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Avaliação das condições bucais, da qualidade de vida e das características craniofaciais em indivíduos com doença de Gaucher

Tese apresentada à Faculdade de Odontologia de Piracicaba da Universidade Estadual de Campinas, para a obtenção do Título de Doutor em Odontologia – Área de Odontopediatria.

Orientador: Profª Drª Maria Beatriz Duarte Gavião

Piracicaba

2009

FICHA CATALOGRÁFICA ELABORADA PELA
BIBLIOTECA DA FACULDADE DE ODONTOLOGIA DE PIRACICABA
Bibliotecária: Marilene Girello – CRB-8ª. / 6159

G141a

Gambareli, Flávia Riqueto.
Avaliação das condições bucais, da qualidade de vida e das características craniofaciais em indivíduos com doença de Gaucher. / Flávia Riqueto Gambareli. -- Piracicaba, SP: [s.n.], 2009.

Orientador: Maria Beatriz Duarte Gavião.
Tese (Doutorado) – Universidade Estadual de Campinas, Faculdade de Odontologia de Piracicaba.

1. Ossos - Doenças. 2. Saúde bucal. 3. Qualidade de vida. I. Gavião, Maria Beatriz Duarte. II. Universidade Estadual de Campinas. Faculdade de Odontologia de Piracicaba. III. Título.
(mg/fop)

Título em Inglês: Evaluation of oral aspects, quality of life and craniofacial characteristics in subjects with Gaucher Disease

Palavras-chave em Inglês (Keywords): 1. Bone diseases. 2. Oral health. 3. Quality of life

Área de Concentração: Odontopediatria

Titulação: Doutor em Odontologia

Banca Examinadora: Maria Beatriz Duarte Gavião, Eduardo Rodrigues Fregnani, Gustavo Hauber Gameiro, Sara Teresinha Olalla Saad, Marinês Nobre dos Santos Uchoa

Data da Defesa: 03-11-2009

Programa de Pós-Graduação em Odontologia

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A Comissão Julgadora dos trabalhos de Defesa de Tese de Doutorado, em sessão pública realizada em 03 de Novembro de 2009, considerou a candidata FLÁVIA RIQUETO GAMBARELI aprovada.

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Dedico esse trabalho

Aos meus pais, ***Cida*** *e* ***Lázaro****, aos quais devo agradecer por tudo o que sou hoje! O amor incondicional que sempre dispensaram a mim pode fazer com que eu atingisse os meus objetivos, mesmo que para isso eles tivessem que colocar seus sonhos em segundo plano. Se hoje conquisto mais essa etapa é porque sei que vocês estão ao meu lado, lutando e torcendo por mim! Vocês são exemplos de dedicação e perseverança! Essa vitória é nossa!*

Aos meus irmãos ***Fernanda*** *e* ***Rodrigo****, companheiros para todas as horas. Compreensivos quando fui ausente e amigos quando precisei de apoio. Hoje vocês podem ficar muito felizes por essa conquista, afinal a ajuda de vocês foi fundamental. Sem o amor e a amizade de vocês eu não conseguiria caminhar tão tranqüila por essa estrada que escolhi.*

Ao meu marido ***Graziano****, pelo amor, carinho, e pelo incentivo tão importante. As minhas ausências foram difíceis, mas a sua paciência me ajudou a trilhar esse caminho. O seu orgulho pela minha conquista me faz seguir mais forte. Obrigada por entender e abraçar os meus objetivos junto comigo de forma tão carinhosa.*

AGRADECIMENTOS ESPECIAIS

Agradeço em especial a minha orientadora, ***Profa. Dra. Maria Beatriz Duarte Gavião****, exemplo de profissionalismo e amor à docência e à pesquisa. O seu carinho e a sua paciência em momentos de difíceis escolhas me ajudaram a tomar decisões corretas. Obrigada pela confiança em mim depositada. Obrigada pela sua prontidão em sempre me orientar e ajudar quando preciso. Termino mais essa etapa com a certeza de ter aprendido muito, tanto no aspecto profissional quanto no pessoal.*

Agradeço também em especial a ***Profa. Dra. Maria Elvira Pizzigatti Côrrea****, que me acolheu carinhosamente. Obrigada pelas orientações tanto teóricas quanto clínicas, que certamente, acrescentaram muito. Você tem um jeito especial de lidar com as pessoas, transmitindo seus conhecimentos de forma desprendida, desejando o sucesso de seus aprendizes. Agradeço pela oportunidade de ter te conhecido e de ter feito uma grande amiga!!*

AGRADECIMENTOS

Agradeço a ***Deus*** *pela vida, pelas pessoas colocadas em minha vida e por todas as possibilidades de crescimento e evolução pessoal.*

À Universidade Estadual de Campinas, nas pessoas do Magnífico Reitor ***Prof. Dr. Fernando Ferreira Costa*** *e Coordenador Geral da Universidade* ***Prof. Dr. Edgar Salvadori de Decca.***

À Faculdade de Odontologia de Piracicaba, da Universidade de Campinas, nas pessoas do Diretor ***Prof. Dr. Francisco Haiter Neto*** *e do Diretor Associado,* ***Prof. Dr. Marcelo de Castro Meneghim.***

Ao Centro de Hematologia e Hemoterapia – Hemocentro – Unicamp, na pessoa do Coordenador ***Prof. Dr. Cármino Antônio de Souza.***

Ao ***Prof. Dr. Jacks Jorge Júnior****, coordenador geral dos cursos de Pós-Graduação e a* ***Profª Dra. Maria Beatriz Duarte Gavião****, coordenadora do Programa de Pós-Graduação em Odontologia.*

Ao Instituto de Radiodiganóstico Odontológico (IRO), nas pessoas do Diretor Presidente ***Dr. José Luiz Cintra Junqueira****, e da* ***Dra. Saori Okajima Nakamoto*** *pela importante parceria, possibilitando a realização das radiografias necessárias.*

À ***Dra. Jordana Torri Regazzo Fuzato****, médica hematologista responsável pelo Grupo de Gaucher do Centro de Hematologia e Hemoterapia, pela conribuição médica dada a este trabalho.*

Ao ***Roberto Zulli,*** *pela importante contribuição estatítica dada a esse trabalho.*

A ***Raquel Suzana Foglio,*** *pela importante ajuda na revisão do inglês dos capítulos dessa tese.*

Aos ***Profs. Drs. Márcio Ajudarte Lopes*** *e* ***Gustavo Hauber Gameiro*** *pela significante contribuição apresentada no exame de pré-qualificação desta tese.*

Aos ***Profs. Drs. Márcio Ajudarte Lopes, Paula Midori Castelo e Eliana Rodrigues*** *pela significante contribuição apresentada no exame de qualificação desta tese.*

Aos ***Profs. Drs. Eduardo Rodrigues Fregnani, Gustavo Hauber Gameiro, Sara Teresinha Olalla Saad e Marinês Nobre dos Santos Uchoa,*** *pela significante contribuição apresentada no exame de defesa desta tese.*

Às professoras do Departamento de Odontologia Infantil, Área de Odontopediatria da Faculdade de Odontologia de Piracicaba, ***Profª Drª Marinês Nobre dos Santos Uchoa, Profª Drª Maria Beatriz Duarte Gavião, Profª Drª Regina Maria Puppin Rontani*** *pelo exemplo de pesquisadoras competentes e dedicação à vida acadêmica. Agradeço a oportunidade proporcionada para que eu pudesse realizar esse trabalho.*

À ***Profª Drª Cecília Gatti Guirado*** *(in memorian), pelo carinho e gentileza característicos, e pelo exemplo de força.*

À ***Profª Drª Regina Célia Rocha Peres,*** *pelo exemplo e pelo convívo sempre agradável.*

Ao ***Prof. Dr. Érico Barbosa Lima****, por sua carinhosa dedicação à docência, que sempre nos trouxe novos ensinamentos.*

Ao ***Prof. Dr. Francisco Nocitti Júnior****, pela contribuição dada na finalização desse trabalho .*

Ao ***Marcelo Corrêa Maistro,*** *pela convivência amigável e pela ajuda no laboratório da Odontopediatria.*

À ***Maria de Lourdes Gaspar Correa Campos,*** *secretária da Área de Odontopediatria, pelo trabalho que realiza, proporcionando-nos a ajuda necessária.*

À ***Niceté Rommämo,*** *secretária do Centro de Hematologia e Hemoterapia, pela ajuda e pelo trabalho eficientemente realizado.*

À ***Maria Elisa dos Santos*** *e* ***Eliane Melo Franco de Souza*** *pelo comprometimento com que realizam seus trabalhos, pela prontidão em ajudar e pelo carinho dispensado à todos os alunos de pós-graduação.*

À ***Érica A. Pinho Sinhoreti, Raquel Q. Marcondes César Sacchi e Tatiana Cristina Gava,*** *pelo profissionalismo com que tratam os alunos de pós-graduação.*

E a todos os ***funcionários*** *da Faculdade de Odontologia de Piracicaba, que sempre nos recebem com sorrisos e disposição.*

À amiga ***Fernanda Gabriele da Costa Raven*** *pela importante amizade construída ao longo desses anos, e por ocupar preciosas horas de seu consultório para contribuir com a realização deste trabalho.*

Às amigas do doutorado da Área de Odontopediatria:

Carolina Steiner Oliveira *– obrigada pelo exemplo de dedicação e pela ajuda sempre disponível.*

Fernanda Miori Pascon *– obrigada pela amizade fortalecida e pelo exemplo de verdadeira Odontopediatra, que realiza com tanto carinho e competência o seu trabalho.*

Kamila Rosamilia Kantovitz *– obrigada pelo exemplo de que sempre podemos mais do que imaginamos!*

Karlla Almeida Vieira *– obrigada por se fazer sempre presente em nossos momentos, mesmo que à distância.*

Marcia Diaz Serra Vicentin *– obrigada pela amizade verdadeira e pelo carinho desses anos de convivência.*

Moara de Rossi *– obrigada pelo bom-humor e pela alegria sempre presentes em seu coração.*

Renata Andréa Salvitti de Sá Rocha *– obrigada pela amizade e pela gentileza em todos os seus gestos.*

Vocês foram importantes, cada uma do seu jeito, para que eu continuasse a seguir os meus caminhos e atingisse os meus objetivos. Obrigada por me mostrarem o valor da amizade e do companheirismo.

Às amigas do Hemocentro:

Vanessa Schcaira *pelo exemplo de dedicação e perseverança, acreditando no crescimento contínuo.*

Thaís Emídio *pelos agradáveis momentos compartilhados.*

A amizade de vocês foi muito importante para que eu conseguisse manter o meu equilíbrio perante momentos exigentes.

Às amigas do Programa de Pós-Graduação em Odontologia, Área de Odontopediatria, ***Eliana Rodrigues, Éfani Caroline de Freitas Banzi, Fernanda Frasseto, Larissa Ferreira Pacheco, Marcela Pinto Monteiro de Oliveira, Marina Severi Leme****, pelo carinho com que sempre me trataram e pela convivência divertida.*

Às colegas do Programa de Pós-Graduação em Odontologia, Área de Odontopediatria, ***Anna Maria Cia De Mazer Papa, Aline Rogéria Freire de Castilho, Annicele da Silva Andrade, Cintia Maria de Souza e Silva, Maria Claudia de Morais Tureli, Patricia Almada Sacramento, Renata Valvano Cerezetti, Tais de Souza Barbosa, Thaís Manzano Parisotto*** *obrigada por me mostrarem o quanto a amizade é importante em uma equipe bem sucedida.*

Aos adultos e crianças que participaram dessa pesquisa e seus respectivos responsáveis. Foram mais que voluntários, foram alvo de cuidados e preocupações ao longo deste período. Sem esta colaboração não seria possível a realização deste trabalho.

A todos os demais amigos, que se não agradeço nominalmente, levo-os em meu coração. Como meus amigos da graduação da FOP, de minha e de outras turmas; meus amigos de Campinas, que sempre estiveram presentes e os companheiros de profissão de Vinhedo, que sempre me alegraram para que meus dias se encerrassem bem.

"Recorda-te de que a vida é curta; esforça-te, pois, por conquistar, enquanto o podes aquilo que vieste aqui realizar: o verdadeiro aperfeiçoamento. Possa teu espírito partir desta Terra mais puro do que quando nela entrou!"

(Léon Denis)

Resumo

A Doença de Gaucher (DG) é uma doença de origem genética, autossômica recessiva, causada por mutações do gene da glucocerebrosidase, o qual codifica a enzima beta-glucocerebrosidase, determinando deficiência na produção e/ou na sua atividade. O objetivo desse estudo foi avaliar a saúde oral, a qualidade vida, as condições maxilares e as caracteristicas craniofaciais de individuos com DG. Dezessete pacientes sob tratamento médico no Centro de Hematologia e Hemoterapia (Hemocentro) da Universidade Estadual de Campinas (Unicamp) participaram desse estudo. Destes, oito eram crianças, entre 7 e 15 anos, e nove adultos, entre 27 e 53 anos. Todos os pacientes receberam exame clínico oral completo, avaliando-se tecidos moles e dentes cariados, perdidos ou obturados, decíduos (ceo) e permanentes (CPOD). Nos pacientes adultos realizou-se exame periodontal, avaliando-se o nível de inserção clínica (NIC), a profundidade de sondagem (PS), a posição da gengiva marginal (PGM), o índice de placa visível (PV) e de sangramento gengival (SG). Realizou-se exame radiográfico panorâmico para avaliar as condições ósseas da maxila e mandíbula, e o momento de erupção da dentição permanente nas crianças. A radiografia lateral foi realizada para avaliar as características craniofaciais pela análise cefalométrica. O crescimento das crianças foi avaliado pela comparação do peso e da altura com gráficos padrões. A idade óssea foi estimada pela radiografia do punho e da mão. A influência da saúde oral sobre a qualidade de vida foi avaliada por questionários auto-administrados pelas crianças – Child Perception Questionnaire – CPQ 8-10 anos e CPQ 11-14 anos; e o questionário Oral Health Impact Profile – OHIP 49 – foi usado para os pacientes adultos. Aplicou-se teste Wilcoxon para se avaliar o momento de erupção dos dentes permanentes e para comparar as variáveis cefalométricas ao padrão. O ceo médio encontrado foi de 2,67 e o CPOD de 0,75. Para os pacientes adultos, um alto índice CPOD (20,44), leve doença gengival e moderada doença periodontal foram observados. As crianças mostraram retardo no crescimento e diferença de 13 e 16 meses, em média, entre a idade cronológica e a idade óssea, na primeira e segunda avaliação, respectivamente. Considerando a idade óssea, erupção precoce foi

observada em 5 pacientes, principalmente nos incisivos centrais e laterais. Considerando a idade cronológica, 7 pacientes exibiram erupção atrasada, significante para o segundo pré-molar. Os achados radiográficos mais encontrados nos maxilares foram rarefação generalizada, borramento do canal mandibular e perda da estrutura trabecular. Pela análise cefalométrica, observou-se que seis crianças mostraram valores lineares de crescimento craniofacial maiores quando comparados ao padrão. O escore médio total do CPQ 8-10 anos foi 17, mostrando moderado impacto da saúde oral na qualidade de vida das crianças nessa faixa etária. O escore médio total do CPQ 11-14 anos foi 38. Os adultos demonstraram impacto expressivo na qualidade de vida relacionada à saúde oral. Concluiu-se que as crianças com DG apresentaram boa saúde oral, erupção precoce de alguns grupos dentários, importante alterações nos maxilares e alterações no crescimento craniofacial. Embora não tenham apresentado saúde oral deficiente, algumas condições orais interferiram na qualidade de vida. Os pacientes adultos apresentaram envolvimento ósseo dos maxilares, pobre saúde oral e conseqüentemente prejudicada qualidade de vida relacionada à saúde oral.

Palavras-chave: Doença de Gaucher, doenças ósseas, saúde bucal, qualidade de vida

Abstract

Gaucher disease (GD) is an autosomally recessive inherited disorder, caused by mutations of the glucocerebrosidase gene, which codify the enzyme glucocerebrosidase, determining deficiency in its production or activity. The aim of this study was to evaluate the oral health and related quality of life in patients with Gaucher disease, and to evaluate jaw conditions, growth and craniofacial development. Seventeen patients undergoing treatement at the Hematology and Blood Transfusion Center (Hemocentro) of University of Campinas (Unicamp) participated of this study. Eight were children, aged from 7 to 15 years old, and nine adults, aged from 27 to 53 years old. Each patient received a complete soft tissue examination and a clinical examination of decayed, missing and filled primary (dmft) and permanent (DMFT) teeth. Periodontal examination was performed in the adult patients evaluating clinical attachment level (CAL), probing depth (PPD), position of the gingival margin (PGM), visible plaque (VPI) and gingival bleeding index (GBI). Panoramic radiography was used to evaluate the bone conditions of the maxilla and mandible, and the eruption timing of the children's permanent dentition. Lateral radiography was used to evaluate the craniofacial characteristics by cephalometric analysis. Growth was assessed for the children through body weight and height, plotted against standard growth charts; and bone age was estimated by X-ray of the wrist and hand. The influence of the oral health about the quality of life was evaluated by a questionnaire self-filled by the children – Child Perception Questionnaire – CPQ 8-10 years and CPQ 11-14 years – and the Oral Health Impact Profile questionnaire – OHIP 49 – was used for the adult patients. Wilcoxon test was applied to evaluate the eruption timing of the permanent dentition and to evaluate the values of the cephalometric analysis compared to the standard. The mean dmft found (2.67) was higher, and the DMFT (0.75) was lower than was counseled by the WHO. For the adults, a high DMFT index (20.44) and a slightly gingival and moderate periodontal disease were observed. The children showed growth retardation and a mean difference of 13 months on the first evaluation and of 16 months on the second between the chronologic and bone age. Considering bone age, early eruption was observed in 5

patients, mainly in the central and lateral incisors. Considering chronologic age, 7 patients showed delay eruption, significant for the second premolar. The most prevalent radiological findings in the jaw comprised generalized rarefaction, effacement of the mandibular canal and loss of trabecular structure presented by children and adults. Through the cephalometric analysis all children were observed to present higher values of craniofacial growth confronting with the standards. The mean overall score for the CPQ_{8-10} years was low (17), showing little impact of the oral health upon quality of life. The mean overall scale for the CPQ_{11-14} years was 38. According to the results obtained by adults, they perceived substantial impact of oral health upon their quality of life. We concluded that children with GD presented good oral health, early eruption of some permanent teeth groups and important alterations in the jaw. Children may manifest alterations at craniofacial growth. Although the children did not present a poor oral health, some oral conditions interfered with their quality of life. The adult patients showed bone involvement in the jaw and poor oral health, consequently poor oral health-related quality of life.

