ÉRICA CRISTINA MARCHIORI

NEUROPATHIC PAIN FOLLOWING SAGITTAL SPLIT RAMUS OSTEOTOMY OF THE MANDIBLE: PREVALENCE, RISK FACTORS AND CLINICAL COURSE

DOR NEUROPÁTICA APÓS OSTEOTOMIA SAGITAL DOS RAMOS MANDIBULARES: PREVALÊNCIA, FATORES DE RISCO E CURSO CLÍNICO

Piracicaba
2014

UNIVERSIDADE ESTADUAL DE CAMPINAS
FACULDADE DE ODONTOLOGIA DE PIRACICABA
ÉRICA CRISTINA MARCHIORI

NEUROPATHIC PAIN FOLLOWING SAGITTAL SPLIT RAMUS OSTEOTOMY OF THE MANDIBLE: PREVALENCE, RISK FACTORS AND CLINICAL COURSE

DOR NEUROPÁTICA APÓS OSTEOTOMIA SAGITAL DOS RAMOS MANDIBULARES: PREVALÊNCIA, FATORES DE RISCO E CURSO CLÍNICO

Thesis presented to Piracicaba Dental School / State University of Campinas in partial fulfillment of the requirements for the degree of Doctor in Dental Clinic in the area of Oral and Maxillofacial Surgery.

Tese apresentada à Faculdade de Odontologia de Piracicaba da Universidade Estadual de Campinas, como parte dos requisitos exigidos para obtenção do Título de Doutora em Clínica Odontológica, Área de Concentração em Cirurgia e Traumatologia Buco-maxilo-faciais.

Orientador: Prof. Dr. Roger William Fernandes Moreira

Este exemplar corresponde à versão final da tese defendida por Érica Cristina Marchiori e orientada pelo Prof. Dr. Roger Willian Fernandes Moreira.

Assinatura do Orientador

PIRACICABA

2014

Ficha catalográfica
Universidade Estadual de Campinas
Biblioteca da Faculdade de Odontologia de Piracicaba
Marilene Girello - CRB 8/6159

M332n

Marchiori, Érica Cristina, 1982-
Neuropathic pain following sagittal ramus split osteotomy of the mandible: prevalence, risk factors and clinical course / Érica Cristina Marchiori. – Piracicaba, SP : [s.n.], 2014.

Orientador: Roger William Fernandes Moreira.
Tese (doutorado) – Universidade Estadual de Campinas, Faculdade de Odontologia de Piracicaba.

1. Neuropatia. 2. Dor pós-operatória. 3. Dor orofacial. I. Moreira, Roger William Fernandes,1971-. II. Universidade Estadual de Campinas. Faculdade de Odontologia de Piracicaba. III. Título.

Informações para Biblioteca Digital

Título em outro idioma: Dor neuropática após osteotomia sagital dos ramos mandibulares: prevalência, fatores de risco e curso clínico
Palavras-chave em inglês:
Neuropathy
Postoperative pain
Orofacial pain
Área de concentração: Cirurgia e Traumatologia Buco-Maxilo-Faciais
Titulação: Doutora em Clínica Odontológica
Banca examinadora:
Roger William Fernandes Moreira [Orientador]
Alessandro Costa da Silva
José Rodrigues Laureano Filho
Fábio Ricardo Loureiro Sato
Marcelo Marotta Araújo
Data de defesa: 30-01-2014
Programa de Pós-Graduação: Clínica Odontológica

UNIVERSIDADE ESTADUAL DE CAMPINAS
Faculdade de Odontologia de Piracicaba

A Comissão Julgadora dos trabalhos de Defesa de Tese de Doutorado, em sessão pública realizada em 30 de Janeiro de 2014, considerou a candidata ÉRICA CRISTINA MARCHIORI aprovada.

Prof. Dr. ROGER WILLIAM FERNANDES MOREIRA

Prof. Dr. ALESSANDRO COSTA DA SILVA

Prof. Dr. JOSÉ RODRIGUES LAUREANO FILHO

Prof. Dr. FÁBIO RICARDO LOUREIRO SATO

Prof. Dr. MARCELO MAROTTA ARAÚJO

RESUMO

Objetivos: Avaliar a prevalência, fatores de risco e curso clínico da dor neuropática (DN) após osteotomia sagital dos ramos mandibulares (OSRM) em uma grande amostra de pacientes. **Materiais e Métodos:** Estudo retrospectivo realizado em dois centros médicos do Hospital Kaiser Permanente da Norte da Califórnia, no período de janeiro de 2007 até setembro de 2012, nos pacientes submetidos à OSRM. Fatores demográficos, clínicos e cirúrgicos foram identificados nos prontuários dos pacientes, bem como comorbidades associadas. A prevalência, sinais e sintomas, características da dor e a resposta ao tratamento nos pacientes afetados foram analisados. **Resultados:** Os autores identificaram 1.778 pacientes que foram submetidos à OSRM e, destes, 107 foram excluídos de acordo com critérios pré-definidos. A média de idade dos pacientes (1.671) foi de 24 anos (intervalo interquartil de 19 a 35 anos) e 62,4% eram do gênero feminino. Sete pacientes desenvolveram DN após OSRM, cuja prevalência foi de 0,42%. Todos eles eram mulheres, cuja média de idade foi de 48 anos. Os fatores de risco para o desenvolvimento de DN após OSRM incluíram: idade superior a 40 anos (p = 0.0098), depressão (p = 0.0100), e gênero feminino (p = 0.0497). O inicio da DN ocorreu em uma média de 30 dias de pós-operatório (18 a 56 dias), com média de duração de 52 dias (30 a 69,5 dias). Todos os pacientes responderam favoravelmente à medicações anticonvulsivantes (n = 6) ou antidepressivas tricíclicas (n = 1), além de nenhum dos pacientes ter desenvolvido dor crônica pós-cirúrgica. **Conclusões:** A dor de origem neuropática é uma complicação infrequente após OSRM, acometendo 1 a cada 238 pacientes nesta amostra. A curta duração e a reposta favorável às medicações empregadas reforça esse achado. Os resultados dessa investigação chamam a atenção para a necessidade de futuros estudos prospectivos para melhor compreensão da DN pós-operatória.

Palavras-chave: neuropatia; dor pós-operatória; dor orofacial.

ABSTRACT

Purpose: To estimate the prevalence of, risk factors for, and clinical course of neuropathic pain (NPP) after sagittal split ramus osteotomy (SSRO) of the mandible in a large cohort of patients. **Materials and Methods:** A retrospective cohort of all patients who underwent SSRO at 2 medical centers within Kaiser Permanente Northern California from January 2007 through September 2012 was assembled. Demographic, clinical, and surgical factors were collected from medical records and relevant comorbidities were identified. The prevalence of NPP in the cohort was calculated and the clinical signs, symptoms, temporal characteristics and treatment response in affected patients were noted. **Results:** The authors identified 1.778 patients who underwent SSRO and excluded 107 patients according to predefined criteria. The remaining 1.671 patients had a median age of 24 years (interquartile range from19 to 35 years) and 62.4% were women. Seven patients developed NPP after SSRO, which was an overall prevalence of 0.42%. All patients with NPP in this cohort were women and had a median age of 48 years. The risk factors for developing NPP after this surgery were age over 40 years (p = 0.0098), depression (p = 0.0100), and female gender (p = 0.0497). NPP developed an average of 30 days postoperatively (range, 18 to 56 days) and persisted for a median duration of 52 days (range, 30 to 69.5 days). All patients responded favorably to anticonvulsant (n = 6) or tricyclic (n = 1) medications, and no patients developed chronic postsurgical pain. **Conclusions:** NPP was an infrequent complication after SSRO, occurring in 1 of 238 patients in this cohort. The short duration and positive response to medication are reassuring findings. The results of this investigation highlight the need for prospective studies to further understand the spectrum of postoperative NPP.

Key-words: neuropathy; pain, postoperative; orofacial pain.

SUMÁRIO

Dedico essa dissertação ao homem mais importante da minha vida – ***Flávio Irineu Marchiori***. Meu pai, meu exemplo de dedicação, perseverança e competência. Pessoa honesta, humilde e humana. Pai presente, em todos os momentos da minha vida.

AGRADECIMENTOS

Finalizada essa etapa singular e de extrema importância em minha vida, não poderia deixar de agradecer a todos aqueles que fazem parte da minha história e que me fizeram uma pessoa mais humana e muito mais feliz.

À ***Deus***, por me permitir viver. Por me permitir o fôlego da vida. Por me conceder a honra de ser filha de quem sou, de ser irmã de alguém tão especial, de pertencer à família que pertenço. Por me permitir o dom de viver.

À ***Faculdade de Odontologia de Pernambuco*** – Universidade de Pernambuco, na qual me graduei cirurgiã-dentista e onde tive o privilégio de conhecer e conviver com meus queridos professores, ***Ricardo José de Holanda Vasconcellos, José Rodrigues Laureano Filho e Luiz Carlos Ferreira da Silva***, principais incentivadores no início da minha formação, em especial, em nossa especialidade.

À ***Escola de Bahiana de Medicina e Saúde Pública da Bahia e Hospital geral Roberto Santos*****,** onde iniciei a formação em minha especialidade, me concedendo a honra de conhecer grandes amigos e mestres.

À ***Faculdade de Odontologia de Piracicaba*** – Universidade Estadual de Campinas, pela possibilidade oferecida para minha formação e por toda infra-estrutura disponível aos alunos.

Ao reitor da Universidade Estadual de Campinas, ***José Tadeu Jorge***, e ao diretor da Faculdade de Odontologia de Piracicaba, ***Jacks Jorge Júnior***, pelo excelente trabalho realizado em nossa instituição.

À ***University of the Pacific - Arthur A. Dugoni School of Dentistry***, ***Kaiser Permanent Oakland Medical Center*** e ***Highland Hospital***, grandes centros mundias no tratamento de pacientes portadores de deformidades dentofaciais, onde tive o imenso privilégio de conhecer e conviver com os professores ***Dr. Thomas Indresano, Dr. Felice O'Ryan, Dr. David Poor e Dr. Chan Park***. Possibilitaram não apenas a realização do meu doutorado sanduíche, mas o conhecimento diferenciado da minha especialidade, com a humildade e paciência de verdadeiros seres humanos. Muito, muito obrigada!

À ***Capes*** – Coordenação de Aperfeiçoamento de Pessoal de Nível Superior, pelo apoio financeiro para a realização dessa tese.

Ao professor ***Renato Sawazaki***, que me ensinou que paciência é uma virtude entre nós, e que a sabedoria depende de como se emprega o conhecimento conquistado ao longo dos anos. Muito obrigada.

Ao professor ***Renato Mazzonetto***, muito obrigada pela amizade e ensinamentos durante esses anos de vida acadêmica.

Ao professor ***Alessandro Costa da Silva***, pela confiança e incentivo em um dos momentos mais delicados e importantes da minha vida.

À professora ***Vânia Célia Vieira de Siqueira*****,** pelo sorriso e incentivo de cada dia. Muito obrigada!

Ao professor ***Paulo Henrique Ferreira Caria***, por ser um verdadeiro exemplo de profissional e professor a todos os alunos desta casa, sem distinção.

De forma especial ao meu amigo, orientador e eterno professor, ***Roger William Fernandes Moreira.*** É tanta coisa que eu gostaria de agradecer que me

faltam palavras neste momento. Hoje acredito que Deus o colocou em meu caminho na forma de um presente. Obrigada pelo convívio, pelo ensinamentos pessoais e profissionais, pelo "sim", pelo "não", pelos elogios, pelas críticas, pelas discussões, pelas oportunidades, pelo carinho e, sobretudo, pela amizade. Meus sinceros agradecimentos.

Ao querido ***Fábio Ricardo Loureiro Sato***, um exemplo de profissional. Exemplo de dignidade, humildade e paciência. Obrigada por todos os ensinamentos transmitidos até hoje e por ser uma "jóia rara" em nossa equipe.

Às funcionárias da área de cirurgia, especialmente à ***Antônia Ângelica do Godoy Quinhones*** e à gloriosa ***Edilaine Cristina Mendes Felipe.*** Obrigada pela paciência, pela compreensão, pela organização e por proporcionar alegria a todos os nossos dias. Com certeza, nosso trabalho não seria o mesmo sem a ajuda de vocês.

Aos ***estagiários*** que por esta casa já passaram, especialmente ao amigo ***Rodrigo Tavares*** por todo o auxílio, dedicação e amizade.

Aos ***pacientes,*** pela confiança depositada. Por fazerem de mim uma profissional cada vez melhor.

Aos alunos de pós-graduação e graduação que fazem ou que já fizeram parte desta casa, principalmente ***Leandro Klüppel, Rafael Grotta, Eduardo Serena, Heric Iamaschita, Miguel Pérez, Sergio Olate, Adriano de Assis, Felipe Nascimento e Jaime Rodrigues***, pelos ensinamentos, incentivo, amizade e companheirismo que compartilhamos. Agradeço de coração por todos os momentos que passamos juntos.

Aos meu queridos amigos ***Sergio Monteiro Lima Júnior*** (meu irmão mineiro), ***Saulo Ellery Santos e Patrício de Oliveira Neto*** (meus irmãos cearenses), e ***Cláudio Ferreira Nóia*** (meu irmão rondoniano) pelos ensinamentos, incentivo, amizade e companheirismo. Por serem pessoas de bem e fiéis à minha amizade. Pessoas que se prestaram a dividir sempre as dificuldades do dia-a-dia, o peso das decisões, as experiências vividas e o conhecimento alcançado, além da conta do final de semana! Obrigada pela amizade sincera e espero que ela permaneça por toda a vida.