Key Words: Gaucher disease, bone diseases, oral health, quality of life

SUMÁRIO

Introdução

A Doença de Gaucher (DG) é uma doença de origem genética, autossômica recessiva, causada por mutações do gene da glucocerebrosidase, ácido B-glucosidase EC 3.2.1.45 – (GBA), localizado no braço longo do cromossomo 1 (1q21). Esse gene codifica a enzima beta-glucocerebrosidase, sendo que defeitos genéticos determinam deficiência na produção e/ou na atividade (Fischman et al., 2003; Sorge et al., 1985).

A DG é caracterizada pelo acúmulo intralisossomal do glucocerebrosídeo nos tecidos do sistema reticuloendotelial, principalmente no fígado, baço, nódulos linfáticos e medula óssea e nas células do sistema macrófago-monócito (Fischman et al., 2003; Meikle et al., 1999). Os monócitos e macrófagos com o acúmulo de glucocerebrosídeo são chamados células de Gaucher, originando assim a respectiva doença (Beutler & Grabowski, 1995).

Apesar de ser considerada rara (Finkelstein et al., 1992), a DG é a mais comum das doenças de depósito lisossomal (Beutler, 1998). A estimativa precisa da freqüência da doença é difícil de ser obtida (Oliveira et al., 2002). É considerada como a doença genética mais comum entre os judeus Ashkenazi da Europa Oriental (Charrow et al., 1998) com incidência de 1:400 a 1:1000 (NIH, 1996; Horowitz et al., 1998), devido aos casamentos consaguíneos frequentes nesse grupo populacional.

Entretanto, registros da DG, em vários países estimam que a doença ocorra na freqüência de 1:40.000 a 1:200.000 na população geral não-judaica (Grabowski et al., 1996). Estima-se que nos Estados Unidos, a incidência seja de 1:40.000 – 1:60.000 (NIH, 1996).

As manifestações clínicas ou fenotípicas da DG dependem do grau de deficiência da beta-glicosidase ácida e do acúmulo dos glicolipídios, que são variáveis (Wenstrup et al., 2002; Martins et al., 2003). Classicamente, três formas clínicas são delineadas, baseadas na ausência (tipo I) ou presença (tipo II e III) de sinais neurológicos (Kaplan et al., 2006), assim caracterizadas:

– Tipo I: forma não-neuropática mais freqüente, correspondendo a 95% dos casos de DG (Altarescu et al., 2000; Grabowski et al., 1998; NIH, 1996). Manifestações clínicas incluem esplenomegalia, hiperesplenismo e até infarto esplênico, envolvimento do fígado causando hepatomegalia, anemia, trombocitopenia, envolvimento da medula óssea bem como envolvimento ósseo (Dayan et al., 2003). A heterogeneidade clínica é uma característica do tipo I e o curso da doença é variável.

– Tipo II: apresenta-se de forma aguda e tipicamente mais uniforme, com sinais viscerais e envolvimento neurológico grave, durante os seis primeiros meses de vida. Compromete cérebro, baço, fígado e pulmão.

– Tipo III: apresentam algumas características da doença na infância e manifestarão envolvimento neurológico no decorrer dos anos.

Doença Óssea

Embora as anormalidades hematológicas e viscerais possam ser graves e potencialmente fatais, é o acometimento ósseo, em geral, o principal determinante da morbidade e incapacidade dos portadores (Hermann et al., 1986).

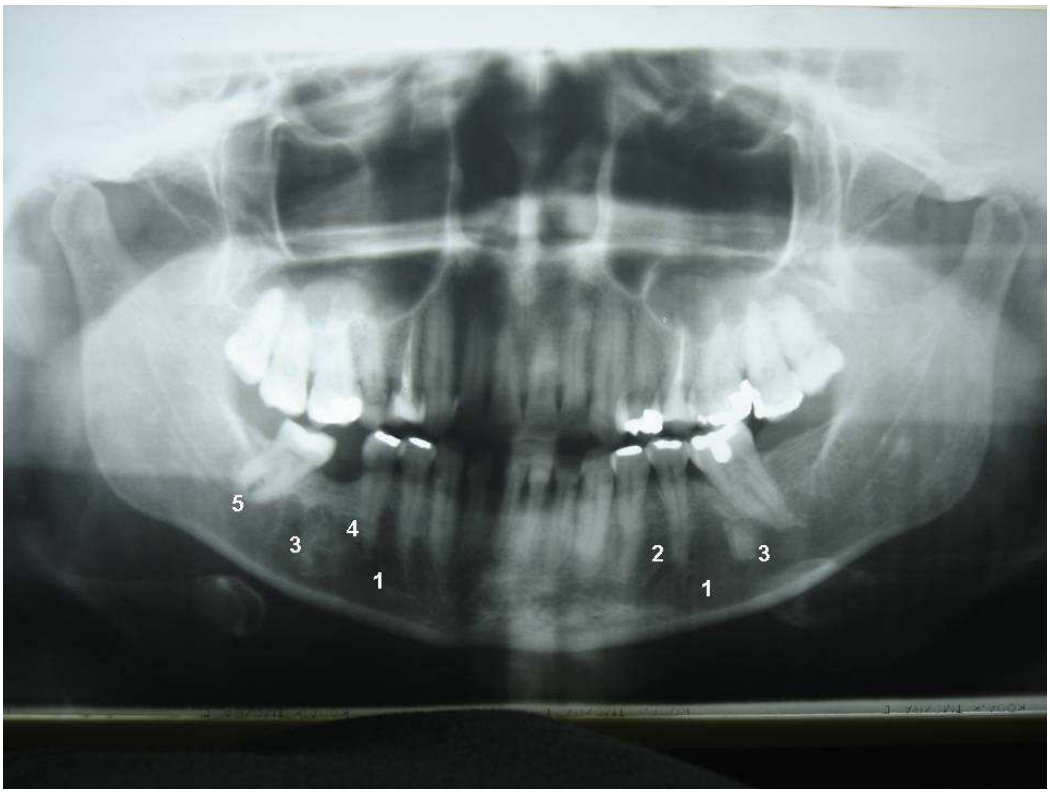
As manifestações esqueléticas são diversificadas na etiopatogenia e na sintomatologia, incluindo um espectro de dor óssea, crises ósseas, deformidades assintomáticas em formato de Erlenmeyer, osteopenia, osteoporose (Pastores et al., 1996), fraturas patológicas, retardo no crescimento e falha em atingir o pico de massa óssea, osteomielite, e necroses avasculares (El-Beshlawy et al., 2006). O fêmur é o sítio mais comumente afetado, ainda que o envolvimento da pélvis, calvarium, vértebras, mandíbula, costelas, e falanges também têm sido relatados (Beutler & Grabowski, 1995).

Carter et al. (1998), em um estudo onde foi avaliado um grupo de 28 pacientes voluntários, entre 8 e 66 anos de idade com Doença de Gaucher, notaram atraso na erupção da dentição permanente em cinco (56%) dos nove pacientes com menos de 20 anos de idade e ainda correlacionaram esse evento com o envolvimento ósseo da DG. Interessantemente, os resultados desse trabalho demonstraram que todas as crianças avaliadas apresentaram algum grau

de atraso na idade óssea, também observado na avaliação da erupção dentária através das radiografias panorâmicas.

Entretanto, Elstein et al. (2002) comentaram que esses achados poderiam ser considerados inconsistentes, uma vez que as radiografias panorâmicas não são indicadas para esta finalidade diagnóstica. Os autores ainda ressaltam que a idade óssea em crianças com todos os subtipos da Doença de Gaucher deveria ser mais estudada, visto a literatura ser escassa nesse assunto (Elstein et al., 2002).

O envolvimento mandibular na Doença de Gaucher é freqüentemente assintomático e é comumente detectado como um achado acidental em radiografias de rotina. Os achados radiográficos que são descritos na mandíbula e na maxila incluem osteoporose e rarefação generalizada, com perda da arquitetura trabecular, e presença de pseudocistos ou lesões radiolucentes, em formato de colméia de abelha. Também há diminuição da lâmina dura, *scalloping* endosteal, e reabsorção apical das raízes dos dentes adjacentes às lesões (Bender & Bender, 1996).



1 – rarefação generalizada; 2 – perda de estrutura trabecular; 3 – osteoesclerose; 4 – diminuição da lâmina dura; 5 – reabsorção de raízes

Segundo Elstein et al. (2002), parece não haver evidências de progressão agressiva em pacientes que desenvolveram a Doença de Gaucher em meia idade e naqueles com sintomatologia leve. Entretanto segundo os mesmos autores e Zimran et al. (1992), pacientes com Doença de Gaucher que desenvolvem sinais e sintomas precocemente na infância parecem ser mais propensos à progressão da doença se não tratadas.

Kaplan et al. (1996) avaliaram 54 crianças portadores da DG e relataram que aproximadamente 50% apresentavam retardo grave do crescimento, ou seja, abaixo do 5º percentil. Kauli et al. (2000) demonstraram que pacientes com doença tipo I, tratados ou não, tiveram atraso no surto de crescimento, mas a maioria (83,3%) atingiu a altura prevista baseada na altura dos pais.

Os exames radiográficos para pacientes adultos e pediátricos com DG objetivam avaliar a gravidade e a progressão da doença, caracterizar as complicações ósseas, e avaliar a resposta às terapias, além de permitir estabelecer o padrão de crescimento (Bembi et al., 2002).

Achados orais

Alguns relatos de caso observaram presença de doença gengival e periodontal em indivíduos com DG, mas a associação dessas alterações com a DG não está estabelecida (Fischman et al., 2003; Horwitz et al., 2007). Envolvimento da mucosa por pigmentação amarelada ou petéquias tambem foram relatadas (Horwitz et al., 2007; Bender & Bender, 1996; Browne, 1977). Dayan et al. (2003) encontraram hiposalivação em 35,4% dos pacientes avaliados. A principal ocorrência clínica de interesse para o dentista está relacionada ao envolvimento da medula óssea que pode resultar em anemia, leucopenia e trombocitopenia (Browne, 1977; Carter et al., 1998). Hemorragia gengival espontânea associada à gengivite pode ser parte do quadro clinico em pacientes com trombocitopenia (Carter et al., 1998). Relatos clínicos sugerem que hemorragia pós-cirúgica secundária à trombocitopenia representa o achado clínico mais freqüente em indivíduos com DG (Carter et al., 1998). As exodontias são frequentemente seguidas por processo de reparo prolongado e pobre resolução

da loja cirúrgica, devida às condições de osteopenia dos maxilares (Carter et al., 1998).

Terapia de reposição enzimática (TRE)

Com o desenvolvimento de técnicas de purificação, a glucocerebrosidase foi obtida primeiramente de tecidos da placenta humana (Ceredase®, Genzyme Corporation, Cambridge, MA, USA) e posteriormente por tecnologia recombinante (Cerezyme®, Genzyme Corporation, Cambridge, MA, USA). Esse tratamento possui boa tolerabilidade e eficácia na normalização dos níveis de hemoglobina e da contagem de plaquetas, além de reduzir a hepatoesplenomegalia (Barton et al., 1991; Fallet et al., 1992; Figueroa et al., 1992; Hollak et al., 1992; Zimran et al., 1994; Grabowski et al., 1998).

A TRE melhora significativamente a dor óssea embora aparentemente não possa reverter nem estacionar o curso das complicações esqueléticas destrutivas pré-existentes (Elstein et al., 2002).

O conhecimento do curso clínico da DG torna-se particularmente importante em relação às decisões quanto à melhor abordagem para os pacientes afetados pela doença. Dois aspectos relevantes são fundamentais na compreensão das questões da abordagem atual da DG: primeiro, a marcante heterogeneidade da doença em relação à apresentação, ao curso clínico e ao prognóstico; segundo, o desenvolvimento de novas terapêuticas de custo elevado, como a terapia de reposição enzimática e o transplante de medula óssea (Oliveira et al., 2002).

O presente estudo justifica-se, considerando os seguintes aspectos: indivíduos com DG apresentam comprometimento esquelético, trompocitopenia, além de outras alterações citadas, que podem também se manifestar nas estruturas bucofaciais, como considerado por Carter et al. (1998), Fischman et al. (2003) e Heasman (1991). Deste modo considera-se de importância a avaliação das condições bucais e esqueléticas do crânio e da face em pacientes portadores de DG. O crescimento craniofacial e o desenvolvimento das dentições são fatores de importância para o equilíbrio das funções do sistema estomatognático, referentes à mastigação, deglutição, fonação e respiração. Assim, o diagnóstico

precoce de alterações morfológicas e funcionais pode favorecer a implementação de ações educativas, preventivas e interceptoras que poderão favorecer o crescimento e desenvolvimento adequado das estruturas craniofaciais e das respectivas funções. Pacientes adultos portadores da doença que não tiveram a oportunidade de receber a TRE, podem ter as referidas alterações estabelecidas, com necessidade de implementação de ações curativas e corretivas. Além disso, radiografias dentárias podem levar a detecção precoce da DG, especialmente na ausência de sintomas clínicos.

Oral aspects of children and adolescents with Gaucher disease

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Brief title: Oral aspects in Gaucher disease

Key words: Gaucher disease, bone diseases, oral health

Abstract

Gaucher Disease (GD) could cause bone alterations and delay of tooth eruption. The aim of this study was to evaluate the oral health and jaw conditions in patients with GD. Eight patients received complete oral examination. Eruption timing of the permanent dentition and jaw conditions were determined by panoramic radiography. Bone age was estimated by X-ray of the wrist and hand. Wilcoxon test was applied to evaluate the eruption timing of the permanent dentition. Carious lesions were different of what was established by WHO. Seven children presented eruption alteration, significant for some dental groups. The mean bone age alteration was of 14 months. All the children presented generalized rarefaction and effacement of the mandibular canal. Two patients presented limitation of the mouth opening. We concluded that children with Gaucher disease present good oral health, early eruption of some permanent teeth groups and important alterations in the jaw, requiring constant follow-up.

Introduction

Gaucher disease (GD), the most prevalent lysosomal storage disorder, is a result of a genetic defect in the production or activity of the B-glucocerebrosidase enzyme, and the consequent accumulation of the glucocerebroside glycolipid, in the cells of the monocyte-macrophage system.[1] National incidence rates vary widely; in the United States, the estimated incidence is 1:40,000–60,000[2] and among those of Ashkenazi–Jewish descent, 1:400 to 1:1000.[2] There are no estimates of GD prevalence in Brazil, however there are approximately 400 diagnosed cases,[3] the third largest patient population undergoing enzyme replacement therapy (ERT) in the world.[4] This therapy was available in Brazil since 1995. In 2004 the Ministry Health of Brazil created a program to centralize the purchasing and distribution, allowing gratuitous accessibility of Brazilian patients. On average, the annual cost per patient ranges from US$50,000.00 to US$100,000.00 for the Brazilian government.

The disease occurs in three distinct phenotypic subtypes which are delineated by the absence (Type I), presence and severity of neurological involvement (Types II and III). Most patients (approximately 95%) have Type I GD, characterized by a remarkable clinical diversity of clinical manifestation onset time, number of organ systems involved, degree of organomegaly, extent of skeletal involvement and rate of progression.[1,5] Type II, or acute neuronopathic Gaucher disease, appears during infancy. In addition to hepatosplenomegaly, the patients manifest rapid progressive neurologic involvement, and usually die of secondary complications during the first two years of life. Patients with Type III, or the juvenile form of the disease, have less severe neurologic involvement and a longer course than those with the infantile form.[6]

More than 90% of Gaucher patients have some radiological evidence of bone disease.[7] Osseous complications secondary to bone involvement are frequent and include joint pain, bone pain (which sometimes mimics osteomyelitis), pathologic fractures, and aseptic necrosis. Osteopenia and osteoporosis may be important findings even among young adults with the disease.[8] The most

commonly involved bones are the femur and vertebrae,[6] although involvement of the pelvis, skull, vertebrae, jaw, ribs, and phalanges has also been reported.[1,6]

Jaw involvement is often asymptomatic and can be detected as an incidental finding on routine dental radiographs.[9] The mandible has been noted in case reports as a nidus of Gaucher's cell infiltration and/or bone crisis.[6,10-12] Several radiographic findings in the jaw have been described: generalized osteopenia, loss of trabecular structure, effacement of lamina dura, displacement of the mandibular canal, pseudocystic radiolucent lesions, and apical root resorption of teeth adjacent to the lesions, all of which mostly appear in the mandible.[12] In addition, oral findings may include yellow pigmentation of the oral mucosa and patechiae.[13] Delayed eruption of permanent teeth has also been reported.[5]

Approximately 110 cases of GD with mandibulo-maxillofacial involvement have been reported in the literature, usually as single cases. The aim of this study was to evaluate oral health and jaw conditions in a group of children and adolescents with Gaucher disease at the Hematology and Blood Transfusion Center (Hemocentro) of the University of Campinas (Unicamp) in Brazil.

Material and methods

All aspects of the study were approved by the Ethics Committee of Medical School (N° 757/2007), University of Campinas. The Hematology and Blood Transfusion Center (Hemocentro) from University of Campinas (Unicamp) included 32 patients with GD. Eleven are children aged from 7 to 15 years. Eight children, who accepted to participate in this study, were under enzymatic treatment at the Hemocentro. The other three were being treated at another Hematological Service.

The children received a complete clinical oral examination, which included panoramic radiographic examination. Data regarding oral health, such as decayed, missing, filled deciduous (dmft), and permanent teeth (DMFT) were collected during the first patient's dental appointment.[14] Bone age was estimated by wrist and hand X-rays according to Greulich and Pyle (1959).[15]

The eruption timing of permanent dentition was determined according to Marques et al. (1978).[16] Delay and early eruption was considered when the development of the teeth differed over 6 months from the standard adopted by the authors above.

The panoramic radiographs were evaluated under optimum viewing conditions in a darkened room by two evaluaters, simultaneously, using an X-Ray illuminator. Presence or absence of generalized rarefaction, loss of trabeculae, cortical thinning, osteoesclerosis, effacement of lamina dura, root resorption and effacement of mandibular canal were taken into consideration. The radiographies were performed in an oral radiology institute (Instituto de Radiodiagnóstico Odontológico – IRO – Campinas, São Paulo, Brazil).

The following parameters were obtained from medical records: gender, age at the diagnosis, enzyme replacement therapy status, hematological, visceral (hepatosplenomegaly), and bone involvement.[17]

Wilcoxon test was applied to evaluate the eruption timing of the permanent dentition considering chronologic and bone age. This analysis was carried out using R version 2.9.1 (2009, Vienna, Austria).

Results

The demographic characteristics of the population, as well as some clinical parameters are shown in Table 1. Of the 8 individuals, ages ranging from 7 to 15 years (mean 10.1 years), 3 were male and 5 were female. Seven patients had Type I GD, and one patient had GD Type III (Patient 3). At the time of the study, all patients were receiving ERT (age at start 2–10 years, mean 5.75 years).