Ao meu amigo de ontem, hoje e sempre, ***Josué Lolli Júnior*** e aos meus queridos ***Blair Alexander Isom*** (meu irmão americano), ***Cristian Milton Cougo*** (amigo do peito), ***Danillo Costa Rodrigues*** (homem de bem, bom caráter e humilde), por tornarem todos os meus dias muito mais felizes. Obrigada pelo respeito, amor e amizade.

Ao meu querido amigo de ontem, hoje e sempre, ***Carlos Alexandre Bueno.*** Por ter sido uma das pessoas mais presentes em minha vida quando tudo parecia vazio. Por ter me trazido paz, segurança e amor. Muito obrigada. Amo muito você!

Às minhas amigas ***Itana Fernandes, Pauline Magalhães Cardojso, Adriana Barbosa Firmo, Thaiz Carrara Arrabal, Karina Giovanetti, Ana Paula Pitarello, Mariana Ambrosio, Renata Morgental, Livia Mota, Livia Faria, Maryara Zeraick, Ana Flávia Zeraick, Jéssyka Moreira, Valéria Lima, Kathlyn Miike, Kelly Damalio e Juliana Stecke*** por serem as MELHORES amigas do mundo!!! Amo vocês de coração!!!

.

À minha **família**, MELHOR FAMÍLIA DO MUNDO!!!! Família que me acolhe sempre, família que eu tenho muito orgulho e que me faz extremamente feliz!

Ao meu ***pai – Flávio Irineu Marchiori***, homem corajoso, honesto, humilde e extremamente competente. Meu grande exemplo em todos os aspectos da minha vida. Sem dúvidas, o homem mais importante da minha vida.

À minha ***mamis – Sueli Pitarello Marchiori***, por ser MÃE todos os dias da minha vida. Indiscutivelmente, um exemplo de mãe. Não tenho palavras jque expressem toda a minha gratidão por você.

Ao meu querido irmão, ***Daniel Marchiori***. Aprendemos um com o outro que a única coisa que realmente vale a pena na vida é a família. Meu irmão, meu anjo da guarda, mesmo longe você é presença diária em meus pensamentos.

À minha tia, ***Tânia Marchiori***. Insubstituível.

À ***primos*** mais importantes do Brasil! ***Daniele Marchiori, Rafael Marchiori, Ana Paula Pitarello, Carlos Renato Pitarello, Tiago Marchiori e todos os "agregados",*** por serem os melhores primos que eu poderia ter! Amo vcs!

Aos meus alunos ***Magno Liberato*** e ***Fernando Pando***, por me ensinarem com carinho diariamente a maravilhosa tarefa de educar.

Às queridas ***Daiana Tonin*** e ***Ingrid Gama,*** por toda a dedicação em nosso trabalho e pela amizade.

Há muito mais a quem agradecer... À todos aqueles que, embora não nomeados, brindaram-me pelo simples fato de fazerem parte da minha vida, por fazerem parte da minha história. Muito obrigada!

INTRODUÇÃO

A dor é uma sensação complexa e não totalmente elucidada cujo entendimento permanece desafiador, fortemente afetada por fatores cognitivos (Cruccu *et al*., 2004; Cruccu *et al*., 2010). A Associação Internacional para o Estudo da Dor (AIED) a define como "uma experiência sensorial e emocional desagradável associada à dano tecidual real ou potencial, ou descrita em termos de tal lesão". É uma sensação emocional e inquestionavelmente subjetiva, que faz parte do corpo humano (Merskey & Bogduk, 1994). Tem início a partir da ativação de nociceptores e neurônios primários aferentes, gerando estímulos dentro do sistema nociceptivo (Treede *et al*., 2008).

Muitos conceitos e classificações de dor foram propostos. A dor aguda é definida como "dor que surge repentinamente e tem sua duração limitada". Este tipo de dor é frequentemente presente em cirurgia buco-maxilo-facial uma vez que a maioria dos procedimentos cirúrgicos podem produzir graus variados de dor aguda, cuja duração e intensidade são bem previsíveis, assim como o tratamento farmacológico (Szumita *et al*., 2010). Em relação à dor crônica, esta pode ser definida como "dor que persiste por longos períodos de tempo, com duração maior que o tempo necessário para a cura da lesão". Frequentemente a causa não é identificada (Johnson, 1997). Já a AIED definiu dor crônica como "dor que perdura por mais de três meses" (Merskey & Bogduk, 1994). No entanto, classificar a dor de acordo com sua duração pode não ser o melhor método para diferenciar a dor aguda de dor crônica, uma vez que a primeira pode persistir por vários meses, enquanto a segunda pode ter um início mais rápido. Neste sentido, a dor aguda é mais relacionada ao dano tecidual e, por isso, responde melhor ao tratamento farmacológico dirigido à alteração neurossensorial (Okeson, 1996). Por outro lado, a dor crônica é resultado de alterações nas vias somatossensoriais do que a interpretação de estímulos nocivos periféricos, como ocorre na dor aguda. Portanto, o tratamento farmacológico para a dor aguda é ineficaz para dor crônica (Szumita *et al*. , 2010).

A dor crônica pós-operatória pode estar presente na ausência de danos nervosos, como um resultado de inflamação permanente, ou ainda pode ser uma manifestação da dor neuropática (Kehlet *et al*., 2006). A AIED definiu dor neuropática como "dor causada por uma lesão ou disfunção do sistema nervoso" (Merskey & Bogduk , 1994). No entanto, a inclusão da palavra " disfunção " atribui uma definição muito ampla para este tipo específico de dor. Desta forma, outras condições também poderiam ser classificadas como dor neuropática, tais como a fibromialgia e enxaqueca (Cruccu *et al*., 2004; Bouhassira *et al*., 2005). Assim, uma nova definição foi proposta por Treede *et al.* (2008), estreitando este conceito para "dor que surge como consequência direta de uma lesão ou doença que afeta o sistema somatossensorial". Ela é descrita pelos pacientes como sensação de queimação dolorosa (Okeson, 2008), tendo uma combinação de duas características principais: hipoestesia e hipersensibilidade paradoxal. Este fenômeno positivo inclui alguns achados distintos: dor espontânea, disestesia, alodinia, hiperalgesia e hiperpatia (Merskey & Bogduk, 1994; Kehlet *et al*., 2006). Disestesia é definida como sensação alterada não comumente presente, mas associada a um leve desconforto e sensação desagradável não necessitando de tratamento farmacológico, referida pelo paciente como queimação, ardor e sensibilidade aumentada (Phillips *et al*., 2006), podendo ser espontânea ou provocada (Merskey & Bogduk, 1994). Alodinia é a dor provocada por um estímulo inócuo, como toque e pressão leve, ou frio e calor moderado. Enquanto que a hiperalgesia refere-se a um aumento da resposta dolorosa à estímulos nocivos que normalmente provocariam dor (Merskey & Bogduk, 1994; Kehlet *et al*., 2006), a hiperpatia é uma sensação de dor explosiva aos mesmos estímulos. Todas estas sensações de hipersensibilidade podem mascarar a hipoestesia que está sempre presente quando o dano nervoso ocorre (Merskey & Bogduk, 1994; Okeson, 2008; Kehlet *et al.*, 2006; Guastella *et al*., 2011) . Quanto ao curso da dor neuropática, também pode ser temporária ou contínua. Normalmente episódios intensos de dor são vistos seguido por remissão total da dor (Okeson, 2008). Dor paroxística também pode ocorrer, definida como "dor lancinante, espontânea e

repentina, com duração de segundos" (Rasmussen *et al*., 2004). Normalmente o paciente não tem dor entre os episódios de dor paroxística, mas, se episódios frequentes estão presentes, desconforto doloroso persistente pode ocorrer (Okeson, 2008) .

Em medicina, a dor neuropática vem sendo exaustivamente estudada em algumas patologias, podendo ser distinguida em periférica ou central baseado na localização anatômica da lesão (Dworkin *et al*., 2003). Em relação ao sistema nervoso central, exemplos desta condição são dor pós- acidente vascular cerebral, dor pós-lesão medular e esclerose múltipla. Já a neuralgia do trigêmeo, neuralgia pós-herpética, polineuropatia diabética dolorosa, polineuropatia em pacientes portadores do vírus da imunodeficiência humana e dor pós-cirúrgica são exemplos deste distúrbio no sistema nervoso periférico (Finnerup *et al*., 2005; Finnerup *et al*., 2010). Em cirurgia buco-maxilo-facial, a dor neuropática pode se manifestar na região da pele e mucosa correspondente ao trajeto do nervo alveolar inferior quando a OSRM é realizada (Jääskeläinem *et al*., 2004; Popat *et al*., 2012). A dor pode se desenvolver imediatamente após a cirurgia e persistir mesmo na ausência de inflamação do tecido contínuo ou estímulo nocivo periférico (Kehlet *et al*., 2006). É mais frequente em pacientes do gênero feminino, com idade superior a 40 anos de idade (Krause & Backonja, 2003; Bennett *et al.,* 2005; Bouhassira *et al*., 2005; Freynhagen *et al*., 2006; Portenoy *et al*., 2006; Dworkin *et al*., 2007; Scholz *et al*., 2009; Santos *et al*., 2010; Unal-Evik *et al*., 2010; Martinez *et al*., 2012).

Embora a dor de origem neuropática pós-cirúrgica ser bem documentada na literatura na área médica, pouco estudos foram publicados a respeito desta condição em cirurgia buco-maxilo-facial após OSRM (Jääskeläinen *et al*., 2004; Popat *et al*., 2012). Desta forma, o presente estudo objetivou identificar a prevalência, fatores de risco e curso clínico da dor neuropática em pacientes submetidos à OSRM.

CAPÍTULO

NEUROPATHIC PAIN FOLLOWING SAGITTAL SPLIT RAMUS OSTEOTOMY OF THE MANDIBLE: PREVALENCE, RISK FACTORS AND CLINICAL COURSE

Purpose: To estimate the prevalence of, risk factors for, and clinical course of neuropathic pain (NPP) after sagittal split ramus osteotomy (SSRO) of the mandible.

Materials and Methods: A retrospective cohort of all patients who underwent SSRO at 2 medical centers within Kaiser Permanente Northern California from January 2007 through September 2012 was assembled. Demographic, clinical, and surgical factors were abstracted from medical records and relevant comorbidities were identified. The prevalence of NPP in the cohort was calculated and the clinical signs, symptoms, temporal characteristics, and treatment response in affected patients were noted.

Results: The authors identified 1.778 patients who underwent SSRO and excluded 107 patients according to predefined criteria. The remaining 1.671 patients had a median age of 24 years (interquartile range,19 to 35 yr) and 62.4% were women. Seven patients developed NPP after SSRO, which was an overall prevalence of 0.42%. All patients with NPP in this cohort were women and had a median age of 48 years. The risk factors for developing NPP after this surgery were age over 40 years (p = 0.0098), depression (p = 0.0100), and female gender (p = 0.0497). NPP developed an average of 30 days postoperatively (range, 18 to 56 days) and persisted for a median duration of 52 days (range, 30 to 69.5 days). All patients responded favorably to anticonvulsant (n = 6) or tricyclic (n = 1) medications, and no patients developed chronic postsurgical pain.

Conclusions: NPP was an infrequent complication after SSRO, occurring in 1 of 238 patients in this cohort. The short duration and positive response to medication are reassuring findings. The results of this investigation highlight the need for prospective studies to further understand the spectrum of postoperative NPP.

Key-words: neuropathy; pain, postoperative; orofacial pain.

1 INTRODUCTION

Mandibular sagittal split ramus osteotomy (SSRO) is among the most frequently performed procedures for correction of mandibular deformities. This technique involves separation of the lateral and medial mandibular cortices with movement of the distal segment anteriorly or posteriorly, with or without rotation. The inferior alveolar nerve (IAN), located within the mandibular canal, is often manipulated during the SSRO. Intraoperative damage to the IAN can be caused by nerve manipulation, mobilization of the osteotomized segments, stretching during mandibular advancement or compression during mandibular setback, bony adherence or entrapment of the IAN, and trauma from bony spicules between the proximal and distal segments (Takeuchi *et al*., 1994; Yamamoto *et al*., 2002). These maneuvers can result in postoperative neurosensory deficits, with reported prevalence rates as high as 95% (Gianni *et al*., 2002; Jääskeläinen *et al*., 2004; Park *et al*., 2011; Monnazzi *et al*., 2012). Older age at the time of surgery and concomitant mandibular procedures, such as genioplasty, may increase the risk of neurosensory disturbances (Park *et al*., 2011; Monnazzi *et al*., 2012).

Altered sensation after nerve injuries may include hypoesthesia, paresthesia, and dysesthesia (Table 1). Standardized word lists or verbal descriptors have been associated with each type of neurosensory deficit involving the IAN (Phillips *et al*., 2006; Phillips *et al*., 2007). Hypoesthesia is a state of decreased sensitivity and is often described as numb, rubbery, and swollen.

Paresthesia is defined as an abnormal sensation that is not unpleasant and is characterized by terms such as tingling, tickling, and itching. In contrast, dysesthesia refers to an abnormal sensation that is unpleasant and is typically described as tender, pricking, stinging, and burning.

Table 1: Definition of neurosensory disturbances and verbal descriptors commonly associated with pain typology.