Table 1. Demographic characteristics, disease involvement, enzyme replacement therapy (ERT) status, dmft and DMFT scores (n=8)

Patients	1♀	2♀	3 ♂	4♀	5 ♂	6 ♂	7♀	8♀	Mean±SD
Age at Diagnostic	NA	2	1.4	3	4	5	10	3.10	4.8±3.11
Age at the study evaluation	15	10.11	9.11	10.1	7.5	8.10	13.5	10.10	10.1±2.57
Type of Disease	I	I	III	I	I	I	I	I	-
Systemic Involvement									
Visceral	Y	Y	Y	Y	Y	Y	Y	N	-
Haematological	N	N	N	N	N	N	N	N	-
Bone	Y	Y	Y	Y	Y	Y	Y	Y	-
Body osteopenia	Y	N	N	Y	Y	N	N	N	-
ERT Administration									
Period (years)	10	9	8	7	3	3	3	3	5.75±3.06
Status	UID	UID	UID	ID	UID	UID	ID	ID	-
dmft Índex									
decayed	-	0	0	3	6	4	-	0	2.17±2.56
missing	-	0	1	0	0	0	-	0	0.17±0.41
filled	-	0	1	0	1	0	-	0	0.33±0.52
dmf	-	0	2	3	7	4	-	0	2.67±2.66
DMFT Índex									
Decayed	0	0	0	0	2	0	0	0	0.25±0.71
Missing	0	0	0	0	0	0	0	0	0.00±0.00
Filled	0	0	0	0	0	0	4	0	0.50±1.41
DMF	0	0	0	0	2	0	4	0	0.75±1.49

UID = under ideal dose; ID = ideal dose; Y = yes; N = no; NA = no available data

Oral findings

The dfmt index medium was 2.67 (range 0 - 7) determined by children 2, 3, 4, 5, 6 and 8, who presented primary teeth. Child 5, who had the greatest number of primary teeth, presented the highest dmft index (7) that contributed to increase the mean. Decayed and filled permanent teeth were found only in child 5 (DMFT=2) and 7 (DMFT=4), respectively (Table 1). The other 6 children presented sound permanent teeth (DMFT=0). Gingival alterations were not observed during the clinical examination of any of the children.

The individual results regarding eruption timing are shown in Table 2.

Delayed and early eruption of permanent teeth was observed in both arches and in all dental groups. When bone age was considered, early eruption was observed in 5 patients, mainly the central (CI) and lateral incisors (LI) (p=0.027). On the other hand, when chronologic age was considered, 7 children exhibited delayed eruption, significant for the second premolar (2PM) (p=0.03). In addition, comparing bone and chronologic age, CI, LI, 2PM and second molar (2M) groups were statistically different (p=0.037, 0.037, 0.037 and 0.03, respectively).

Radiological findings

The results of chronologic and bone age evaluation are shown in Table 2. The mean difference between both ages was 14 months. Four patients (patients 1, 2, 3 and 5) showed advanced chronologic age (higher than 18 months) when compared with the bone age. Four patients (patients 4, 6, 7, 8) showed few months of difference between both, chronologic and bone age.

All 8 evaluated children displayed radiographic evidence of jaw involvement by GD (Table 3). Generalized rarefaction, effacement of the mandibular canal and loss of trabecular structure were the most frequent image findings.

Only 1 patient presented no evidence of delayed development and also lacked generalized bone involvement, exhibiting discreet bone lesions in the jaws and in the femur as well. No cortical thinning, osteoesclerosis, effacement of lamina dura and root resorption was observed.

Table 2. Bone age and eruption timing of children with Gaucher disease (n=8)

Children	Chronologic Age (month)	Bone age (month)	Difference (month)	Eruption Timing															
				Considering Bone Age								Considering Chronologic Age							
				CI	LI	C	1PM	2PM	1M	2M	3M	CI	LI	C	1PM	2PM	1M	2M	3M
1♀	180	162	18	N	N	N	N	N	N	D	D	N	N	N	N	N	N	D	D
2♀	131	94	37	E	E	E	N	N	E	E	E	N	N	N	D	D	D	D	N
3♂	119	96	23	E	E	N	E	N	N	E	E	N	N	D	N	D	D	N	N
4♀	121	120	1	E	E	N	N	D	N	N	N	E	E	N	N	D	N	N	N
5♂	89	60	29	E	E	E	E	E	E	E	-	N	N	D	N	N	N	N	N
6♂	106	108	-2	E	E	E	E	N	N	N	E	E	E	E	E	N	N	N	E
7♀	161	156	5	N	N	N	N	N	N	N	N	D	D	D	D	D	D	D	D
8♀	130	132	-2	N	N	N	D	D	N	D	N	N	N	N	D	D	N	D	N
MEAN±SD	130±29.08	116±33.96	14±15.17	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

SD = standard deviation
D = delay
E= early
Y = with alterations
N = without alterations
CI = central incisor
LI = lateral incisor
C = canine
1PM = first premolar
2PM = second premolar
1M = first molar
2M = second molar
3M = third molar

Table 3. Bone involvement in children with Gaucher disease (n=8)

Children	Generalized Rarefaction	Trabecular Loss	Cortical Thinning	Osteoesclerosis	Lamina Dura Effacement	Root Resorption	Effacement Mandibular Canal	Bone Involved
1♀	Y	Y	N	N	N	N	Y	MAND/ MAX
2♀	Y	Y	N	N	N	N	Y	MAND
3♂	Y	Y	N	N	N	N	Y	MAND
4♀	Y	Y	N	N	N	N	Y	MAND
5♂	Y	Y	N	N	N	N	Y	MAND
6♂	Y	Y	N	N	N	N	Y	MAND
7♀	Y	N	N	N	N	N	Y	MAND
8♀	Y	Y	N	N	N	N	Y	MAND

Max. = maxilla

Mand. = mandible

Y= with alterations

N = without alterations

Discussion

Oral findings

The results of the oral conditions showed a great variability among the patients, as three of them were free of caries (Children 1, 2 and 8). From those six children with mixed dentition, four showed dental caries in primary teeth. In addition, the Child 5 contributed to increase this mean, as this patient had the highest dmft (7). This child was considered as being the youngest, and had a greater number of primary teeth than the other children. Moreover, this child was one of the two who presented dental caries in permanent teeth, showing a high caries experience, whereas the others had no caries. Considering both dentition, children 1, 2 and 8 reached the World Health Organization (WHO) recommendation,[14] whereas children 3, 4, 5, 6 and 7 were far from this recommendation. As caries experience in primary teeth is the best predictor for caries in permanent teeth, the children 3, 4, 6 should have been encouraged to adopt preventive measures, as well as the others, on an individual basis. Despite the fact that the children enrolled in this study presented a systemic disease, the results regarding oral health were in line with the results of the oral survey conducted in a Brazilian general population in 2002-2003, when permanent dentition was verified, and approximately 70% of the 12 year old children presented decay in at least one permanent tooth.[18]

Scutellori et al. (1994)[19] found similar incidence of dental caries with B-thalassemia subjects and their controls. On the other hand, Al-Wahadni et al. (2002)[20] evaluated patients with thalassemia major and found a mean DFMT of 8.7±6.57 what was almost twice as high as that in the parallel healthy control group (4.3±1.6). Although the difference between these sudies, both agreed with previous studies which reported that similar systemic condition was not associated with significant increased levels of gingivits or periodontitis.[21,22] As in Gaucher patients, the incidence of tooth decay in children with talassemia seemed likely related to local factors such as poor mouth hygiene and malocclusion, evidencing dental neglect.

The results of the bone study, showed a bone age retardation of 14 months in average. This difference was shorter than that previously described by Kauli et al. (2000),[23] who reported bone age retardation of 2–4 years on a similar patient population.

Delayed and early eruption of permanent teeth was observed in both arches and in all dental groups. When bone age was considered, there were more groups of teeth and more number of patients (n=5) presenting an early rather than a delayed eruption, and this situation was different from the study of Marques et al. (1978)[16] for a larger number of months, 16.5 months average.

The results may suggest that some dental groups are more susceptible to alterations than other groups. Additionally, the eruption had not followed a common pattern and was not in accordance with bone or with chronologic age. If we considere the bone age as the most reliable information about the bone maturation, it could be observed that five individuals showed early eruption. Maybe, this alteration could be due the jaw bone condition, since it showed generalized rarefaction, what could provide a porous state of the bone favouring the dental eruption. It is important to accompany these children and assure that they have a healthy development of their permanent dentition, esthetical and functionally. Carter et al. (1998)[5] showed that chronologic development of the permanent dentition was altered in 56% of the Gaucher Disease patients under 20 years of age. However, in our study, considering bone and chronologic age, 7 (87.5%) and 8 (100%) children, respectively, showed this disturbance. This could be due to the fact that individuals with Type I and III Gaucher disease vary in severity in different geographic regions of the world, in accordance with Sobreira et al. (2007).[24] In addition, most of the published literature on Type I Gaucher disease comes from different countries such as United States, Europe, and Israel where a higher proportion of patients are of Ashkenazi–Jewish ethnicity, and who may manifest a more restricted disease phenotype.[24]

Radiological findings

Generalized rarefaction and effacement of the mandibular canal were the most prevalent radiological findings in the jaws of all children, followed by loss of trabecular in 7 children. These findings are in accordance with Carter et al. (1998)[5] who reported that 25 of the 28 patients displayed radiographic evidence of jaw involvement. As we used only panoramic radiographs we could not infer that these jaw lesions were osteopenia as formerly reported,[12] even with the osteopenia diagnosis in other squeletal bones of children 1, 4 and 5.

Plain radiography is less sensitive and precise than magnetic resonance imaging (MRI) to assess the skeletal status of patients with GD,[25,26] and to detect osteopenia that could be detected as a decrease in bone mineral density (BMD) using dual-energy X-ray absorptiometry (DXA).[27] None of the patients had these exams to evidence the bone involvement pattern. In some parts of the world, including Brazil, access to MRI and DXA technologies is limited, and thus, physicians must use plain radiograph studies to assess patient status.[25] Although the pathophysiology of bone lesions are poorly understood, the complications are thought to be related to presence and accumulation of pathological Gaucher cells, which replace normal bone marrow and reduced osteoblastic activity.[27]

The mandible was more affected than the maxilla, and the maxilla was not affected alone which was in accordance with other authors.[5,12,28] The distribution pattern of the prior case reports suggested that the mandible, that has endochondral and intramembranous ossification, is affected more frequently than the maxilla, an exclusively membranous bone. In addition, the mandibular and maxillary lesions were located, respectively, mainly in the premolar-molar and in the canine-premolar areas, as described by Lustmann et al. (1991),[11] Karabulut et al. (1997)[28] and Carter et al. (1998).[5] Bone lesion involvement could have initiated at the premolar and molar region, soon after the mental foramen, probably caused by the extrinsic vessel compression due to increased intraosseous pressure and/or occlusion by thrombosis or embolism, leading to the formation of localized bone lesions in GD.[29]

Limitation of mouth opening was found in Children 1 and 3. Although child 1 had an associated storage disease (mucopolysaccharidosis) and the other had Type III, we could not infer that these conditions led to a more severe damage of the craniofacial structures.

Some lesions previously described,[5,12] such as cortical thinning, effacement of the lamina dura, apical root resorption of adjacent teeth to the lesions and areas of osteosclerosis were not found in these patients, probably as these alterations tend to appear with the progression of the disease over the years. The early diagnosis and ERT could possibly prevent the appearance of these alterations, which would imply that a long follow up of those patients was required. None of the cases presented tooth mobility or loss of tooth vitality as previously reported.[11]

Corroborating with the literature,[5] none of the children evaluated exhibited any complaint as to jaw involvement, demonstrating the characteristically asymptomatic course.

As previously noted,[5] gingival changes were not found. None of the children presented gingivitis, nor alterations in size, shape or structure of the teeth, except for dental caries. The mucosa was not affected with oral pigmentation, as found in adults by Browne (1977).[13]

As patients with Gaucher disease who develop signs and symptoms during early childhood tend to present a more severe course of the disease,[30] monitoring of bone lesions is essential so that treatment can be adjusted as required to prevent irreversible skeletal damage.[31] Panoramic radiographic is an easy and inexpensive exam that could represent a useful tool for the evaluation of bone lesions in the jaw bones.

Bone lesions X Enzyme replacement therapy

In children, early and sustained ERT can prevent or reverse skeletal complications.[26] In addition ERT has been shown to reduce infiltration of Gaucher cell and improve lipid concentration of bone marrow.[32] Andersson et al. (2008)[33] affirmed that to achieve the goals in these children, early treatment with ERT is crucial.

The mean time of ERT in our patients was approximately 5 years, however this period did not seem to be enough to prevent or reverse bones jaw involvement. As previously reported, skeletal responses to ERT occur significantly later on than hematological and visceral responses,[26] and may be dependent on the degree of bone involvement at the time therapy is initiated. These children could have their bone condition improved unless the administration of enzyme therapy were delayed beyond a point of irreversible bone changes, where the effect of enzyme therapy on skeletal abnormalities could be limited.[34]

There are no markers that accurately predict which signs and symptoms will occur in any particular patient.[35] The degree of bone involvement may not be correlated with the severity of organomegaly or of any of the hematological parameters of Gaucher disease[36] as demonstrated in this study, in which all chidren presented bone involvement, 7 of them (87,5%) presented visceral involvement (hepatosplenomegaly) however none of them exhibited hematological involvement.

Osteomyelitis and pathologic fractures were not observed in the bone jaw of our children. However, child 4 had been hospitalized due to an episode of osteomyelitis in the femur epiphysis. These conditions seem to occur with the progression of bone lesion, evidencing the importance of early diagnosis and periodical evaluation of Type I and III GD patients. If there is evidence of bone involvement, the value of good dental hygiene should be stressed to avoid odontogenic infections and secondary osteomyelitis of the involved bone.[37]

Dental radiographs may lead to early detection of GD, especially in the absence of clinical symptoms; therefore dentists should be aware of possible oral and radiographic manifestations of the disease.[38]

Follow-up of all pediatric patients, whether undergoing treatment or not, should be carried out at frequent intervals, minimally every 6 months, and should include assessments of disease parameters.[39] Comprehensive and reproducible evaluation and monitoring of all clinically relevant aspects are vital for the effective management of Gaucher disease patients.[40]

To our knowledge, the present study represents the first analysis of osseous mandibulo-maxillofacial alterations in GD in Brazil and demonstrates that osseous involvement of the jaws in GD may be more prevalent than had been previously suspected.

Conclusion

Children with Gaucher disease presented good oral health, early eruption of some permanent teeth and alterations in the jaws, requiring constant follow-up. Future studies should include a larger number of patients and a multicentre evaluation.

Acknowlodgments

The authors thank Mr. José Luiz Cintra Junqueira and Ms. Saori Okajima Nakamoto for the indispensable support, offering free radiographs exams, Ms. Raquel Suzana Foglio, for English review and Mr. Roberto Zulli for statistics analysis.

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Oral aspects and jaw lesions in adults with Gaucher disease

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Abstract

The aim of this study was to evaluate the conditions of oral health of 9 adult patients with Gaucher disease (GD), under treatment at Hematology and Blood Transfusion Center (Hemocentro) of the University of Campinas (Unicamp), Brazil. Patients were submited to a complete oral examination, where an oral health index, including the decayed, missing and filled teeth (DMFT index) was performed. A periodontal examination was carried out evaluating clinical attachment level (CAL), probing depth (PPD) and position of the gingival margin (PGM), visible plaque (VPI) and gingival bleeding index (GBI). Panoramic radiography was used for jaw evaluation. A high DMFT index (20.44) and slight gingival and moderate periodontal disease were observed. Five individuals showed VPI and 2 showed GBI. The CAL mean was 3.4mm, the PGM mean was 2.47 mm and PPD mean was 1.73mm. The most prevalent radiological findings in the jaw were loss of trabecular structure and effacement of the mandibular canal. Generalized rarefaction and effacement of lamina dura was found in 6 (85.71%) and in 5 (71.43%) patients, respectively. Osteomyelitis and pathologic fractures were not observed. In conclusion, our results showed that adult patients with Gaucher disease presented jaw involvement related to the underlying disease, and poor oral health, similar to the general Brazilian population.

Introduction

The physiopathology of the Gaucher disease (GD) implies in a deficiency of the enzyme glucosylceramidase, which is responsible for the cleavage of glucose from glucosylceramide, an intermediate in the biosynthesis and degradation of cellular components. Glucosylceramide is abundantly found in leukocytes[1] and to a lesser degree in the spleen, liver, aorta, lung, intestine, and serum.[2]

There are no estimates of GD prevalence in Brazil, however there are approximately 400 diagnosed cases,[3] the third largest patient population undergoing enzyme replacement therapy (ERT) in the world. GD has a variable incidence in the general population 1:50,000,[4] 1:100,000 – 1:200,000,[5] a high incidence though, is cited among Ashkenazi–Jews descent, 1:500 to 1:1000, considered the most frequent genetic disease in this group.[6]

GD is divided into three clinical entities which are delineated by the absence (Type I) or presence and severity of neurological involvement (Types II and III). Type I, or the chronic visceral form, which occurs in adults and is the most common form of GD, with a wide range of presenting signs and symptoms. Common presenting signs include hepatosplenomegaly, leucopenia, thrombocytopenia, and mild microcytic anemia.[7] Spleen, liver and bones are the primarily involved organs by the Gaucher cells (GC).[8] ERT is the standard treatment for type I and III GD patients. In adults, it has been shown to reduce GC infiltration, improve lipid concentration of bone marrow, and increase bone mineral density.[9]

Radiolucent bone lesions due to GC infiltration in the bone marrow is present in up to 75% of patients.[7] This infiltration leads to bone alterations such as expansion cortical and vascular impairment.[2,10] In addition to the bone marrow infiltration, other factors, such as hematologic abnormalities, for example anemia over a long period of time, can contribute to the osseous changes in GD.[11] The results of an *in vitro* study suggest that GC may secrete lysosomal enzymes that attract and activate osteoclasts.[12]

Patients with GD often complain of intense bone pain in various parts of the skeletal system except in the jaws.[13] Thus, the jaws, particularly the mandible, is

often ignored in skeletal surveys.[13] Nevertheless, Carter et al. (1998)[14] reported that from a series of 28 Type I Gaucher patients, 89.3% presented radiographic changes in the mandible.

The radiographic findings in the jaw that have been described are: generalized osteopenia and osteoporosis, loss of trabecular structure, effacement of lamina dura, displacement of the mandibular canal, pseudocystic radiolucent lesions, and apical root resorption of teeth adjacent to the lesions, all of which mostly appear in the mandible.[13] Oral findings have been included yellow pigmentation of the oral mucosa, patechiae and poor oral hygiene.[15]

The most description of the dental literature in Gaucher's patients is focusing the bone conditions of the jaws. There are few studies describing the oral health conditions in these patients and most are case reports.

The aim of this study was to evaluate the oral health conditions in a group of adults with GD. Moreover, due to the bone involvement, the craniofacial characteristics were also evaluated.