Pain Term	Definition
Allodynia	Painful response to an innocuous stimulus
Analgesia	Absence of pain to a noxious stimulus
Dysesthesia	Unpleasant abnormal sensation (spontaneous or evoked) - descriptors include: tender, pricking, stringing, burning, electric, cold
Hyperalgesia	Increased painful response to a noxious stimulus
Hyperpathia	Explosive abnormal pain that outlasts a noxious stimulus
Hypoesthesia	Reduced sensation to stimulation -- descriptors include: numb, rubbery, swollen, wooden
Neuralgia	Pain in the distribution of a specific nerve
Neuropathic Pain	Spontaneous pain caused by a lesion or disease of the somatosensory nervous system - involves sharp paroxysmal pain not associated with painful stimuli - descriptors include: throbbing, electric shock, burning, excruciating, wrenching
Paresthesia	Abnormal sensation (spontaneous or evoked) which is *not* unpleasant -- descriptors include: tingling, tickling, itching, crawling

Merskey & Bogduk, 1994; Bennett, 2001; Backonja & Krause, 2003; Jensen & Baron, 2003; Bouhassia *et al*., 2005; Portenoy, 2006; Dworkin, 2009; Guastella *et al*., 2011

A less common consequence of nerve injury is neuropathic pain (NPP). NPP is defined by the International Association for the Study of Pain (IASP) as

‘‘pain arising as a direct consequence of a lesion or disease affecting the somatosensory system" (Treede *et al,* 2008). NPP is a clinical description that requires a demonstrable lesion or known trauma of the involved nerve. NPP is commonly described as a burning sensation, although it may be perceived as throbbing, wrenching, excruciating, and electric shocks (Okeson, 2008; Guastella *et al*., 2011). NPP occurs in conjunction with hypoesthesia and paradoxical hypersensitivity. Thus, patients with NPP experience sensory loss and the so-called positive phenomena, which include distinct findings of spontaneous pain, dysesthesia (spontaneous or evoked), allodynia, hyperalgesia, and hyperpathia (Merskey & Bogduk, 1994; Kehlet *et al*., 2006). Allodynia is pain evoked by an innocuous stimulus that usually does not elicit pain, such as light touch, pressure, or cold, whereas hyperalgesia (IASP) is an increased response to a noxious stimulus (Merskey & Bogduk, 1994; Kehlet *et al*., 2006). Hyperpathia is an explosive abnormal pain that outlasts the stimulus. NPP can be episodic or continuous, and severe episodes of pain can be seen followed by total pain remission (Merskey & Bogduk, 1994; Kehlet *et al*., 2006; Okeson, 2008; Guastella *et al*., 2011). Paroxysmal pain also can occur, defined as ‘‘spontaneous, sudden, jabbing pain of seconds’’ (Rasmussen *et al*., 2004). There is usually no pain between the episodes of paroxysmal pain, but, if frequent episodes are present, persistent pain can occur (Okeson, 2008).

Although studies have examined the prevalence of and risk factors for NPP after thoracic, abdominal, gastrointestinal, and gynecologic surgeries, there is limited knowledge about NPP after SSRO of the mandible. Prevalence estimates have ranged from 2.5 to 13.0%, but these have been derived from just a few small case series (Jääskeläinen *et al*., 2004; Rasmussen *et al*., 2004; Popat *et al*., 2012). The current understanding of NPP after SSRO has been limited by the methodologic heterogeneity of studies and a lack of consensus regarding the characteristics of NPP. Therefore, the authors sought to identify the prevalence of, risk factors for, and clinical course of NPP after SSRO in a large patient cohort.

2 MATERIAL AND METHODS

2.1 STUDY DESIGN

This was a retrospective observational cohort study designed to investigate the prevalence, clinical course, risk factors, and treatment responses in patients with NPP arising from injury to the IAN after SSRO. The Kaiser Foundation Research Institute's institutional review board approved the study (annex 1).

2.2 PATIENTS

Subjects eligible for inclusion were consecutive patients who underwent SSRO, with or without genioplasty, or Le Fort I osteotomy. All were treated in the Division of Maxillofacial Surgery at Kaiser Permanente Medical Center in Oakland or Santa Clara from January 2007 through September 2012 and had at least 2 postoperative examinations. Exclusion criteria included normal IAN function immediately after SSRO; preexisting neurologic disorders involving orofacial sensory impairment, orofacial pain, or cranial nerve disorders; history of mandibular trauma or surgery; history of radiation therapy to the head and neck region; history of bisphosphonate exposure; and inability to describe signs and symptoms in English. Health plan databases, medical charts, and clinic files, including relevant imaging, were abstracted to collect patient characteristics, demographic classification, potential risk factors, and relevant comorbidities that might be associated with development of NPP after SSRO. SSROs were performed using a standardized surgical technique in all cases.

2.3 STUDY VARIABLES

2.3.1 Outcome Variables

The primary outcome of this study was the presence of NPP in the distribution of the IAN (lower lip, chin, mucogingiva, and teeth) after SSRO. NPP is a clinical description and, as noted, is defined by the IASP as ‘‘pain caused by a lesion or disease of the somatosensory system’’ (Merskey & Bogduk, 1994). The IASP notes that ‘‘lesion’’ includes cases of known nerve trauma such as that which occurs during the SSRO. Because charts may not explicitly list a diagnosis of NPP, the authors identified descriptors commonly used in association with the condition, including electric shocks, wrenching, excruciating, severe burning, aching, piercing, stabbing, sharp pain, squeezing, and cold-freezing pain (Bennett, 2001; Backonja & Krause, 2003; Jensen & Baron, 2003; Bouhassia *et al*., 2005; Portenoy, 2006; Dworkin, 2009; Guastella *et al*., 2011). To differentiate patients with NPP from those with dysesthesia, only patients who reported these symptoms at more than 1 appointment and required pharmacologic treatment specifically for the symptoms were categorized as having NPP.

Using pharmacy and medical records, the date of onset and duration of NPP in relation to the date of the SSRO were documented. Date of onset was defined as the date of the first prescription for pharmacologic treatment of NPP, and duration was determined from pharmacy refills and clinical complaints.

2.3.2 Predictor Variables

The following predictor variables were ascertained using electronic medical records and maxillofacial clinic files:

1. Demographic factors: patients’ age at time of surgery, gender, race;
2. Lifestyle factors: patient-reported alcohol, tobacco and drug use;

3. Comorbidities: cardiovascular disease, diabetes, migraine headache, depression, psychiatric disorders, sleep apnea, neurologic disorders, herpes simplex labialis;
4. Surgical factors: concomitant procedures, characteristics of distal segment movement (direction, amount and symmetry), method of internal fixation, presence or absence of mandibular third molar teeth, intraoperative blood loss, complications involving the mandible such as unfavorable sagittal split, partial or total IAN transection;
5. Postoperative complications: infection, hematoma, wound dehiscence, bony malunion, or nonunion.

2.4 STATISTICAL ANALYSIS

Standard descriptive statistics were used to describe the characteristics of the cohort. Fisher exact, Kolmogorov-Smirnov, and c2 tests were used for comparison between NPP and non-NPP subgroups ($p<0.05$). All analyses were conducted using SAS 9.2.3 (SAS Institute, Cary, NC).

3 RESULTS

The initial study sample consisted of 1.778 patients treated from January 2007 through September 2012, and among these, 107 were excluded (Figure 1). The final cohort consisted of 1.671 patients, 62.4% were women, and the median age was 24 years (interquartile range [IQR], 19 to 35 yr; Table 2). Relevant comorbidities, identified in 29.4% of patients, included cardiovascular disease, depression, migraine headaches, psychiatric history, sleep apnea, diabetes, and herpes simplex labialis. All patients underwent bilateral SSRO as an isolated procedure (n = 556, 33.3%), with a genioplasty (n = 97, 5.8%), or in conjunction with maxillary surgery (n = 763, 45.7%) and genioplasty (n = 255, 15.3%). Postoperative complications related to the SSRO occurred in 23.5% of patients

and included local wound infection (n = 307, 18.4%), wound dehiscence (n = 73, 4.4%), and hematoma (n = 62, 3.7%).

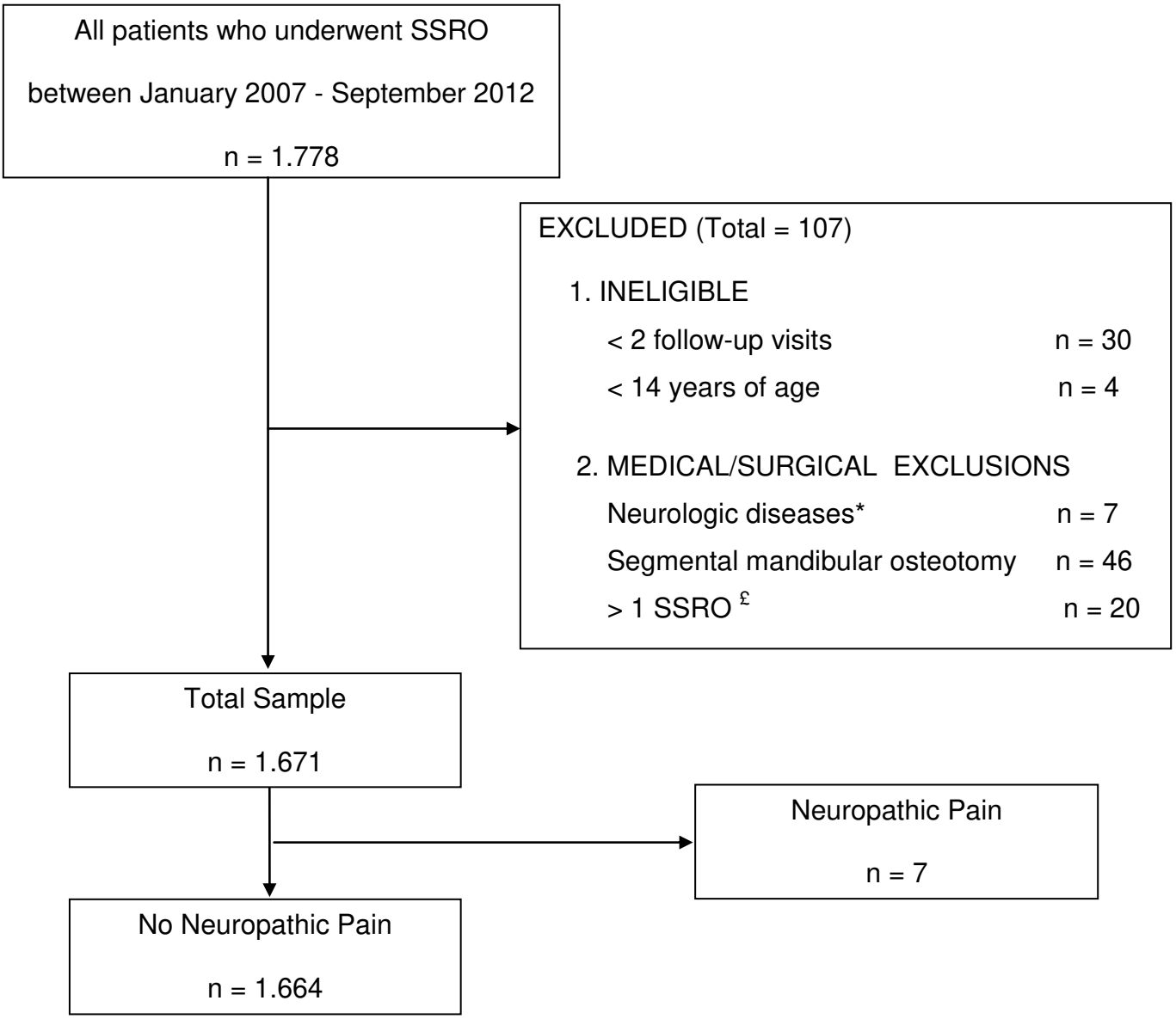

Figure 1: Flow chart for SSRO cohort treated from January 2007 through September 2012. * Patients with neurologic disease included: cerebral palsy and numbness of the face, scalp and neck. £ >SSRO indicates revision of a prior SSRO.

Table 2: Demographics of overall cohort including patients with neuropathic pain

	Overall Cohort (n = 1671)	NPP (n = 7)	Univariate *p*-Value
AGE (yr), median (IQR)	24 (19-35)	48 (28-54)	0.0098
WOMEN, n (%)	1042 (62.4)	7 (100)	0.0497
COMORBIDITY, n (%)	491 (29.4)	5 (71.4%)	0.0258
Cardiovascular	181 (10.8)	1 (14.3)	0.5525
Depression	119 (7.1)	3 (42.9)	0.0100
Migraine headache	108 (6.5)	2 (28.6)	0.0702
Psychiatric disorder	97 (5.8)	1 (14.3)	0.3426
Sleep apnea	89 (5.3)	2 (28.6)	0.0495
Diabetes	60 (3.6)	1 (14.3)	0.2262
Herpes simplex labialis	17 (1.0)	1 (14.3)	0.0692
SURGERY, n (%)			0.1781
BSSO	556 (33.3)	4 (57.1)	
BSSO/Genio	97 (5.8)	1 (14.3)	
BSSO/Le Fort	763 (45.7)	1 (14.3)	
BSSO/Le Fort/Genio	255 (15.3)	1 (14.3)	
POSTOPERATIVE COMPLICATION, n (%)*	393 (23.5)	2 (28.6)	0.6190
Infection	307 (18.4)	2 (28.6)	0.6190
Wound Dehiscence	73 (4.4)	0 (0.0)	1.0000
Hematoma	62 (3.7)	0 (0.0)	1.0000

The authors identified 7 patients who developed features of NPP in this cohort of 1.671 patients. Thus, the prevalence of NPP in this surgical population was 0.42%. All patients were Caucasian women, with a median age of 48 years (IQR, 28 to 54 yr). NPP developed approximately 1 month postoperatively (median, 30 days; IQR, 19 to 55 days) and persisted for a median of 52 days (IQR, 28 to 71 days).