Patients and methods

All aspects of the study were approved by the Ethics Committee of Medical School (N° 757/2007), University of Campinas. Twenty one adult patients undergoing treatment for GD at the Hematology and Blood Transfusion Center (Hemocentro - Unicamp), age ranging from 27 – 53 years of age, were invited to participate in this study. From those, nine, who were under enzyme replacement treatment, accepted. This therapy is offered gratuitously by the Brazilian government, through a program, created by the Ministry Health of Brazil, that centralize the purchasing and distribution of the enzyme.

Patients received a complete clinical oral examination, verifying the soft tissues and the decayed (D), missing (M) and filled (F) teeth (T) (DMFT) index.[16] Periodontal examination was also performed on the four quadrants, assessing all fully erupted teeth, excluding third molars. The mesio-buccal, mid-buccal, disto-buccal, and palatal/lingual surfaces were assessed in millimeters for probing attachment level and probing depth measurements.[17]

The position of the gingival margin (PGM) was measured from the cemento-enamel junction to the gingival margin and the clinical attachment level (CAL) was defined as the distance from the cemento-enamel junction to the bottom of the periodontal pocket/sulcus. Probing depth (PPD) was defined as the distance from the soft tissue margin to the tip of the probe.[17]

The Visible Plaque Index (VPI)[18] and Gingival Bleeding Index (GBI)[18] were measured dichotomously at the same sites. For GBI a blunt pocket probe was used for gentle probing of the gingival crevice orifice. No pain was supposed to be caused by the probing. If bleeding occured within about 10 seconds after testing, a positive finding was recorded. The number of positive findings was then expressed as a percentage of the number of gingival margins examined.[18] In the VPI, the occurrence of clearly visible plaque at the sites was examined.

The patients were encouraged to present for the panoramic radiographic for evaluation of the maxilla and mandible bone conditions. The radiography was performed in an oral radiology institute (Instituto de Radiodiagnóstico Odontológico – IRO – Campinas, São Paulo, Brazil). The panoramic radiographs were evaluated under optimum viewing conditions in a darkened room by two evaluaters, simultaneously, using an X-Ray illuminator. Presence or absence of generalized rarefaction, loss of trabeculae, cortical thinning, osteoesclerosis, effacement of lamina dura, root resorption and effacement of mandibular canal were taken into consideration.

Results

Nine adults were evaluated, 2 male and 7 female, mean age 44.4 years old (27 to 53). All of them presented GD type I. The demographic characteristics of this patient population and clinical parameters are shown in Table 1. The mean age at diagnostic was 36.56 years (ranged 22-50 years), and their mean period of diagnostic was 8.11 years. At the time of the study, all patients were receiving ERT, for a mean period of 3.22 years.

The mean of the DMFT index was 20.44 (range 14-28) (Table 1). Of the three components of DMFT, FT (45.64%) was the most prevalent, followed by MT

(43.49%) and DT (10.76%). Patient 6 and 8 did not receive periodontal examination as they were edentulous and wore complete removable dental prosthesis. The other patients evaluated showed slight gingival disease, even though 2 patients showed slight and 4 patients showed moderate periodontium involvement.

Seven individuals responded to radiographic examination. Table 2 summarized the observations regarding bone involvement. The most prevalent radiological findings were loss of trabecular structure and effacement of the mandibular canal found in all patients. Generalized rarefaction and effacement of lamina dura was found in 6 and 5 patients, respectively.

Table 1. Patient demographic characteristics, DMFT index scores and periodontal index results (n=9)

Patient		**1♀**	**2♀**	**3♀**	**4♀**	**5♂**	**6♀**	**7♂**	**8♀**	**9♀**	**MEAN± SD**
Age at Diagnostic (year)		41	22	29	38	38	50	49	24	38	36.56±9.93
Period of Diagnostic (year)		7	5	7	7	8	1	4	25	9	8.11±6.77
Period of ERT (year)		6	5	1	6	4	1	3	2	1	3.22±2.11
Body bone involvement (osteopenia)		YES	YES	-	YES	NO	YES	-	YES	YES	
DMFT Index											
Decayed		0	4	13	2	0	0	1	0	0	2.22±4.27
Missing		3	5	1	2	1	28	3	28	9	8.89±11.11
Filled		15	6	0	12	21	0	17	0	13	9.33±8.06
Total		18	15	14	16	22	28	21	28	22	20.44±5.2
Periodontal Evaluation											
VPI (%)		9	29.55	64.29	1.92	0	-	100	-	0	29.25±38.95
GBI (%)		0	3.4	0	0	0	-	100	-	0	14.77±37.6
PGM (mm)	**mean± SD**	2.6±1.4	2.5±1.91	1±0	2.11±0.78	3.21±1.12	-	2.89±1.05	-	3±0	2.47±0.74
PPD (mm)	**mean± SD**	0	3±0	3±0	0	3±0	-	3.13±0.35	-	0	1.73±1.62
CAL (mm)	**mean± SD**	2.6±1.4	4.4±2.7	4±0	2.11±0.78	4.06±2.05	-	3.92±1.85	-	3±0	3.44±0.87

DMFT = decayed, missing and filled teeth

SD = standard deviation

ERT = enzyme replacement therapy

VPI = visible plaque index

GBI = gengival bleeding index

PGM = position of the gingival margin

PPD = probing depth

CAL = clinical attachment level

Table 2. Gnathic radiologic findings in Gaucher Disease patients

Patient	Age	Generalized Rarefaction	Loss of Trabecular Structure	Cortical Thinning	Esclerosis	Pseudocystic	Effacement Lamina Dura	Root Resorption	Effacement Mandibular Canal	Bone Involved
1♀	48	YES	YES	NO	NO	NO	YES	NO	YES	Mandible/Maxilla
2♀	27	YES	YES	NO	NO	NO	YES	NO	YES	Mandible/Maxilla
3♀	37	-	-	-	-	-	-	-	-	-
4♀	44	YES	YES	NO	YES	NO	YES	NO	YES	Mandible/Maxilla
5♂	45	YES	YES	NO	NO	NO	YES	NO	YES	Mandible
6♀	51	YES	YES	NO	NO	NO	NO	NO	YES	Mandible/Maxilla
7♂	53	-	-	-	-	-	-	-	-	-
8♀	49	NO	YES	NO	NO	NO	NO	NO	YES	Mandible
9♀	47	YES	YES	YES	NO	NO	YES	NO	YES	Mandible/Maxilla

Discussion

Oral findings

The mean of the 20.44 for the DMFT index in this study showed a high prevalence of filled and missing teeth among GD adult patients. These findings were in accordance to the results of the oral health survey conducted in a Brazilian general population during the period of 2002-2003.[19] The survey showed that the result of the DFMT index for adults was 20.13. Considering only the missing teeth, patients 6, 8 and 9 had less than 20 functional teeth. In accordance with WHO,[16] 75% of the population aged 35 to 44 years old should have, at least, twenty functional teeth. Unfortunately, 3 of our patients were below the WHO objective. Furthermore, the DFMT index showed that our patients presented a high caries experience and were a long way off the WHO[16] goals established for 2010. Comparing the results of this study with patients who have Thalassemia Major (TM), another chronic disease, Gaucher patients showed higher DMFT values, since Lugliè et al. (2002)[20] found a mean DMFT score of 10.3±7.3 which was not statistically signifcant difference of the control group. Laurence et al. (2006)[21] suggested that African-American with sickle cell anemia may be at increased risk for dental caries than control group. These authors afirmed that TM patients might be considered at risk for caries, however, they did not state whether this difference is related to the systemic disease, as in our study.

In our study, 5 individuals presented 30% of the dental faces with VPI. GB was found in 2 adults in 14.7% of the dental faces, which was lower than the mean of the general population,[17] or even of the previous report on renal chronic disease[22] or Gaucher's patients.[15,23,24] On the other hand, the periodontium showed moderate involvement, since severe periodontitis has been defined as CAL ≥5 mm,[15,17,22,24] and our patients showed a mean CAL of 3.4 mm, PGM of 2.47 mm and PPD of 1.73 mm. In fact, patient 1 and 4 showed slight and patients 2, 3, 5, 7 and 9 showed moderate periodontal involvement. In agreement with Fischman et al. (2003),[23] we could not determine an association between GD and gingival disease, however attention to the possible complications due to haematologic abnormalities, such as thrombocytopenia inducing to patechiae or spontaneous

bleeding is necessary. In addition, the difference between the gengival and the periodontal condition could show an improving of the present oral health compared to the past. Maybe the enzyme replacement therapy could have an influence on this condition, or the patients were aware of their Gaucher disease status and may have had a higher health awareness, including a greater concern for their oral health.[23] A healthier diet and better personal oral might also explain the observed differences in DT and MT scores.[23]

Radiological findings

Jaw involvement seemed to follow the same world wide pattern.[13,14,23] The most prevalent radiological findings in the jaw found in all our patients were loss of trabecular structure and effacement of the mandibular canal that were in accordance with previous study.[13,14,23] In addition, generalized rarefaction and effacement of lamina dura was very common, found in 6 (85.7%) and 5 (71.4%) patients, as have been reported by Bender & Bender (1996).[13] From the seven patients evaluated, six showed osteopenia in conventional radiographs of the body. Although these panoramic radiographs were not the most appropriate exam to determine bone involvement, these finds could suggest that the generalized rarefaction found in the jaw bones could also be osteopenia. Only patient 5 underwent bone mineral density evaluation, revealing neither osteopenia nor osteoporosis.

The pathophysiology of bone involvement in GD is not yet well understood, however the literature has shown that complications could be explained by the infiltration of GC into bone and bone marrow. The mechanisms by which GC displaces normal bone marrow cells and causes edema and ischaemia are not yet known either.[25]

The mandible was more affected than the maxilla, 7 and 5 cases respectively. The predilection sites involved were the premolar and molar areas of the mandible, and in the canine-premolar areas in the maxilla, as reported by Karabulut et al. (1997).[8] Compromised vascularization, from extrinsic vessel compression due to increased intraosseous pressure and/or occlusion by

thrombosis or embolism, may lead to the formation of localized bone lesions in GD.[26] Those vessel alterations could explain the predilection area for these bone alterations, near to the mental foramen. Hemorrhage may also occur, and these events may result in necrosis and raised intraosseous pressure.[27]

Esclerosis was found only in patient 4, corroborating the literature, since few reports of mandibular radiopacities have been reported for this population. Radiopacites could represent a temporary bone regeneration following splenectomy and extraction of teeth[28] or a chronic diffuse osteosclerotic type of reaction to an initial GC infiltration.[29] Wenstrup et al. (2002)[25] affirmed that osteosclerosis can occur as an aberrant remodelling after bone infarction with the deposition of calcium into the bone. In the present case, esclerosis seemed to be caused by bone regeneration, as the regeneration was observed next to the region of an extracted tooth.

The occurrence of mandibular disease Type I GD patients suggested that all patients should be evaluated periodically to detect mandibular skeletal involvement. The consequences of medullary bone loss in the mandible may be severe.

Some studies reported that osteomyelitis is a major concern.[30,31] We found no cases of osteomyelitis reported at Hemocentro, despite the high prevalence of bone jaw involvement. If Gaucher-involved bone has an increased susceptibility to infection which is most likely due to the presence of necrotic material and decreased blood supply, providing an optimal environment for microorganisms,[30] we have to keep in mind that osteomyelitis is a potential disease in these patients, obligating us to maintain a constant follow-up. If there is evidence of bone lesions, then the importance of good dental hygiene should be stressed to avoid odontogenic infections and secondary osteomyelitis in the bone involved.[32]

Another consequence of medullary bone loss is the potential for pathologic fractures, which usually occur in areas of pre-existing bone lesions where the cortex is thin and the trabeculae weakened.[32] Again, we did not observe this situation in our study, which could be due to the fact that even though all of them showed loss of trabecular structure, only patient 9 showed cortical thinning. In

addition, none of our patients had to be submitted recently to invasive procedures, such as extractions, that could lead to pathologic fractures.

Moreover, they did not exhibit the severe complications of jaw involvement, possibly corroborating the findings of Zimran et al. (1992)[33] who reinforced that GD becomes less progressive as the patients grow older and has a tendency to stabilize in adulthood.

ERT X Bone lesions

At the time of the study, all the patients evaluated were receiving ERT (age at start 25–52 years, median 41.3 years old), however this therapy has been available only for a short period of time, approximately 3.22 years (range 1-6), which did not seem to be enough to reverse the skeletal involvement in the jaw. The skeletal responses to ERT are slower than the hematological and visceral changes, and may be dependent on the degree of bone involvement at the time therapy is initiated. The effect of ERT on skeletal abnormalities may be limited when administration is delayed beyond the point of irreversible bone changes.[34]

We could not affirm that the bone changes had reached an irreversible point, however the mean age at diagnosis of these patients was 36.5 years and the mean age of the beginning of the therapy was 41.3 years, which could have provided years of damage of the disease before starting the treatment.

The findings point to the importance of asking for a panoramic radiographic exam during the first appointment, as a routine procedure, for all the patients independently to their general health conditions.

Due to the clinical heterogeneity, comprehensive and reproducible evaluation and monitoring of all clinically relevant aspects of GD are vital to assess patterns of the disease and effective management of patients.[35] It is important for dentists to keep in touch with patients' physicians, in order to be informed as to their medical condition. Furthermore, we suggest that future studies should include a larger number of patients and a multicentre evaluation.

Conclusion

Adult Gaucher patients showed poor oral health not associated to GD and important alterations of the jaw bone. Patients with GD require oral health monitoring, with the respective treatment provided, as well as instruction on oral hygiene as part of their dental education in order to improve their oral health history. Even in the absence of infection or pain, radiographic examinations should be asked for periodically in order to investigate the presence of any bone lesions in the jaw and to better comprehend GD jaw involvement.

Acknowlodgments

The authors thank Mr. José Luiz Cintra Junqueira and Ms. Saori Okajima Nakamoto for the indispensable support, offering free radiographs exams, Ms. Raquel Suzana Foglio, for English review and Mr. Roberto Zulli for statistics analysis.

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Oral Health-Related Quality of Life in a Group of Patients with Gaucher Disease

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Abstract

The aim of this study was to assess the oral health-related quality of life among a group of patients with Gaucher disease. Seven children, aged from 7 to 15 years old, and eight adults, aged from 27 to 53 years old, under treatment at the Hematology and Blood Transfusion Center (Hemocentro) of the University of Campinas (Unicamp) participated of this study. Each patient received a complete soft tissue examination and a clinical examination of decayed, missing and filled primary (dmft) and permanent (DMFT) teeth. Periodontal examination was performed in the adult patients evaluating clinical attachment level (CAL), probing depth (PPD), position of the gingival margin (PGM), visible plaque (VPI) and gingival bleeding index (GBI). The influence of oral health on the quality of life was evaluated by a questionnaire filled by the children themselves – a Child Perception Questionnaire, specific for each range of age – CPQ 8-10 years and CPQ 11-14 years – and the Oral Health Impact Profile questionnaire – OHIP 49 – was used for the adult patients. In the children group, the mean dmft found was 3.2 and the DMFT 0.86. For the adults, the mean DMFT was 21.25. Five patients presented visible plaque and 2, gingival bleeding. The CAL mean was 3.0 mm, PGM was 3.0 mm, and PPD 1.2 mm. The mean overall score for CPQ 8-10 years was 17, showing moderate impact of oral health upon quality of life for children at these ages. The highest mean values were recorded for the domain of oral symptoms, followed by functional limitations, emotional and social well-being. The mean overall scale for the CPQ 11-14 years showed the highest mean values for the domain of emotional well-being, followed by functional limitations, oral symptoms and social well-being, and the medium value was 38. Among the adults, the perception of substantial impact of oral health on their quality of life was high, since the mean overall score of the questionnaire was 58.63. The highest mean values were recorded for the domain of functional limitations and physical pain, followed by physical disability and psychological discomfort. Although the children did not present poor oral health, some oral conditions, such as pain during eruption, or esthethics alterations could interfere in their quality of life. On the other hand, the adults showed poor oral health-related quality of life.

Introduction

Gaucher Disease (GD) is an autosomal, recessively inherited, lysosomal storage disease that results from deficiency of the lysosomal enzyme glucocerebrosidase. Consequently, the enzyme's substrate, glucocerebroside, accumulates in the macrophages of the reticuloendothelial system, particularly in the spleen, liver, bone marrow, and lung.[1]

Clinically, 3 major forms of GD have been recognized. GD type I, a panethnic disease with an increased prevalence in Ashkenazi Jews, which is the most common.[2,3] The rare GD type II is acutely neuronopathic. GD type III is less common than GD type I and is characterized by severe visceromegaly and variably progressive neurologic involvement.[4-6]

Some patients with GD can present hemorrhagic diathesis,[7] pigmentation in the cheek,[8] or petechia in the mucosa.[9] A tendency to bleeding is one of the more common presenting signs described in the literature.[10] Case reports suggest that postsurgical hemorrhage secondary to thrombocytopenia represents the most frequent dental finding.[11] Moreover, cases report have showed poor oral conditions.[8,9] Delayed eruption of permanent teeth in both arches from the canines distally was observed by Carter et al. (1998).[11]

Quality of life is actually a rather broad concept that applies to the level of a person's general feeling of a well-being and encompasses an extensive range of physical and psychological characteristics and limitations that describe ability to function and derive satisfaction in doing so.[12] Therefore, quality of life is probably best defined as the perceived discrepancy between the reality of what a person has and the concept of what that person wants, needs or expects.[12] If this definition is evaluated with the view on the part of a dentist, a new phenomenon occurs with the name of Oral Health Related Quality of Life (OHRQoL), that characterizes a person's perception of how oral health influences their life quality and overall well being.[13]

The clinical indicators used in dentistry research have been restricted to the symptoms an individual perceives, such as pain, discomfort and esthetic alterations.[14] Despite the increasing number of rigorous studies focusing on quality

of life we still know relatively little on how oral conditions affect people feelings of wellbeing.[15]

The aim of this study was to assess the OHRQoL among a group of patients with GD.

Patients and Methods

All aspects of the study were approved by the Ethics Committee of Medical School (N° 757/2007), University of Campinas. There are 32 patients with GD, 11 children and 21 adults submitted to medical treatment at the Hematology and Blood Transfusion Center (Hemocentro) of the University of Campinas (Unicamp). All of them were invited to participate in this study, which included an oral examination and application of a questionnaire. Fifteen patients were submitted to both oral examination and assessment of OHRQoL, seven children, aged from 7 to 15 years old, and eight adults, aged from 27 to 53 years old.

The clinical oral examination described in details previously (Chapters 1 and 2). Briefly, examination of soft tissue and evaluation of decayed, missing and filled teeth (dmft or DMFT) were performed. Adult patients received also a periodontal assessment for all teeth in the mesio-buccal, mid-buccal, disto-buccal, and palatal/lingual surfaces and the measurements obtained in millimeters for probing attachment level and probing depth.[16] The position of the gingival margin (PGM) was measured from the cemento-enamel junction to the gingival margin and the clinical attachment level (CAL) was defined as the distance from the cemento-enamel junction to the bottom of the periodontal pocket/sulcus. Probing depth (PPD) was defined as the distance from the soft tissue margin to the tip of the probe.[16] The Visible Plaque Index (VPI)[17] and Gingival Bleeding Index (GBI)[17] were measured dichotomously at the same sites.