Symptoms involved the chin in 6 of 7 cases and 5 patients described NPP symptoms in the chin and lower lip. One patient reported lower lip pain only and another patient described pain only in her chin (Table 3). One patient with unilateral lip and chin involvement also reported NPP in the ipsilateral dentition and gingiva. Pain topography was consistent with the anatomic distribution of the IAN or mental nerve in all cases; 4 patients reported bilateral NPP of the lip or chin, and 2 had unilateral pain. All patients with NPP described hypoesthesia (decreased sensation) and dysesthesia (abnormal unpleasant sensation) of the involved nerve. Three patients reported mechanical allodynia and 2 reported hyperpathia. NPP was described as burning by most patients (85.7%), but was also characterized as ‘‘sharp’’, "extremely sensitive’’, ‘‘obnoxious’’, ‘‘irritating’’, ‘‘unbearable’’, ‘‘pins and needles’’ and ‘‘terrible’’. Patients also reported that it was ‘‘hard to do every day simple things’’, ‘‘hard to sleep’’, ‘‘hurts every time that I move my mouth’’, ‘‘unbearable when single things touch my chin’’, and ‘‘I can hardly brush my teeth because it just makes me cringe’’.

Older age (p = 0.0098), presence of a comorbidity (p = 0.0258), and female gender (p = 0.0497) were significant risk factors associated with development of NPP. The median age of patients who developed NPP was 48 years (IQR, 28.0 to 54.0 yr) compared with 24 years (IQR, 19.0 to 35.0 yr) in patients who did not develop NPP. When age was examined as a continuous variable, the odds of developing NPP increased by approximately 8% (95% confidence interval, 3.2 to 14.7peryear.

Table 3. Clinical details of patients with neuropathic pain of the inferior alveolar nerve following OSRM.

CASE	GENDER	AGE	COMORBITIES	PO COMPLICATION	LOCALIZATION	DESCRIPTORS	NPP PO START DAY	NPP DURATION (Days)	TREATMENT
1	F	61	Migraine, Neuropathic low back pain	L SSRO wound infection	Chin B, Inferior lip B	Burning pain	19	68	Anticonvulsant
2	F	20	Herpes simplex labialis	None	Chin L, Inferior lip L, Left mandibular teeth - adjacent mucosa and gingiva	Burning pain, Sharp pain, Pins and Needles, Extremely sensitive	56	52	Anticonvulsant, NSAID, Opioid, Antidepressant, Antihistamine
3	F	28	Depression, Sleep apnea	R SSRO wound infection	Chin B	Burning pain	55	72	Anticonvulsant, NSAID, Non-steroid + Opioid,
4	F	32	None	None	Chin R, Inferior lip R	Sensitivity, Irritating pain	55	28	Anticonvulsant, Non-opioid, NSAID + Opioid
5	F	48	Depression, Migraine, Anxiety disorder	None	Chin L, Inferior lip L	Burning pain, Ache and pain	30	71	Anticonvulsant
6	F	49	None	None	Inferior lip B	Burning pain, Obnoxious pain	24	32	Homeopathic topical cream
7	F	54	Cardiovascular, Depression, Diabetes, Sleep apnea	None	Chin B, Inferior lip B	Burning pain, Sharp pain, Terrible pain	18	22	Anticonvulsant, Non-opioid

Abbreviations: PO Complication: Postoperative complication involving SSRO surgical site; NPP PO Start Day: Number of days postoperatively when NPP first diagnosed and required treatment; B: Bilateral; L: Left; R: Right.

Five of the 7 patients with NPP (71.4%) had at least 1 relevant comorbid condition, which was more than double the rate of patients with SSRO as a whole (29.4%). The most common comorbidity in the NPP group was depression. Three patients with NPP (42.9%) had comorbid depression, whereas 7.1% of patients had depression in the non-NPP group. Surgery type (including genioplasty), intraoperative factors, surgical time, presence of third molars, and distance and direction of surgical movement were not associated with NPP.

Most patients with NPP responded well to anticonvulsant medication (gabapentin) with or without nonsteroidal anti-inflammatory medications. One patient had continued NPP with gabapentin, but was successfully treated with a tricyclic antidepressant (amitriptyline). Another patient refused medication and used a homeopathic topical cream. All patients responded favorably and none developed chronic postsurgical pain.

4 DISCUSSION

The authors' overall goal was to determine the prevalence and clinical course of NPP after SSRO and to identify possible risk factors for development of NPP. To the authors' knowledge, this is the largest cohort used for this purpose to date. In addition, the integrated health care delivery system allowed the authors to document comorbidities and monitor pharmacologic compliance and treatment response in this large cohort. NPP developed within the first several months postoperatively, had a short duration, and showed a positive response to pharmacologic treatment with gabapentin or amitriptyline.

The prevalence of NPP in this surgical cohort was 0.42%, which is markedly lower than rates estimated in previous studies. Although there are numerous investigations of IAN function after SSRO, few studies have documented persistent postsurgical pain or NPP. Moreover, existing prevalence estimates are derived

from small case series and individual case reports. Jääskeläinen *et al.* (2004) reported NPP in 2 patients (5%) 1 year after SSRO, although the 2 patients had documented, intraoperative, axonal injuries of the IAN. They concluded that the overall prevalence of NPP after SSRO was 5%, but the prevalence increased to 13% in patients with documented axonal injuries. In a systematic literature review of the neuropathic component of postsurgical pain, Haroutiunian *et al*. (2013) reported an NPP prevalence after SSRO of 10%. However, they cautioned that this prevalence estimate was based on 1 study. The present data, derived from a relatively large cohort, suggest that the actual prevalence of NPP may be lower than estimated in previous case series.

Patients with NPP in the present cohort tended to be older and all were Caucasian women. This finding is consistent with reports of NPP after general surgical procedures showing higher prevalence rates in Caucasian women older than 50 years (Krause & Backonja, 2003; Bennett *et al*., 2005; Bouhassia *et al*., 2005; Freynhagen *et al*., 2006; Dworkin *et al*., 2007; Scholz *et al*., 2009; Maier *et al*., 2010; Santos *et al*., 2010; Unal-Cevik *et al*., 2010; Martinez *et al*., 2012). The present results suggest that older age and female gender are clinically relevant risk factors for predicting NPP after SSRO, with the caveat of a low overall prevalence rate.

Despite the small number of patients affected with NPP after SSRO, sleep apnea and depression appear to be risk factors. Although the causal relation is poorly understood, sleep disturbances are commonly reported in patients with NPP (Zelman *et al*., 2006; Langley *et al*., 2013). Increased levels of inflammatory mediators and a shift in thermal and mechanical pain thresholds toward hyperalgesia have been found in response to acute and chronic sleep deprivation (Haack *et al*., 2007; Schuh-Hofer *et al*., 2013). Freynhagen *et al* (2006) reported a significantly higher prevalence of moderate and severe depression in patients with NPP compared with those with nociceptive pain and found a greater frequency of

sleep disturbances in patients with NPP. Thus, the role of these comorbidities in the development of NPP warrants further investigation.