The influence of the oral health on the quality of life was evaluated by a questionnaire self-filled by the children – Child Perception Questionnaire (CPQ),[18] translated and validated for using in Brazilian Children.[19] There was a specific questionnaire for each range of age – CPQ_{8-10} and CPQ_{11-14}. These questionnaires were a Child Oral Health Quality of Life questionnaire and assess the

repercussions of oral health problems on the quality of life of children between 8 and 10 years of age (CPQ_{8-10}), and between 11 and 14 years of age (CPQ_{11-14}), respectively.

At the CPQ_{8-10} the items addressed the frequency of events during the previous four weeks and the CPQ_{11-14} during the previous three months. The questionnaire was structurally composed of 25 and 37 items, respectively, distributed among 4 domains: oral symptoms (5 and 6 questions), functional limitation (5 and 10 questions), emotional well-being (7 and 9 questions) and social well-being (8 and 12 questions). A 5-point Likert scale was used, with the following options: 'Never' = 0; 'Once/twice' = 1; 'Sometimes' = 2; 'Often' = 3; and 'Every day/almost every day' = 4. They were computed by summing all of the item scores. Since there were 25 and 37 questions, the final score could vary from 0 to 100 and from 0 to 148, respectively, for which a higher score denoted a greater degree of impact of oral conditions on the quality of life of the respondents.

The influence of oral health upon quality of life for adults was evaluated by a Portuguese translation of the self-filled questionnaire – Oral Health Impact Profile – OHIP 49. The questionnaire measured people's perception of the social impact of oral disorders on their well-being.[20] This measure consisted of 49 items divided into seven different domains and the possible score range for each one was: 'functional limitation' (nine items) – from 0 to 36; 'physical pain' (nine items) – from 0 to 36; 'psychological discomfort' (five items) – from 0 to 20; 'physical disability' (nine items) – from 0 to 36; 'psychological disability' (six items) – from 0 to 24; 'social disability' (five items) – from 0 to 20; 'handicap' (six items) – from 0 to 24; and finally 'Overall OHIP score' (49 items) – from 0 to 196. The respondents were asked, regarding each item, how often during the previous 12 months had they experienced a certain problem regarding their teeth or mouth. They responded using a Likert-type scale, which was coded as follows: 'Never' = 0; 'Hardly ever' = 1; 'Sometimes' = 2; 'Fairly often' = 3; and 'Very often' = 4. In this model, the higher scores indicated a poorer state of health.

Results

The individual data for age, gender and oral conditions are shown in Table 1. One child (C3 ♂) presented Type III GD, and the others Type I. At the time of the study, all patients were receiving enzyme replacement therapy (ERT). (For more details, please see Chapters 1 and 2). The periodontal examination was not carried out in adults A6 and A8 as they were edentulous and used complete denture prosthesis.

The dfmt index medium for the children was 3.2 (ranged 0-7) and the DMFT was 0.86 (ranged 0- 4) (Table 1). Child 5, who had the greatest number of primary teeth, also had the highest dmft index which helped to raise the mean. In addition, 6 patients showed the DFMT index equal zero, however 2 patients resulted in the mean DMFT index found, since children 5 and 7, showed high DMFT values, 2 and 4 respectively. For the adult patients, the mean DMFT was 21.25 (ranging 14-28) (Table 1). Except for the adults A6 and A8, who wore complete dentures, the other patients with tooth losses did not wear any other oral prosthesis.

The results indicated that the measure detected variability in the quality of life of the child and adult participants. The CPQ_{8-10} scores ranged from 2 to 32, with a mean of 17 and a standard deviation of 15.2. The CPQ_{11-14} ranged from 15 to 65, with a mean of 38 and a standard deviation of 25.2. The individual values for the overall scale and for the four domains of the CPQ_{8-10} and CPQ_{11-14} are described in Table 2. For the CPQ_{8-10}, the highest domain was oral symptoms and for the CPQ_{11-14}, emotional well-being. The social well-being domain was the lowest for both age ranges. Moreover, only child C2♀ complained about her esthetics due to a severe open bite.

Table 3 describes the adults' individual values for the overall scale and for the seven domains of the OHIP 49. The scores ranged from 7 to 111, with a mean of 58.63 and a standard deviation of 34.1. The highest values were found for functional limitation followed by physical pain domains, the lowest one was handicap and social disability.

Table 1. Demographic characteristics, and oral conditions of children and adults with Gaucher disease

Children	**C1**♀	**C2**♀	**C3** ♂	**C4**♀	**C5** ♂	**C6** ♂	**C7**♀		Mean±SD
Age (y.m)	15	10.11	9.11	10.1	7.5	8.10	13.5		10.8±2.78
dmft Index	-	0	2	3	7	4	-		3.2±2.59
DMFT Index	0	0	0	0	2	0	4		0.86±1.57
Adults	**A1**♀	**A2**♀	**A4**♀	**A5** ♂	**A6**♀	**A7** ♂	**A8**♀	**A9**♀	
Age (year)	48	27	44	45	51	53	49	47	45.50±8.04
DMFT Index	18	15	16	22	28	21	28	22	21.25±4.92
Periodontal Evaluation									
VPI (%)	9	29.55	1.92	0	-	100	-	0	27.25±48.69
GBI (%)	0	3.4	0	0	-	100	-	0	20.00±44.72
PGM (mm)	2.6±1.4	2.5±1.91	2.11±0.78	3.21±1.12	-	2.89±1.05	-	3±0	3.00±0.40
PPD (mm)	0	3	0	3	-	3.13±0.35	-	0	1.20±1.64
CAL (mm)	2.6±1.4	4.4±2.7	2.11±0.78	4.06±2.05	-	3.92±1.85	-	3±0	3.00±0.91

SD = standard deviation y.m = year.month dmft = = decayed, missing and filled primary teeth DMFT = decayed, missing and filled permanent teeth
VPI = visible plaque index GBI = gingival bleeding index PGM = position of the gingival margin PPD = probing depth CAL = clinical attachment loss

Table 2. Children's oral health-related quality of life: individual values, mean and sd for domains and total scores

	Children	Total Scale	Subscale			
			Oral Symptoms	Functional Limitation	Emotional Well-Being	Social Well-Being
CPQ_{8-10}	C3 ♂	28	10	4	7	7
	C4♀	6	3	1	2	0
	C5 ♂	2	2	0	0	0
	C6 ♂	32	9	12	7	4
	Mean±SD	17±15.19	6±4.08	4.25±5.44	4±3.56	2.75±3.40
CPQ_{11-14}	C1♀	15	7	6	1	1
	C2♀	65	10	20	24	11
	C7♀	34	5	6	23	0
	Mean±SD	38±25.24	7.3±2.52	10.7±8.08	16±13.00	4±6.08

SD = standard deviation

CPQ = Child Perception Questionnaire

Table 3. Adults' oral health-related quality of life: individual values, mean and sd for domains and total scores for OHIP 49

Patient	Total Scale	Subscale						
		Functional Limitation	Physical Pain	Psychological Discomfort	Physical Disability	Psychological Disability	Social Disability	Handicap
A1♀	76	23	20	4	15	6	6	2
A2♀	111	17	26	19	16	13	9	11
A4♀	75	20	19	10	11	12	2	1
A5♂	14	5	5	2	0	2	0	0
A6♀	71	18	17	11	12	6	0	7
A7♂	55	20	14	5	11	5	0	0
A8♀	60	24	16	12	4	2	0	2
A9♀	7	1	4	2	0	0	0	0
Mean±SD	58.63±34.10	16.00±8.42	15.13±7.45	8.13±5.94	8.63±6.41	5.71±5.06	2.13±3.48	2.88±4.02

SD = standard deviation

OHIP 49 = Oral Health Impact Profile

Discussion

Contemporary concepts of health suggest that oral health should be defined in terms of general physical, psychological and social well-being and in relation to oral status.[20]

In the present study, oral disease and disorders have been evaluated in population studies using clinical measures, such as the DMFT and periodontal indexes, which indicate the presence and severity of an oral condition. However, perceptions of oral health and positive or negative impacts on the quality of life must necessarily be reported by the people who experience the conditions.[21]

In general, we observed that the oral health of our children was good. On the other hand, the adults presented poor dental and periodontal conditions.

Children

Considering the primary teeth, patient C2♀ was caries free (dmft = 0) reaching the recommendation by the World Health Organization (WHO)[22] for 2010, however patients C3♂, C4♀, C5 ♂ and C6♂ were far off. Nevertheless, their high dmft value (2, 3, 7 and 4, respectively), determined a moderate impact on their quality of life, since their total CPQ score were 28, 6, 2 and 32. Conversely, the patient C5♀, showed the highest dmft value and the lowest total CPQ rate. Patient C2♀, who was caries-free, showed the highest total CPQ score. This finding could be explained by the impact of malocclusion upon the quality of life of this child, as the child reported great dissatisfaction with her facial appearance due to a severe open bite.

On the other hand, when permanent teeth were evaluated, our children were inclined to reach those goals that established a DMFT smaller than 1.00 at 12 years old. However, 2 patients still had high values for DMFT, showing that the caries lesions were not uniformly distributed among children with GD, as in the general population. Even though they were caries free, the oral results presented substantial impact upon their quality of life. Patients C3♂, C4♀ and C6♂ did not have sound primary teeth, which could have influenced their total CPQ values. Patient C1♀ experienced situations other than those detected, instead of the

carious lesions that determined their CPQ value, whereas for patient C2♀ malocclusion could be the reason.

The mean overall score for CPQ_{8-10} was 17 (SD:15.19). Patients **C4**♀ (6) and **C5** ♂ (2) showed little impact of oral health upon their quality of life, while patients **C3**♂ (28) and **C6**♂ (32) showed moderate impact. These last patients showed overall CPQ_{8-10} scores higher than those reported for healthy children 8.5 (SD: 6.2), children with cleft lip and palate 7.9 (SD: 8.0) and children with rare oral diseases 16.3 (SD:8.4).[23] As previously reported,[21] the highest mean values were recorded for the domain of oral symptoms, followed by functional limitations, then emotional and social well-being. Oral diseases and teeth alterations during childhood could have a negative impact upon the life of children. Dental caries can lead to toothaches, which can be distressful and worrying for the affected child,[21,24] explaining the highest mean value found for oral symptoms. Pain can interfere in the masticatory activities leading to functional limitations that were also perceived by our patients, demonstrated by the second highest mean value. This domain was closely followed by the emotional well-being, showing that the disability could cause some annoying situations.

The mean overall scale for the CPQ_{11-14} did not show the same pattern as for the youngest patients, showing the highest mean values for the domain of emotional well-being, followed by functional limitations, oral symptoms and social well-being. Perhaps, their dental appearance could be more worrying leading to frustrating feelings. In fact, Gherunpong et al. (2004)[25] showed that the difficulty with smiling was an important aspect of children's OHRQoL, affecting 40% of children aged 11–12 years. For Drotar et al. (1998),[26] it was evident that children's concern about their oral appearance was important when they reach adolescence. Indeed, patient 2 who complained about her esthetic because of open bite had a great CPQ_{11-14} value, being "emotional well-being" domain the highest one.

Furthermore, although these patients were caries-free, they could experience previous problems related to aphthous ulcer or dental eruption as previously described by Tubert-Jeannin et al. (2005)[27] who found high prevalence of oral impacts in a population with a low incidence of caries. It must be taken into

consideration that health outcomes experienced by an individual are not determined only by the nature and severity of the disease/disorder but also by the personal and environmental characteristics.[28]

Patients **C1**♀(15) **C2**♀(65) and **C7**♀(34) showed overall CPQ_{11-14} scores higher than those reported for healthy children 10.5 (SD: 7.6) and for children with cleft lip and palate 10.2 (SD: 7.2).[23] Patients **C2**♀ and **C7**♀ also had higher scores than children with rare oral disease 17.8 (SD: 8.8) and children with orthodontic appliances 24.4 (SD: 12.5).[23] Foster Page et al. (2005)[29] described lowest CPQ_{11-14} values for 4+ DMFS group (21.8;SD:18.2) and malocclusion 'Handicapping' category (21.6;SD:18.0) compared to our children.

Adults

The mean DMFT in the adults subjects in this study was high (21.25) with filled and missing teeth being more prevalent. These findings were in line with the results of the oral survey conducted in Brazil in 2002-2003.[30]

Five individuals leading to, in median, 27.3% of the dental faces presented visible plaque and gingival bleeding was found in 2 adults, 20% of the dental faces, which was lower than the mean of the general population. Although they showed slight gingival involvement, they presented moderate periodontal disease with mean CAL of 3.0 mm, PGM of 3.0 and PPD of 1.2 mm.

In the light of these data, we estimated that their poor oral health caused the poor level of oral health quality. Overall we observed that, the group of adults in this study perceived substantial impact of oral health upon their quality of life, since the mean overall score of the questionnaire were 58.63.

The highest mean values were recorded for the domain of functional limitations and physical pain, followed by physical disability and psychological discomfort. The domain of social disability was the lowest value. Indeed, the wearers of complete dentures, patients A6♀ and A8♀, presented high scores for the OHIP 49, showing highest values for functional limitations and physical pain, (18 and 17 for the A6♀ and 24 and 16 for A8♀, correspondingly), showing the impact of the prosthesis on the equilibrium of the functions of the stomatognathic

system and consequently the influence of oral health upon quality of life. These results were in agreement with a result demonstrated by the healthy Spanish population that also showed the highest oral health impact within the following domains: 'psychological discomfort', 'functional limitation' and 'physical pain'.[15]

The perception of the OHRQoL has been shown in previous studies to be related to oral health status, especially the caries status.[31-33] Although the decayed teeth were the lowest value representing 4.1% of the DMFT index, the highest values found were related to functional limitation and physical pain. Actually, there were only 3 questions on the physical pain domain that were specifically related to toothaches, maybe indicating that other oral problems, such as inadequately filled teeth, bad adapted prosthesis or dentin hypersensitivity could cause functional limitation and pain. In addition, MT corresponded to 46.5% of the DMFT index, which influenced the masticatory function in a meaningful way.

Indeed, Reisine et al. (1989)[34] suggested that only if symptoms of disease affected a person's functioning did they view their oral health as being impaired, thus making physical functioning a determinant of oral health. As well, the function limited and pain consequently leads to physical disability that in turn causes psychological discomfort, which were the two following prevalent domains. Even though our patients identified their oral health as poor, this did not influence their social relationships, as the social disability domain was the lowest value found.

In addition, it is known that measurements of perceived health status rely on individual judgments, values, and beliefs, reflecting the extent to which a person experiences function/dysfunction and comfort/discomfort, for example,[35] explaining why patients 5 and 9, who showed high DMFT and low scores of OHIP 49, could have underestimated their oral health. They were affected by a chronic disease that could have some debilitating and disabling aspects, which often have greater impact upon quality of life,[36] leading to lesser attention to oral problems.

Patients with GD were found to have considerably impaired OHRQoL in comparison with other groups of patients and with the general population. The mean OHIP score for our patients was 53.68, higher than the temporomandibular disorder patients that showed a mean score of 42.9 and 15.8 for the general

population.[37] Despite the small number of patients included in this study, our results indicated that our patients with GD experienced decreased OHRQoL compared to patients from other populations.

The results of this study emphasized the importance of perceived health status and psychosocial assessment in the evaluation of Gaucher patients. Health-related quality of life measures, including objective and subjective assessments, are especially useful for evaluating efforts to prevent disabling chronic diseases and their effectiveness.[38] Furthermore, quality of life is increasingly acknowledged as a valid, appropriate, and a significant indicator of service need and intervention outcomes in contemporary public health research and practice.[39]

Conclusion

Measurement of the impact of oral conditions on quality of life should be part of the evaluation of oral health needs as clinical indicators alone are not capable of describing the satisfaction or symptoms of dental patients or their ability to perform daily activities.

Although the children did not present poor oral health, some oral conditions interfered in their quality of life. On the other hand, the adults showed poor oral health and consequently poor OHRQoL.

These patients should be advised as to the importance of oral care; they must be recalled for regular dental visits; and with the help of these measurements, OHRQoL levels of the Gaucher patients should be increased. Moreover, we should assure good oral health in children, leading to a decrease in the impact upon their quality of life.

Acknowlodgments

The authors thank Ms. Raquel Suzana Foglio, for English review.

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Gaucher disease: evaluation of body and craniofacial development

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Abstract

The general growth delay observed in Gaucher children even if under enzyme treatment, could have an influence on the craniofacial development. The aim of this study was to evaluate prospectively, the general growth and craniofacial development in a group of children under enzyme replacement therapy (ERT). The Hematology and Blood Transfusion Center (Hemocentro) from University of Campinas (Unicamp) included 8 children with Gaucher disease (GD) under ERT. All of them were invited to come in for radiographic analysis. Growth was assessed by the body mass index, weight and height plotted against standard growth charts. Bone age was estimated by X-ray of the wrist and hand. The lateral radiography was used to evaluate the craniofacial characteristics by cephalometric analysis. Craniofacial characteristics and growth was evaluated at baseline and 12 months follow-up. At diagnosis, growth was less than the 5^{th} percentile of height for gender and age in 28.6% of children; in 28.6%, from the 5^{th} to 25^{th} percentiles; and, 42.8%, greater than the 25^{th} percentile. There was a slight improve at the second evaluation for the group less than 5^{th} percentile and 5^{th} to 25^{th} percentiles. The children showed a mean difference of 13 months in the first evaluation and of 16 months at the second between the chronologic and bone age. By cephalometric analysis was observed that some children showed higher values of craniofacial growth confronting with the craniofacial standards. After one year, all the patients had craniofacial measures divergent of the standard. The growth of these patients was not in line with what was previous predictable after the first exam. It suggests that children with GD may manifest alterations on the craniofacial growth but it seems that this variation was into normality requiring continuous follow up.

Introduction

Gaucher's disease, the most common lysosomal storage disease, is an autosomal recessive disease caused by a deficiency of the enzyme acid B-glucosidase [EC 3.2.1.45] (ABG), a hydrolase that cleaves the sphingolipid glucosylceramide, a glucocerebroside, to glucose and ceramide.[1,2]

The disease occurs in three distinct phenotypic subtypes which are delineated by the absence (Type I) or presence and severity of neurological involvement (Types II and III).[3]

Some patients have minimal signs or symptoms, while many have debilitating or disabling hematologic, visceral and/or skeletal involvement and/or have required splenectomy.[4] The disease may be life-threatening or even fatal. Such clinical variation may be a function of genetic and/or environmental factors.[4ida]

The skeletal manifestations are strikingly diverse in symptoms and in pathology, including a spectrum of bone pain, bone crises, asymptomatic Erlenmeyer flask deformity, osteopenia, pathological fractures, osteomyelitis, and avascular necrosis, growth retardation and failure to reach peak bone mass.[5]

Kaplan et al. (1996)[6] documented, for the first time, the high prevalence of retarded growth in children and adolescents with type I GD and the acceleration of growth with enzyme replacement therapy. They affirmed that growth failure is often obvious much earlier than teenage years. The cause of the poor growth was not elucidated.

In the study of Ida et al. (1998)[4] the Japanese GD patients had their height stunted more severely than the Israeli ones, showing that 10 (33%) of 30 evaluable patients were below the 3rd percentile.

Enzyme replacement therapy (ERT) with the placental preparation alglucerase (Ceredase, Genzyme Corporation, Cambridge, MA, USA) or the recombinant preparation imiglucerase (Cerezyme, Genzyme Corporation, Cambridge, MA, USA) has been shown to arrest or reverse hematologic, visceral and skeletal involvement, to diminish physical growth retardation and to improve quality of life in patients of a variety of genotypes, ethnicities and ages.[6-9]

Children and adolescents with GD commonly experience growth retardation.[10] Since the disease is progressive, earlier onset usually correlates with a more severe disease course.[11] The growth delay in Gaucher children[5,12-13] lead to a possible correlation with craniofacial development ateration.

The aim of this study was to evaluate growth and the craniofacial development in a group of GD children under enzyme replacement therapy.

Patients and methods

All aspects of the study were approved by the Ethics Committee of Medical School (N° 757/2007), University of Campinas. The Hematology and Blood Transfusion Center (Hemocentro) from University of Campinas (Unicamp) included 11 children with GD. All of them were invited to come in for radiographic analysis and clinical evaluation. For the first evaluation eight were included and for the second, 1 year later, six of them.

Growth was assessed by the body mass index (BMI), weight and height plotted against standard growth charts. Bone age was estimated by X-ray of the wrist and hand according to Greulich and Pyle (1959).[14] The lateral radiography was used to evaluate the craniofacial characteristics by cephalometric analysis of Jarabak (1972).[15]

The lateral radiographies of each subject were taken in an institute of oral radiology (Instituto de Radiodiagnóstico Odontológico – IRO – Campinas, São Paulo, Brazil). All subjects were positioned in the cephalostat with the sagittal plane at a right angle to the path of the X-rays, the Frankfort plane parallel to the horizontal, the teeth in centric occlusion, and the lips slightly closed. The radiographs were hand-traced and measured by the same investigator (F.G.C.R.).

The following landmarks were used for cephalometric analysis: frontal-nasal suture (N), sella turcica (S), articular (Ar), gonial intersection (Go), menton (Me). The linear values evaluated were anterior facial height (N-Me), posterior facial height (S-Go), anterior cranial base (S-N), mandibular corpus (Go-Me), posterior cranial base (S-Ar) and ramus height (Ar-Go). Also were evaluated the N-S-Ar (saddle angle), S-Ar-Go (articular angle), Ar-Go-Me (gonial angle); Ar-Go-N (upper

gonial angle); N-Go-Me (lower gonial angle) and Ar-Go-Me (sum of angles) (Figure 1).

Jarabak has categorized facial morphology on the basis of three distinct patterns defined by the Facial Height Ratio (FHR), a ratio of posterior facial height to anterior facial height: $FHR = \frac{S - Go}{N - Me} \times 100$.

These patterns are commonly associated with rotational growth changes that tend to accentuate the patterns characteristics with growth, so even statics evaluation are identified in terms of growth, as follows:

1. Hyperdivergent growth pattern**: FHR < 59%** and the face rotating downward and posteriorly with growth. Anterior facial height increases more rapidly than posterior height, and Dow's Y-axis and some others angles tend to open.

2. Neutral growth pattern**: FHR 59% - 63%**. Growth direction is downward and forward along Dow's Y-axis, with about the same increments anteriorly and posteriorly and no progressive change in most angular relationships.

3. Hypodivergent growth pattern: **FHR > 63%**, with predominantly horizontal growth.

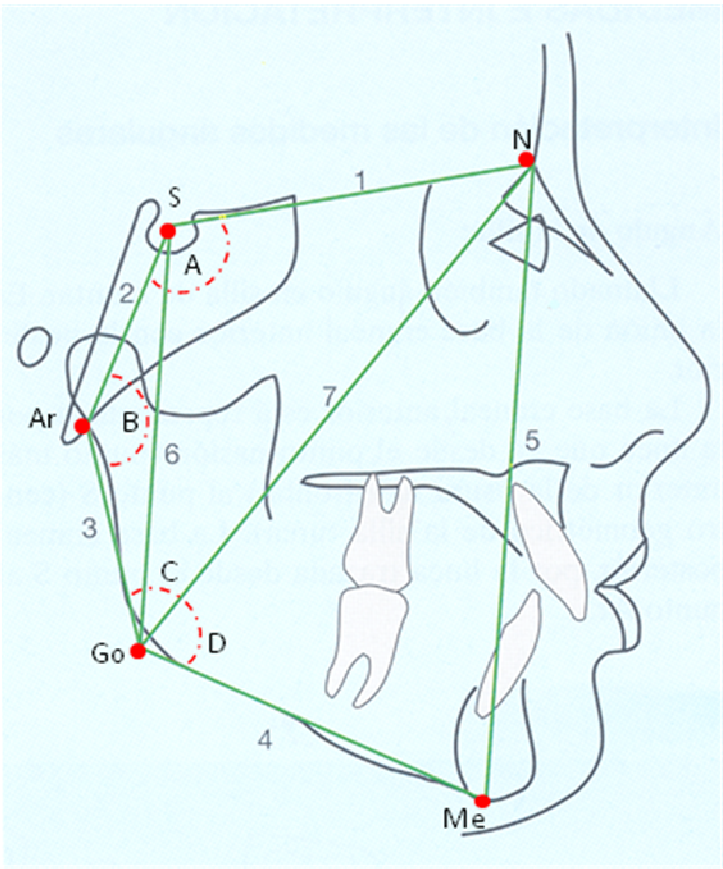

Figure 1. Measurements used for cephalometric analysis

Angular measurements	Linear measurements
N-S-Ar [(A) saddle angle]	1. Anterior cranial base (S-N)
S-Ar-Go [(B) articular angle]	2. Posterior cranial base (S-Ar)
Ar-Go-Me [(C+D) gonial angle]	3. Ramus height (Ar-Go)
Ar-Go-N [(C)upper gonial angle]	4. Mandibular corpus (Go-Me)
N-Go-Me [(D)lower gonial angle]	5. Anterior facial height (N-Me)
Ar-Go-Me [(A+B+C+D)sum of angles]	6. Posterior facial height (S-Go)
	7. Facial depth (N-Go)

Results

The demographic characteristics of the population, as well as the therapy status are shown in Table 1. Of the 8 individuals, ages ranging from 7 to 15 years (mean 10.1 yttears), 3 were male and 5 were female. Seven patients had Type I GD, and one patient had GD Type III (patient 3). At the time of the study, all patients were receiving ERT (age at start 2–10 years, mean 5.75 years).

Two children didn't appear to the second evaluation and 6 children were reevaluated. Growth was divided into the following 3 groups: less than the 5th percentile, 5th to 25th percentile, and greater than the 25th percentile (Table 2). There were 1 patient for BMI, 3 for weight and 2 patients for height considering "less than the 5th percentile" group. The individual values for weight, height and BMI percentiles were exposed at Table 3.

The individual results about the difference between the chronologic and bone age were showed at Table 4. In the first evaluation there was no significative difference between them, however it was significant after one year.

The results of the cephalometric analysis (linear and angular values), showing the growth in one year of follow-up and the craniofacial growth tendencies of the children, were showed at Table 5. It can be noticed that the most obtained cephalometric measurements were correspondent to the standards stated by Jarabak[13] although the craniofacial growth medium, in this period, was 4.5, 3, 4.8, 4, 2.5mm respectively for patients 2, 3, 4, 5 and 6. Because patients 1 and 7, were at puberty period, their craniofacial growth were not evaluated, since they had already had their "boom". Child 1 showed significant higher value to the saddle angle (N-S-Ar), lower gonial angle (N-Go-Me) and mandibular corpus (Go-Me). There was statistically significant difference for the linear measures growth of the mandibular corpus (Go-Me) in children 2 and 3 ($p=0.018$), posterior cranial base (S-Ar) in children 6 ($p=0.016$), and ramus height (Ar-Go) ($p=0.016$). The saddle angle (N-S-Ar) was significant higher in child 4 in both evaluations and the lower gonial angle (N-Go-Me) in children 2 and 3 showed significant difference to the standard in both evaluations. A linear measure, posterior facial height (S-Go) in children 3, 4 and 5, also showed significative difference in both evaluations.

Table 1. Demographic characteristics and enzyme replacement (ERT) therapy status (n=8)

Patients	**1**♀	**2**♀	**3** ♂	**4**♀	**5** ♂	**6** ♂	**7**♀	**8**♀	**Mean±SD**
Age (year)	15	10.11	9.11	10.1	7.5	8.10	13.5	10.10	10.1±2.57
Type of Disease	I	I	III	I	I	I	I	I	-
ERT Administration									
Period (years)	10	9	8	7	3	3	3	3	5.75±3.06
Status	UID	UID	UID	ID	UID	UID	ID	ID	-

Table 2. Number (n) and percentage (%) of patients classified into the growth groups for the body variables

Percentile	BMI n(%)		Weight n(%)		Height n(%)	
	1st	2nd	1st	2nd	1st	2nd
less than 5th	1 (14.28)	1 (14.28)	3 (42.85)	2 (28.58)	2 (28.58)	1 (14.28)
5th to 25th	5 (71.42)	4 (57.15)	2 (28.58)	3 (42.85)	2 (28.58)	3 (42.85)
Greater than 25th	1 (14.28)	2 (28.58)	2 (28.58)	2 (28.58)	3 (42.85)	3 (42.85)

BMI – body mass index

n – Number of patients

Table 3. Individual values for BMI (kg/m^2), weight (Kg) and height (m) at the first and second evaluation

	BMI				Weight				Height			
	1st		2nd		1st		2nd		1st		2nd	
Children	Perc.	kg/m^2	Perc	kg/m^2	Perc	Kg	Perc	Kg	Perc	m	Perc	m
1♀	P25-P50	18.71	P25-P50	19.73	<P5	32.6	<P5	35.95	<P5	1.32	<P5	1.35
2♀	P10	14.84	P10-P25	16.15	P10-P25	31.2	P25	37.8	P50	1.45	P50	1.53
3♂	P10-25	15.19	<P5	15.38	<P5	23.35	<P5	26	<P5	1.24	P10	1.3
4♀	P25	15.67	P10	15.15	P50	28.55	P10	31.85	P25	1.35	P50	1.45
5♂	P5	13.77	P10	14.34	P5-P10	20.5	P50	23.5	P25-P50	1.22	P10	1.28
6♂	P25	15.1	P50-P75	16.67	P50	28.75	P75-P90	35.05	P90	1.38	P50	1.45
7♀	P5-P10	15.71	P10	16.84	P5	35.35	P10	40.45	P10	1.5	P10-25	1.55
8♀	-	-	-	-	-	-	-	-	-	-	-	-
Mean±SD												

Perc. = Percentile Chronol. = Chronologic

Table 4. Individual values for chronologic and bone age (months) at the first and second evaluation

Children	1st			2nd		
	Chronologic	**Bone**	***Difference***	**Chronologic**	**Bone**	***Difference***
1	180	-	-	192	162	*30*
2	131	94	*37*	143	132	*11*
3♂	119	96	*23*	131	120	*11*
4	121	120	*1*	133	120	*13*
5♂	89	60	*29*	101	72	*29*
6♂	106	108	*-2*	118	108	*10*
7	161	156	*5*	173	162	*11*
8	130	132	*-2*	142	-	-
Mean	130	116	*13*	141.6[A]	125.14[B]	*16*
SD	(29.08)	(33.96)	*(16.28)*	(29.08)	(31.45)	(8.98)

Table 5. Individual values of cephalometric linear and angular values (mm) at first and second evaluations

	1♀		2♀		3♂		4♀		5♂		6♂		7♀		8♀	
	1st	2nd	1st	2nd	1st	2nd	1st	2nd	1st	2nd	1st	2nd	1st	2nd	1st	2nd
S-N	70	-	65	71	63	63	70	73	72	73	73	76	71	73	69	-
Go-Me	64	-	62	63	60	66	68	72	65	67	72	75	75	79	66	-
S-Ar	30	-	30	33	33	34	30	32	28	31	34	36	33	34	30	-
Ar- Go	54	-	47	51	36	38	40	47	34	39	40	42	48	50	41	-
S- Go	74	-	74	79	65	68	66	73	59	66	71	74	74	78	61	-
N-Me	111	-	112	120	110	116	110	116	104	110	116	118	117	120	105	-
N-S-Ar (°)	135	-	125	130	128	127	131	132	123	122	125	123	129	130	130	-
S-Ar-Go (°)	120	-	145	140	146	147	142	140	146	142	144	143	135	137	135	-
Ar-Go-Me (°)	144	-	128	127	130	129	125	124	130	134	127	128	132	127	131	-
S+Ar+Go (°)	399	-	398	397	404	403	398	396	399	398	379	394	396	394	396	-
Ar-Go-N (°)	64	-	50	51	51	48	53	53	58	59	54	56	57	54	59	-
N-Go-Me (°)	80	-	78	76	79	81	72	71	72	75	73	72	75	73	73	-
% de Jarabak	66.60%	-	66.0%	66.0%	59.09%	58.60%	66.0%	63.0%	56.73%	60.0%	61.20%	62.70%	63.79%	65.0%	58.09%	-
Facial pattern	Hypodivergent		Hypodivergent		Neutral		Hypodivergent		Hyperdivergent		Neutral		Hypodivergent		Hyperdivergent	

Discussion

Our data confirmed the observation reported by other investigators[6,10,16-19] that growth delay during childhood is a prominent clinical feature of Gaucher disease Type I and III.

Growth was less than the 5th percentile and from the 5th to 25th percentiles of height for gender and age in 2 children each percentile range, and there were 3 children greater than the 25th percentile. Grigorescu Sido et al. (2007)[20] reported that two of 6 GD patients had short stature before enzyme treatment. Drelichman et al. (2007)[21] evaluating 5 children with GD, related that 4 had growth retardation before receiving ERT.

There was a slight improve at the second evaluation for the group less than 5th percentile and 5th to 25th percentiles, since the percentage of the first group decreased for 14.3% and of the second, increased for 42.8%, although the group greater than the 25th percentile sustained 42.8% of children. Also, considering the 5th percentile, 1 patient (14.28%) for BMI and 3 patients (42.85%) for weight were below.

Linear growth retardation is common in the pediatric nonneuronopathic (Type I) GD population; with more than 30% of all children below the fifth percentile for height at the time of diagnosis.[13] Andersson et al. (2008)[10] found that 42% of their patients were below the 5th percentile before the ERT.

The mechanism whereby growth is delayed in Gaucher disease Type I is not clear, but it can be assumed that the underlying metabolic disorder is the main factor, as in other chronic metabolic diseases.[11,22]

Another possible explanation for the poor growth found in this group could be the early manifestations of the disease and maybe a more severe course. Since the literature affirms that the disease is progressive and earlier onset usually correlates with a more severe disease course.[23]

In fact, our results showed that 28.6% of the children were below the 5th percentile for height, although all of them had already initiated enzyme replacement treatment. Previous reports suggested that enzyme replacement therapy significantly improves growth in children with GD.[6]

The data of Kauli et al. (2000)[12] confirm that ERT normalizes growth during childhood, as already reported.[6,16,17] They also observed that the benefit of ERT on growth is sustained and progressive — the longer the treatment period, the greater the improvement.[12]

The goal of treatment is to normalize growth and achieve normal peak skeletal mass within 3 years of initiating enzyme replacement therapy,[24] although it seemed that in our children the objective was not achieved since the average of replacement in our patients was 5.75 years, and they still shown growth retardation.

Indeed, Andersson et al. (2008)[10] affirmed that after 8 years of ERT, the patients' median height was not substantially different from the median for the normal population; perhaps with the prolongation of the treatment our children could reach the normal population median height. In the study of Schaison et al., (2002)[25] with paediatric patient population, ERT resulted in significant weight gain and increase of head circumference but there was no change in height. However, the follow-up of 2 years of this last study might be not enough to observe the benefits of the ERT, what could also had happened to our study, justifying a long term follow-up on grown disorders for this group of patient.

As was previously described, Gaucher children can present decrease in bone maturation rate leading to a bone age retardation of 2–4 years.[12] Carter et al. (1998)[26] also suggested some degree of delayed bone age. Corroborating the literature, our patients showed some difference between the chronologic and bone age, 1 year and 1 month in median at the first evaluation and 1 year and 4 months at the second. The difference found on the second evaluation might suggest that the bone involvement in our children became worse during the period of evaluation even under ERT.

For that reason, the cephalometric analyses were done based at the bone age. Despite of the growth impairment presented for our patients, in general, our results showed that the linear craniofacial growth of these patients is not deficient, even though the growth pattern presented some alterations. This could be due to the type of bone, since the most commonly involved bones are the femur and

vertebrae that are long bones. It can be observed that all of them showed higher values of craniofacial growth determining a significant difference confronting with the standards stated by Jarabak, since the standard growth of each linear value is in median 1mm. Constant follow-up of these children is essential, considering that the growth is a dynamic process and could pass by period of acceleration or reduction.

The most obtained cephalometric measurements were correspondent to the standards stated by Jarabak.[15] However, the % Jarabak's[15] was the most affected parameter at the first and second evaluation, although it was not significative. This variable demonstrated the growth direction of the maxilla and mandible; 4 patients showed higher values presenting a counter-clockwise growth, 2 patient showed lower value promoting an opposite sense of rotation growth, and 2 had neutral growth.

The N-S-Ar(°) [saddle angle] value was significant higher in children 1 and 4 what could determined retrognatism mandibular. The increased value of the lower gonial angle (N-Go-Me) indicates a bigger mandibular inclination downward, and this angle was altered in children 1, 2 and 3, although their growth tendency was different, showing compensation between the craniofacial structures. As well, the posterior facial height (S-Go) was also altered, what could reduce the % Jarabak's[15], leading to a hyperdivergent growth tendency, however just patient 5 confirmed this possibility. It is important to realize that, regarding craniofacial growth, we can not evaluated one measure isolated, since the structures are linked and present mechanism of compensation to determine a more proportional growth. Mandibular corpus (Go-Me) showed significant difference only at the first evaluation showing improvement of these structure after one year, in opposition, posterior cranial base (S-Ar) became worse during these period, in children 6, soliciting attentive follow-up.

Also the Ar-Go-N(°) [upper gonial angle] was the most affected angle, although it was no statistically different, showing different values from the standard in 6 patients (75%) at the first evaluation, and in 4 patients (66.7%) at the second. This angle describes the inclination of the ramus and indicates the growth direction

of the mandible. The patients who showed a higher value will have disposition for a horizontal growth, while the lower values predispose to a vertical growth direction. Based at this angle, it seemed that just 2 patients will have a predisposition for normal growth. Indeed the results of craniofacial growth pattern showed that 2 children (25%) had a tendency of neutral growth and the others or had a hyperdivergent (25%) or hypodivergent (50%) tendency of growth.

Patients 3, 4, 5 and 6 showed improved of some measures that reached the standard, i.e., Go-Me (mandibular corpus) determining better mandible growth, posterior facial height (S-Go) and anterior facial height (N-Me), determining better association between them. However, after one year, all the patients had craniofacial measures divergent of the standard and need a long follow up.

Crossing the lateral radiographies of the first and second evaluation, we observed that patient 2, 3 and 6 maintained the growth pattern between both evaluations that is in line with what was predicted. On the other hand, patient 4 had a tendency of hypodivergent growth and patient 5 had a tendency of hyperdivergent, however in the one year follow-up both children presented neutral growth. The other children 1 and 8 were not evaluated after one year.

It suggested that children with GD may have some measures diferent from the normal parameters but it seems that this variation was into normality requiring continuous follow up. Also we proposed that this area warrants further investigation.

Acknowlodgments

The authors thank Mr. José Luiz Cintra Junqueira and Ms. Saori Okajima Nakamoto for the indispensable support, offering free radiographs exams, Ms. Raquel Suzana Foglio, for English review and Mr. Roberto Zulli for statistics analysis.

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Conclusão Geral

- Crianças com doença de Gaucher apresentaram boa saúde oral, erupção precoce de alguns grupos dentários, importantes alterações nos maxilares e diferenças nos valores da análise cefalométrica comparado ao padrão, requerendo acompanhamento constante.

- Adultos com doença de Gaucher mostraram pobre saúde oral e importantes alterações nos maxilares. Mesmo na ausência de infecção ou dor, exames radiográficos devem ser solicitados periodicamente como procedimento de rotina para investigar lesões ósseas nos maxilares.

- A avaliação do impacto das condições orais sobre a qualidade de vida deve ser parte da avaliação da saúde oral uma vez que indicadores clínicos isolados não podem descrever a satisfação ou os sintomas orais dos pacientes ou sua habilidade em realizar atividades diárias.

- Embora as crianças não tenham apresentado pobre saúde oral, algumas condições orais interferiram na qualidade de vida. Por outro lado, os adultos mostraram pobre saúde oral e consequentemente prejudicada qualidade de vida.

- Pacientes com doença de Gaucher devem ser advertidos sobre a importância do cuidado oral, devendo ser chamados para consultas regulares; com a ajuda dessas medidas, os níveis da qualidade de vida relacionada à saúde oral devem ser aumentados.

- É necessária mais investigação sobre a manifestação da Doença de Gaucher. Estudos futuros devem abranger maior número de pacientes e avaliação multicêntrica.

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ANEXO 1

QUESTIONÁRIO DE SAÚDE BUCAL INFANTIL
8-10 anos

Olá,

Obrigado por nos ajudar com nosso estudo!

Estamos fazendo este estudo para entender melhor as coisas que podem acontecer com as crianças por causa de seus **dentes e sua boca.**

POR FAVOR, LEMBRE-SE:

☺ Não escreva seu nome no questionário.

☺ Isto **não é uma prova** e não existem respostas certas ou erradas.

☺ Responda o mais **honestamente** que puder.

☺ **Não converse com ninguém** sobre as perguntas enquanto as estiver respondendo.

☺ **Ninguém** que Você conhece verá suas respostas.

☺ Leia cada pergunta **cuidadosamente** e pense sobre as coisas que aconteceram com Você nas últimas **4 semanas**.

☺ Antes de responder, pergunte a Você mesmo: "**Isto acontece comigo por causa dos meus dentes ou da minha boca?"**

☺ Coloque um **X** na caixa (□) à frente da resposta que for **melhor** para Você.

QUESTIONÁRIO DE SAÚDE BUCAL INFANTIL 8-10 anos

Data de hoje: _____/_____/_____

Dia Mês Ano

PRIMEIRO, RESPONDA ALGUMAS PERGUNTAS SOBRE VOCÊ

1. Você é um menino ou uma menina?

( ) Menino

( ) Menina

2. Quando você nasceu? _____/_____/_____ Idade _____

Dia Mês Ano

3. Quando você pensa em seus dentes ou boca, Você acha que eles são:

( ) Muito bons

( ) Bons

( ) Mais ou menos

( ) Ruins

4. Quanto seus dentes ou boca lhe incomodam no dia-a-dia?

( ) Nem um pouco

( ) Só um pouquinho

( ) Mais ou menos

( ) Muito

AGORA RESPONDA ALGUMAS PERGUNTAS SOBRE O QUE ACONTECEU COM SEUS DENTES E SUA BOCA **NAS ÚLTIMAS 4 SEMANAS**

5. Você teve dor em seus dentes ou em sua boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

6. Você teve locais doloridos em sua boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

7. Você teve dor em seus dentes quando tomou bebidas geladas ou comeu alimentos quentes?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

8. Você sentiu alimento grudado em seus dentes?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

9. Você teve mau hálito?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

10. Você precisou de mais tempo que os outros para comer seus alimentos devido aos seus dentes ou sua boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

11. Você teve dificuldade para morder ou mastigar alimentos duros, como maçã, milho verde na espiga ou bife devido aos seus dentes ou sua boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

12. Você teve dificuldade para comer o que gostaria devido a problemas nos seus dentes ou na sua boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

13. Você teve dificuldade para dizer algumas palavras devido a problemas aos seus dentes ou sua boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

14. Você teve problemas enquanto dormia devido aos seus dentes ou sua boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

AGORA RESPONDA ALGUMAS PERGUNTAS SOBRE O QUE ACONTECEU COM SEUS SENTIMENTOS NAS ÚLTIMAS 4 SEMANAS

15. Você ficou triste devido aos seus dentes ou sua boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

16. Você se sentiu aborrecido devido aos seus dentes ou sua boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

17. Você ficou tímido devido aos seus dentes ou sua boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

18. Você ficou preocupado com o que as outras pessoas pensam sobre seus dentes ou sua boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

19. Você ficou preocupado porque Você não é tão bonito quanto os outros por causa de seus dentes ou sua boca nas últimas 4 semanas?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

RESPONDA ALGUMAS PERGUNTAS SOBRE O QUE ACONTECEU NA SUA ESCOLA **NAS ÚLTIMAS 4 SEMANAS**

20. Você faltou à escola devido a problemas nos seus dentes ou na sua boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

21. Você teve dificuldade para fazer sua lição de casa devido a problemas com seus dentes ou sua boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

22. Você teve dificuldade para prestar atenção na aula devido a problemas nos seus dentes ou na sua boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

23. Você não quis falar ou ler em voz alta na aula devido a problemas nos seus dentes ou na sua boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

RESPONDA ALGUMAS PERGUNTAS SOBRE VOCÊ JUNTO COM OUTRAS PESSOAS QUE ACONTECERAM NAS ÚLTIMAS 4 SEMANAS

24. Você não quis sorrir ou rir quando estava com outras crianças devido a problemas nos seus dentes ou na sua boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

25. Você não quis conversar com outras crianças devido aos problemas com seus dentes ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

26. Você não quis ficar perto de outras crianças devido aos seus dentes ou sua boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

27. Você não quis participar de esportes e ir ao parque devido aos seus dentes ou sua boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

28. Outras crianças tiraram sarro de você ou lhe apelidaram devido aos seus dentes ou sua boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

29. Outras crianças fizeram perguntas sobre seus dentes ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

PRONTO, ACABOU!

OBRIGADA POR SUA AJUDA

ANEXO 2

QUESTIONÁRIO DE SAÚDE BUCAL DA CRIANÇA
11-14 anos

Olá,

Obrigado por concordar em nos ajudar com nosso estudo!

Este estudo está sendo feito para que haja maior entendimento sobre os problemas que as crianças podem ter por causa de seus **dentes, boca, lábios e maxilares**. Respondendo às perguntas, você nos ajudará a aprender mais sobre as experiências dos jovens.

POR FAVOR, LEMBRE-SE:

☺ Não escreva seu nome no questionário.

☺ Isto **não é uma prova** e não existem respostas certas ou erradas.

☺ Responda o mais **honestamente** que puder.

☺ **Não converse com ninguém** sobre as perguntas enquanto as estiver respondendo. Suas respostas são **pessoais**; ninguém que você conhece verá suas respostas.

☺ Leia cada pergunta **cuidadosamente** e pense sobre as coisas que aconteceram com você **nos últimos 3 meses** enquanto estiver respondendo.

☺ Antes de responder, pergunte a você mesmo: **"Isto acontece comigo por causa de problemas com meus dentes, lábios, boca ou maxilares?"**

☺ Coloque um **X** na caixa (□) à frente da resposta que for **melhor** para Você.

QUESTIONÁRIO DE SAÚDE BUCAL INFANTIL 11-14 anos

Data de hoje: _____/_____/_____
DIA MÊS ANO

PRIMEIRO, RESPONDA ALGUMAS PERGUNTAS SOBRE VOCÊ

1. Você é um menino ou uma menina?

( ) Menino

( ) Menina

2. Quando você nasceu? _____/_____/_____
DIA MÊS ANO

3. Você acha que a saúde de seus dentes, lábios, maxilares e boca é:

( ) Excelente

( ) Muito boa

( ) Boa

( ) Mais ou menos

( ) Ruim

4. Quanto a condição de seus dentes, lábios, maxilares ou boca afetam sua vida no geral?

( ) Nem um pouco

( ) Só um pouquinho

( ) Mais ou menos

( ) Muito

( ) Muitíssimo

PERGUNTAS SOBRE PROBLEMAS BUCAIS

NOS ÚLTIMOS 3 MESES...

5. Você teve dor em seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

6. Você teve sangramento na gengiva?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

7. Você teve feridas em sua boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

8. Você teve mau hálito?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

9. Você teve alimento grudado dentro ou entre dentes?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

10. Você teve alimento preso no céu da boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

11. Você respirou pela boca devido aos seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

12. Você levou mais tempo que os outros para comer uma refeição devido aos seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

13. Você teve problemas enquanto dormia devido aos seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

14. Você teve dificuldade para morder ou mastigar alimentos como maçã, milho verde na espiga ou bife devido aos seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

15. Você teve dificuldade para abrir bastante a boca devido aos seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

16. Você teve dificuldade para dizer alguma palavra devido aos seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

17. Você teve dificuldade para comer comidas que Você gostaria de comer devido aos seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

18. Você teve dificuldade para beber com canudinho devido aos seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

19. Você teve dificuldade para beber ou comer alimentos quentes ou gelados devido aos seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

PERGUNTAS SOBRE SENTIMENTOS

NOS ÚLTIMOS 3 MESES...

20. Você se sentiu irritado ou frustrado devido aos seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

21. Você se sentiu inseguro devido aos seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

22. Você se sentiu tímido ou envergonhado devido aos seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

23. Você ficou preocupado com o que os outros pensam sobre seus dentes, lábios, boca ou maxilares?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

24. Você se preocupou por não ter tão boa aparência como os outros devido aos seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

25. Você ficou chateado devido aos seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

26. Você se sentiu nervoso ou com medo devido aos seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

27. Você se preocupou por não ser tão saudável quanto os outros devido aos seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

( ) Não entendi

28. Você se preocupou por ser diferente das outras pessoas devido aos seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

PERGUNTAS SOBRE A ESCOLA

NOS ÚLTIMOS 3 MESES...

29. Você faltou na escola por causa de dor de dente, consultas ao dentista ou cirurgias?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

30. Você teve dificuldade para prestar atenção na aula devido aos seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

31. Você teve dificuldade para fazer sua lição de casa devido aos seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

32. Você não quis falar ou ler em voz alta na aula devido aos seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

PERGUNTAS SOBRE SUAS ATIVIDADES NO TEMPO LIVRE E SOBRE ESTAR COM OUTRAS PESSOAS

NOS ÚLTIMOS 3 MESES...

33. Você não quis participar de atividades como esportes, clubes, teatro, música, viagens escolares devido aos seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

34. Você não quis conversar com outras crianças devido aos seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

35. Você não quis sorrir ou rir quando estava perto de outras crianças devido aos seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

36. Você teve dificuldade para tocar um instrumento musical como flauta ou gaita devido aos seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

37. Você não quis passar tempo com outras crianças devido aos seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

38. Você discutiu com outras crianças ou com sua família devido aos seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

39. Outras crianças caçoaram (tiraram sarro) de Você devido aos seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

40. Outras crianças fizeram Você se sentir excluído devido aos seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

41. Outras crianças fizeram perguntas sobre seus dentes, lábios, maxilares ou boca?

( ) Nunca

( ) Uma ou duas vezes

( ) Algumas vezes

( ) Várias vezes

( ) Todos os dias ou quase todos os dias

PRONTO, ACABOU!

OBRIGADO POR NOS AJUDAR!

ANEXO 3

Adultos

Instruções

Marque a resposta que indique com qual freqüência cada um dos problemas ocorreu com você no último ano.

1. Você teve dificuldade em mastigar qualquer alimento por causa de problemas com seus dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

2. Você teve problemas em pronunciar alguma palavra por causa de problemas com seus dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

3. Você notou que algum dente parece estar com problemas?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

4. Você sentiu que a sua aparência foi afetada por causa de problemas com seus dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

5. Você sentiu que seu hálito estava mal cheiroso por causa de problemas com seus dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

6. Você sentiu que o seu paladar piorou por causa de problemas nos dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

7. Você teve alimentos presos nos dentes ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

8. Você sentiu que a sua digestão piorou por causa de problemas com seus dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

9. Você teve dores na sua boca?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

10. Você teve dores nos maxilares?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

11. Você teve dores de cabeça por causa de problemas com seus dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

12. Você teve dentes sensíveis, por exemplo, por causa de alimentos ou bebidas frias ou quentes?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

13. Você teve dor de dente?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

14. Você teve dores na gengiva?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

15. Você achou desconfortável mastigar algum alimento por causa de problemas com seus dentes, boca ou dentadura?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

16. Você teve pontos ou locais doloridos na sua boca?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

17. Você sentiu que as suas dentaduras não estavam bem adaptadas?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

( ) não se aplica

18. Você teve desconforto com as suas dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

( ) não se aplica

19. Você esteve preocupado por causa de problemas dentários?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

20. Você já se sentiu constrangido por causa de seus dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

21. Problemas dentários lhe fizeram sentir triste?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

22. Você se sentiu desconfortável com a aparência dos seus dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

23. Você se sentiu tenso por causa de problemas com seus dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

24. Sua dicção foi prejudicada por causa de problemas com seus dentes, boca ou dentadura?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

25. Alguém compreendeu errado algumas de suas palavras por causa de problemas com seus dentes, boca ou dentadura?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

26. Você notou menos sabor em sua comida por causa de problemas com seus dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

27. Você esteve incapaz de escovar adequadamente seus dentes por causa de problemas com seus dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

28. Você teve de evitar algum tipo de alimento por causa de problemas com seus dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

29. Sua alimentação ficou prejudicada por causa de problemas com seus dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

30. Você ficou impossibilitado de comer com suas dentaduras por causa de problemas com elas?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

( ) não se aplica

31. Você evitou sorrir por causa de problemas com seus dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

32. Você teve que parar suas refeições por causa de problemas com seus dentes, boca ou dentadura?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

33. O seu sono foi interrompido por causa de problemas com seus dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

34. Você ficou chateado por causa de problemas com seus dentes, boca ou dentadura?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

35. Você teve dificuldade de relaxar por causa de problemas com seus dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

36. Você ficou deprimido por causa de problemas com seus dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

37. Sua concentração ficou afetada por causa de problemas com seus dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

38. Você ficou envergonhado por causa de problemas com seus dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

39. Você evitou sair por causa de problemas com seus dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

40. Você foi menos tolerante com seu companheiro (a) ou familiares por causa de problemas com seus dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

41. Você teve problemas em se relacionar com outras pessoas por causa de problemas com seus dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

42. Você ficou um pouco irritado com outras pessoas por causa de problemas com seus dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

43. Você teve dificuldades em fazer suas atividades diárias por causa de problemas com seus dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

44. Você sentiu que a sua saúde geral piorou por causa de problemas com seus dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

45. Você teve alguma perda financeira por causa de problemas com seus dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

46. Você deixou de aproveitar a companhia de outras pessoas por causa problemas com seus dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

47. Você sentiu que a vida em geral ficou pior por causa de problemas com seus dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

48. Você ficou totalmente incapaz de exercer qualquer atividade por causa de problemas com seus dentes, boca ou dentaduras?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

49. Você teve sua capacidade de trabalho reduzida por causa de problemas com seus dentes, boca ou dentadura?

( ) muito freqüente ( ) freqüente ( ) ocasionalmente ( ) quase nunca ( ) nunca

ANEXO 4 – Ficha de avaliação clínica dos índices de saúde oral

Avaliação Dentária

Condições Atuais

0 - hígido
1 - cariado
2 - restaurado com cárie
3 - restaurado sem cárie
4 - ausente por cárie
5 - ausente por outros motivos
6 - pilar de prótese
7 - dente não erupcionado
8 - dente excluído
9 - mancha branca ativa

Tratamento Proposto

0 - nenhum
1 - selante
2 - restauração de 1 face
3 - restauração várias faces
4 - tratamento protético
5 - tratamento endodôntico
6 - extração
7 - outros tratamentos

Tratamento Realizado

0 - nenhum
1 - selante
2 - restauração provisória
3 - rest. com amálgama
4 - rest. com ionômero
5 - rest. com resina foto
6 - endodontia
7 - extração
8 - fluorterapia

C -
P –
O –

			55	54	53	52	51	61	62	63	64	65			
18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38
			85	84	83	82	81	71	72	73	74	75			

ANEXO 4 – Ficha de avaliação clínica dos índices de saúde oral (continuação)

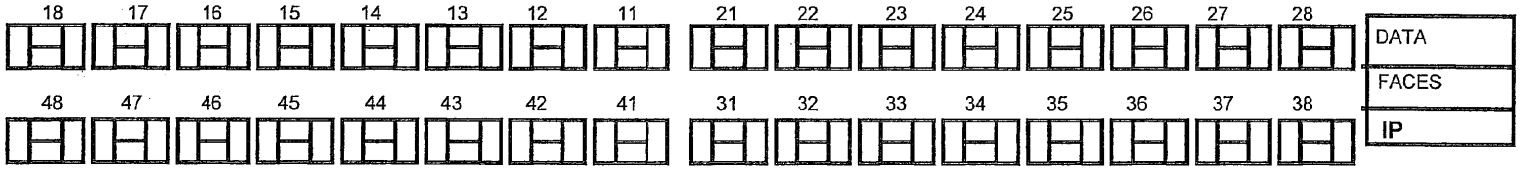
UNIVERSIDADE ESTADUAL DE CAMPINAS

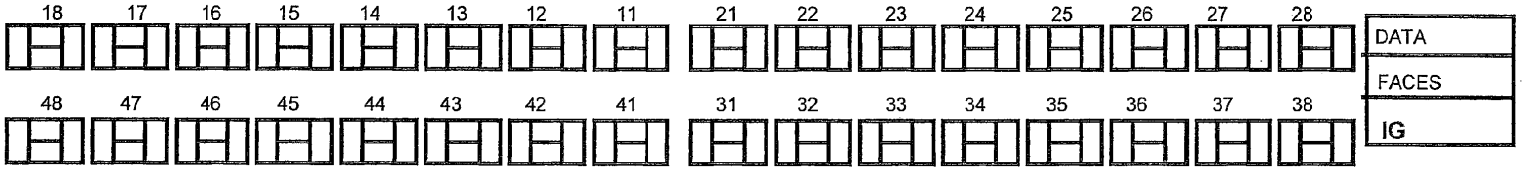
FACULDADE DE ODONTOLOGIA DE PIRACICABA

V / D M / P

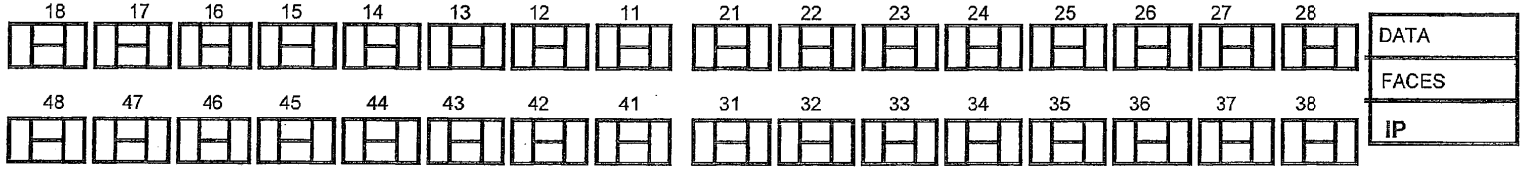
Nome do Paciente: _____ P.G. _____

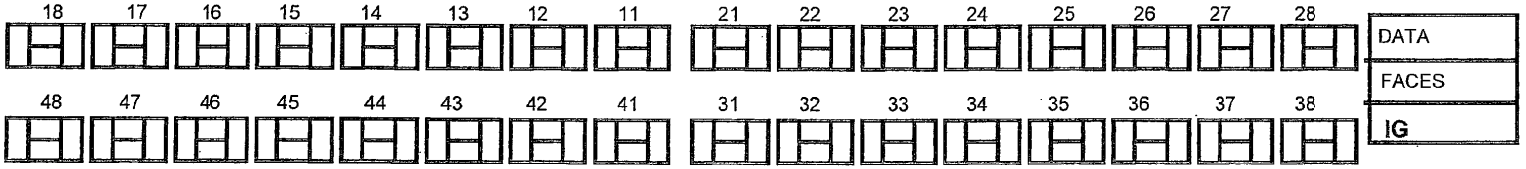
EXAME INICIAL





REAVALIAÇÃO





ANEXO 5 - Resolução CCPG/002/06 a qual dispõe a respeito do formato das teses de mestrado e doutorado aprovados pela UNICAMP (Parte I)

INFORMAÇÃO CCPG/OO2/06[6]

Tendo em vista a necessidade de revisão da regulamentação das normas sobre o formato e a impressão das dissertações de mestrado e teses de doutorado e com base no entendimento exarado no Parecer PG n° 1985/96, que trata da possibilidade do formato alternativo ao já estabelecido, a CCPG resolve:

Artigo 1º - O formato padrão das dissertações e teses de mestrado e doutorado da UNICAMP deverão obrigatoriamente conter:

I. Capa com formato único ou em formato alternativo que deverá conter informações relativas ao nível (mestrado ou doutorado) e à Unidade de defesa, fazendo referência à Universidade Estadual de Campinas, sendo o projeto gráfico das capas definido pela PRPG.
II. Primeira folha interna dando visibilidade à Universidade, a Unidade de defesa, ao nome do autor, ao título do trabalho, ao número de volumes (quando houver mais de um), ao nível (mestrado ou doutorado), a área de concentração, ao nome do orientador e co-orientador, ao local (cidade) e ao ano de depósito. No seu verso deve constar a ficha catalográfica.
III. Folha de aprovação, dando visibilidade à Comissão Julgadora com as respectivas assinaturas.
IV. Resumo em português e em inglês (ambos com no máximo 500 palavras).
V. Sumário.
VI. Corpo da dissertação ou tese dividido em tópicos estruturados de modo característico à área de conhecimento.
VII. Referências, formatadas segundo normas de referenciamento definidas pela CPG da Unidade ou por critério do orientador.
VIII. Todas as páginas deverão, obrigatoriamente, ser numeradas, inclusive páginas iniciais, divisões de capítulos, encartes, anexos, etc... As páginas iniciais poderão ser numeradas utilizando-se algarismos romanos em sua forma minúscula.
IX. Todas as páginas com numeração "impar" serão impressas como "frente" e todas as páginas com numeração "par" serão impressas como "verso".

§ 1º - A critério do autor e do orientador poderão ser incluídos: dedicatória; agradecimento; epígrafe; lista de: ilustrações, tabelas, abreviaturas e siglas, símbolos; glossário; apêndice; anexos.

§ 2º - A dissertação ou tese deverá ser apresentada na língua portuguesa, com exceção da possibilidade permitida no artigo 2° desta Informação.

§ 3º - As dissertações e teses cujo conteúdo versar sobre pesquisa envolvendo seres humanos, animais ou biossegurança, deverão apresentar anexos os respectivos documentos de aprovação.

Artigo 2º - A critério do orientador e com aprovação da CPG da Unidade, os capítulos e os apêndices poderão conter cópias de artigos de autoria ou de co-autoria do candidato, já publicados ou submetidos para publicação em revistas científicas ou anais de congressos sujeitos a arbitragem, escritos no idioma exigido pelo veículo de divulgação.

[6] Disponível em: http://www.prpg.unicamp.br/ccpg_inf002_06.pdf

ANEXO 5 - Resolução CCPG/002/06 a qual dispõe a respeito do formato das teses de mestrado e doutorado aprovados pela UNICAMP (Parte II)

§ único - O orientador e o candidato deverão verificar junto às editoras a possibilidade de inclusão dos artigos na dissertação ou tese, em atendimento à legislação que rege o direito autoral, obtendo, se necessária, a competente autorização, deverão assinar declaração de que não estão infringindo o direito autoral transferido à editora.

Artigo 3º - Dependendo da área do conhecimento, a critério do orientador e com aprovação da CPG da Unidade, a dissertação ou tese poderá ser apresentada em formato alternativo, desde que observados os incisos I, II, III IV, V e VII do artigo 1º.

Artigo 4º - Para impressão, na gráfica da Unicamp, dos exemplares definitivos de dissertações e teses defendidas, deverão ser adotados os seguintes procedimentos:

§ 1º - A solicitação para impressão dos exemplares de dissertações e teses poderá ser encaminhada à gráfica da Unicamp pelas Unidades, que se responsabilizarão pelo pagamento correspondente.

§ 2º - Um original da dissertação ou tese, em versão definitiva, impresso em folha tamanho carta, em uma só face, deve ser encaminhado à gráfica da Unicamp acompanhado do formulário "Requisição de Serviços Gráficos", onde conste o número de exemplares solicitados.

§ 3º - A gráfica da Unicamp imprimirá os exemplares solicitados com capa padrão. Os exemplares solicitados serão encaminhados à Unidade em, no máximo, cinco dias úteis.

§ 4º - No formulário "Requisição de Serviços Gráficos" deverão estar indicadas as páginas cuja reprodução deva ser feita no padrão "cores" ou "foto", ficando entendido que as demais páginas devam ser reproduzidas no padrão preto/branco comum.

§ 5º - As dissertações e teses serão reproduzidas no padrão frente e verso, exceção feita às páginas iniciais e divisões de capítulos; dissertações e teses com até 100 páginas serão reproduzidas no padrão apenas frente, exceção feita à página que contém a ficha catalográfica.

§ 6º - As páginas fornecidas para inserção deverão ser impressas em sua forma definitiva, ou seja, apenas frente ou frente/verso.

§ 7º - O custo, em reais, de cada exemplar produzido pela gráfica será definido pela Administração Superior da Universidade.

Artigo 5º - É obrigatória a entrega de dois exemplares para homologação.

Artigo 6º - Esta Informação entrará em vigor na data de sua publicação, ficando revogadas as disposições em contrário, principalmente as Informações CCPG 001 e 002/98 e CCPG/001/00.

Campinas, 13 de setembro de 2006

Profa. Dra. Teresa Dib Zambon Atvars
Presidente
Comissão Central de Pós-Graduação

ANEXO 6 - Certificado do Comitê de Ética em Pesquisa

CEP, 21/01/07.
(Grupo III)

PARECER CEP: N° 757/2007 (Este n° deve ser citado nas correspondências referente a este projeto)
CAAE: 0547.0.146.000-07

I - IDENTIFICAÇÃO:

PROJETO: **"AVALIAÇÃO CRANIOFACIAL, CONDIÇÕES BUCAIS E QUALIDADE DE VIDA EM INDIVÍDUOS COM DOENÇA DE GAUCHER".**
PESQUISADOR RESPONSÁVEL: Flávia Riqueto Gambareli
INSTITUIÇÃO: Centro de Hematologia e Hemoterapia/Hemocentro
APRESENTAÇÃO AO CEP: 10/10/2007
APRESENTAR RELATÓRIO EM: 27/11/08 (O formulário encontra-se no *site* acima)

II - OBJETIVOS

Avaliar em indivíduos portadores de DG: as características morfológicas e funcionais das estruturas componentes do sistema mastigatório pelo exame clínico; seqüência e cronologia da erupção dentária.

III - SUMÁRIO

Serão adultos e crianças de ambos os sexos, na faixa etária de 8 a 14 anos e 25 a 60 anos respectivamente, diagnosticados com doença de Gaucher, os quais estão em tratamento no Hemocentro da UNICAMP. A responsável pela pesquisa irá convidar os voluntários pessoalmente de forma verbal. Os voluntários terão atendimento odontológico durante a realização da pesquisa no consultório odontológico do Hemocentro - UNICAMP. Serão realizadas radiografias panorâmicas para avaliar as condições orais, e à telerradiografias para avaliar o padrão facial através de análise cefalométrica, com propósito de pesquisa e para diagnóstico preciso. Estas radiografias serão realizadas gratuitamente na Clínica de Radiologia IRO. Além disso, também serão submetidos à análise da idade óssea através de radiografias da mão e do punho esquerdo nesses mesmos intervalos. Será aplicado um Questionário de Qualidade de Vida e Saúde Bucal. Este Questionário abrange escalas que avaliam os sintomas orais, limitações funcionais, bem-estar emocional e bem-estar social. Os questionários serão auto-administrados, ou seja, cada criança, responderá este questionário referente à sua faixa etária.

IV - COMENTÁRIOS DOS RELATORES

O projeto encontra-se adequado a Resolução CNS/MS 196/96 e complementares, bem como o Termo de Consentimento Livre e Esclarecido.

Comitê de Ética em Pesquisa - UNICAMP
Rua: Tessália Vieira de Camargo, 126
Caixa Postal 6111
13084-971 Campinas – SP

FONE (019) 3521-8936
FAX (019) 3521-7187
cep@fcm.unicamp.br

V - PARECER DO CEP

O Comitê de Ética em Pesquisa da Faculdade de Ciências Médicas da UNICAMP, após acatar os pareceres dos membros-relatores previamente designados para o presente caso e atendendo todos os dispositivos das Resoluções 196/96 e complementares, resolve aprovar sem restrições o Protocolo de Pesquisa, bem como ter aprovado o Termo do Consentimento Livre e Esclarecido, assim como todos os anexos incluídos na Pesquisa supracitada. O conteúdo e as conclusões aqui apresentados são de responsabilidade exclusiva do CEP/FCM/UNICAMP e não representam a opinião da Universidade Estadual de Campinas nem a comprometem.

VI - INFORMAÇÕES COMPLEMENTARES

O sujeito da pesquisa tem a liberdade de recusar-se a participar ou de retirar seu consentimento em qualquer fase da pesquisa, sem penalização alguma e sem prejuízo ao seu cuidado (Res. CNS 196/96 – Item IV.1.f) e deve receber uma cópia do Termo de Consentimento Livre e Esclarecido, na íntegra, por ele assinado (Item IV.2.d).

Pesquisador deve desenvolver a pesquisa conforme delineada no protocolo aprovado e descontinuar o estudo somente após análise das razões da descontinuidade pelo CEP que o aprovou (Res. CNS Item III.1.z), exceto quando perceber risco ou dano não previsto ao sujeito participante ou quando constatar a superioridade do regime oferecido a um dos grupos de pesquisa (Item V.3.).

O CEP deve ser informado de todos os efeitos adversos ou fatos relevantes que alterem o curso normal do estudo (Res. CNS Item V.4.). É papel do pesquisador assegurar medidas imediatas adequadas frente a evento adverso grave ocorrido (mesmo que tenha sido em outro centro) e enviar notificação ao CEP e à Agência Nacional de Vigilância Sanitária – ANVISA – junto com seu posicionamento.

Eventuais modificações ou emendas ao protocolo devem ser apresentadas ao CEP de forma clara e sucinta, identificando a parte do protocolo a ser modificada e suas justificativas. Em caso de projeto do Grupo I ou II apresentados anteriormente à ANVISA, o pesquisador ou patrocinador deve enviá-las também à mesma junto com o parecer aprovatório do CEP, para serem juntadas ao protocolo inicial (Res. 251/97, Item III.2.e)

Relatórios parciais e final devem ser apresentados ao CEP, de acordo com os prazos estabelecidos na Resolução CNS-MS 196/96.

VI - DATA DA REUNIÃO

Homologado na XI Reunião Ordinária do CEP/FCM, em 27 de novembro de 2007.

Profa. Dra. Carmen Silvia Bertuzzo
PRESIDENTE DO COMITÊ DE ÉTICA EM PESQUISA
FCM / UNICAMP

Comitê de Ética em Pesquisa - UNICAMP
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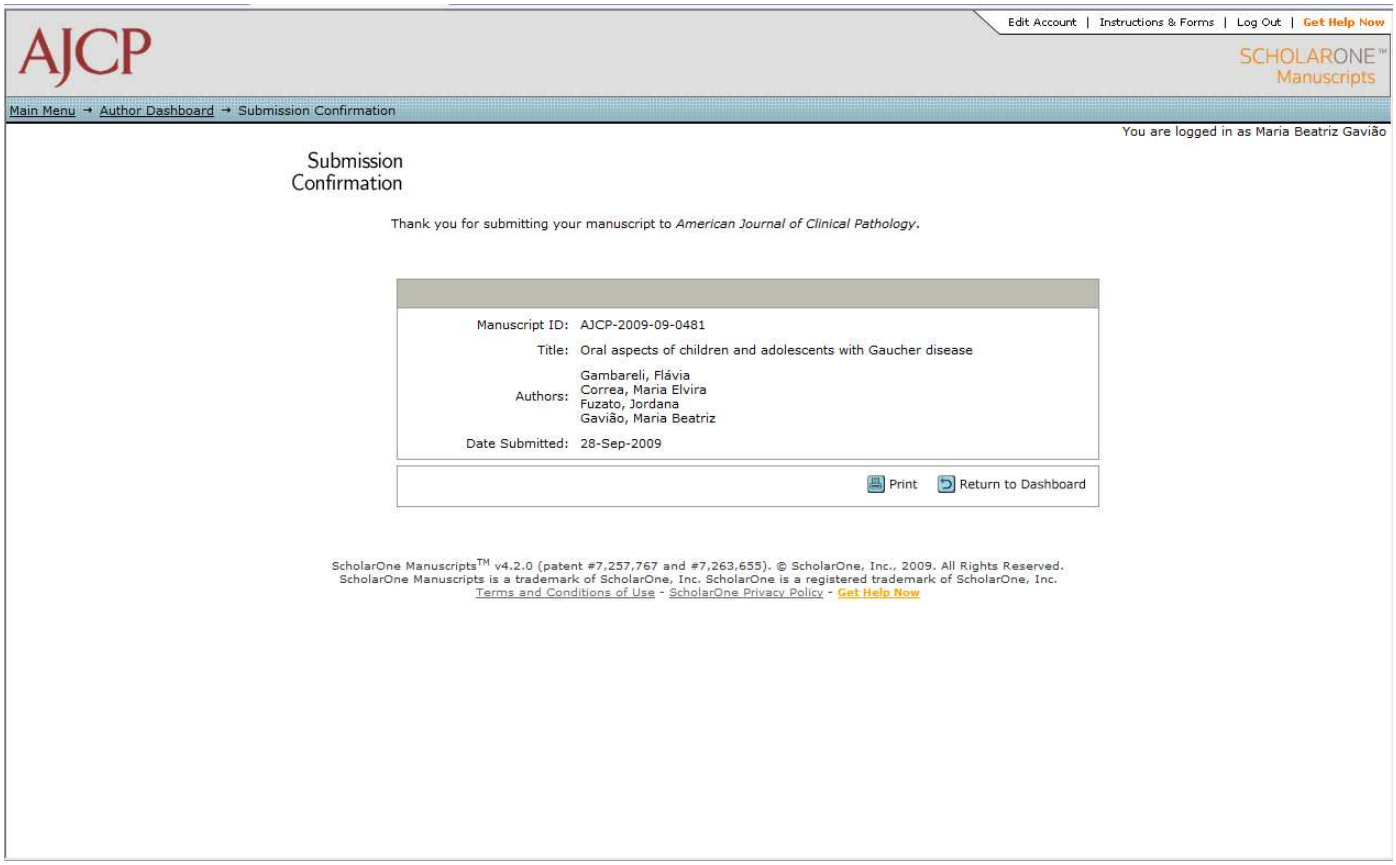
ANEXO 7 - Confirmação de submissão do primeiro artigo apresentado nesta Tese para o periódico *American Journal of Clinical Pathology*.



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Submission Confirmation

Thank you for submitting your manuscript to *American Journal of Clinical Pathology*.

Manuscript ID:	AJCP-2009-09-0481
Title:	Oral aspects of children and adolescents with Gaucher disease
Authors:	Gambareli, Flávia Correa, Maria Elvira Fuzato, Jordana Gavião, Maria Beatriz
Date Submitted:	28-Sep-2009

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