Because there is no diagnostic tool for specifically and unequivocally establishing the diagnosis of NPP, the authors used proxy criteria in the form of verbal pain descriptors to identify NPP. The present cohort of patients consistently used these same verbal descriptors to characterize the multiple positive and negative sensations they perceived in the IAN distribution. Positive sensations refer to sensations that are normally not present, whereas negative sensations refer to loss of sensation. The subjective descriptions of the 7 identified patients were consistent with the expert consensus descriptors that should be present to make a diagnosis of NPP: ‘‘prickling, tingling, pins and needles’’, ‘‘pain evoked by light touch’’, ‘‘electric shocks or shooting pain’’, ‘‘hot or burning pain", and ‘‘brush allodynia on self-examination’’ (Smith *et al*., 2012; Renton & Yilmaz, 2012). They also were significantly different than descriptors documented in the control charts. Most of the present patients with NPP described their pain as ‘‘burning’’ and used sensory descriptors common to many other NPP studies, including ‘‘electric shocks’’, ‘‘tingling’’, ‘‘pins and needles’’, ‘‘sharp’’, ‘‘extremely sensitive’’, ‘‘obnoxious’’, ‘‘irritating’’, ‘‘unbearable’’, and ‘‘terrible’.’ Although it is conceivable that the authors may have underestimated prevalence in cases that were inadequately described by the treating clinician, the 7 identified cases had clear symptoms of NPP.

Owing to the retrospective nature of this study, the authors did not perform neurosensory testing or use a visual analog scale to document pain severity. However, the validity of sensory testing in documenting nerve injuries and NPP has not been proved. Furthermore, most NPP studies have found a poor correlation between subjective symptoms and objective neurosensory testing (Maier *et al*., 2010; Martinez *et al*., 2012). Another potential limitation of this study is that the time to fill prescriptions was used as the time of onset. Although this is likely close

to the actual time of onset, it may underestimate the true duration of NPP symptoms because patients may have not sought or received professional attention immediately. Although all the present patients responded favorably to pharmacologic treatment, surgical exploration of the IAN in instances of ongoing severe NPP or hyperalgesia has been reported by Gregg (1990) and Bagheri *et al*. (2010).

Early pharmacologic management of NPP is thought to be important in the prevention of central sensitization (Kehlet *et al*., 2006). Anticonvulsant and tricyclic antidepressants represent first-line medications for the treatment of NPP in combination with opioids and nonopioid medications as needed. The present patients with NPP received gabapentin or amitriptyline and achieved a favorable response. Interestingly, the patient who used a homeopathic remedy also fully recovered. It is not clear whether this reflects a treatment effect, placebo effect, or the natural course of the illness (ie, some patients may heal without treatment). Nevertheless, the management of patients who develop refractory IAN pain can be challenging (Popat *et al*., 2012; Renton & Yilmaz, 2012). Therefore, early treatment of NPP with standard medications is recommended.

In conclusion, the authors found that NPP was an infrequent complication after SSRO, occurring in 1 of 238 patients (0.42%). Practitioners should be aware that older women with a history of depression may be at greater risk of developing NPP after SSRO than younger patients. The short duration of symptoms and complete, positive response to standard medications are reassuring findings. The results of this investigation highlight the need for prospective studies to further understand the spectrum of postoperative NPP.

5 REFERENCES[1]

1. Backonja MM, Krause SJ. Short report: Neuropathic Pain Questionnaire–Short Form. Clin J Pain. 2003; 19:315-6.

2. Bagheri SC, Meyer RA, Khan HA, Wallace J, Steed MB. Microsurgical repair of the peripheral trigeminal nerve after mandibular sagittal split ramus osteotomy. J Oral Maxillofac Surg. 2010; 68: 2770-82.

3. Bennett M. The LANSS Pain Scale: Leeds Assessment of Neuropathic Symptoms and Signs. Pain. 2001; 92:147-57.

4. Bennett MI, Smith BH, Torrance N, Potter J. The S_LANSS Score for identifying pain of predominantly neuropathic origin: Validation for the use in clinical and postal research. J Pain. 2005; 6: 149-58.

5. Bouhassira D, Attal N, Alchaar H, Boureau F, Brochet B, Bruxelle J *et al*. Comparison of pain syndromes associated with nervous or somatic lesions and development of a new neuropathic pain questionnaire (DN4). Pain. 2005; 114: 29-36.

6. Dworkin RH, Jensen MP, Gammaitoni AR, Olaleye DO, Galer BS. Department of Anesthesiology, University of Rochester School of Medicin Symptom profiles differ in patients with neuropathic versus nonneuropathic pain. J Pain. 2007; 8: 118-26.

---

[1] De acordo com a norma da Unicamp/FOP baseada na norma do International Committee of Medical Journal Editors – Grupo de Vancouver. Abreviatura dos periódicos em conformidade com o Medline.

7. Dworkin RH, Turk DC, Revicki DA, Harding G, Coyne KS, Peirce-Sandner S *et al.* Development and initial validation of an expanded and revised version of the Short-Form McGill Pain Questionnaire (SF-MPQ-2). Pain. 2009; 144: 35-42.

8. Freynhagen R, Baron R, Gockel U, Tölle TR. PainDETECT: A new screening questionnaire to identify neuropathic components in patients with back pain. Curr Med Res Opin. 2006; 22: 1911-20.

9. Gianni AB, D'Orto O, Biglioli F, Bozetti A, Brusati R. Neurosensory alterations of the inferior alveolar and mental nerve after genioplasty alone or associated with sagittal osteotomy of the mandibular ramus. J Craniomaxillofac Surg. 2001; 30: 295-303.

10. Gregg J. Studies of traumatic neuralgia in the maxillofacial region: Symptom complexes and response to microsurgery. J Oral Maxillofac Surg. 1990; 48:135-40.

11. Guastella V, Mick G, Soriano C, Valle L, Escande V, Dubray C, Eschalier A. A prospective study of neuropathic pain induced by thoracotomy: Incidence, clinical description, and diagnosis. Pain. 2011; 152: 74-81.

12. Haack M, Sanchez E, Mullington JM. Elevated inflammatory markers in response to prolonged sleep restriction are associated with increased pain experience in healthy volunteers. Sleep. 2007; 30:1145-52.

13. Haroutiunian S, Nikolajsen L, Finnerup NB, Jensen TS. The neuropathic component in persistent postsurgical pain: A systematic literature review. Pain. 2013; 154: 95-102.

14. Jääskeläinen SK, Teerijoki-Oksa T, Virtanen A, Tenovuo O, Forssell H. Sensory regeneration following intraoperatively verified trigeminal nerve injury. Neurology. 2004; 62: 1951-7.

15. Jensen TS, Baron R. Translation of symptoms and signs into mechanisms in neuropathic pain. Pain. 2003; 102:1-8.

16. Kehlet H, Jensen TS, Woolf C. Persistent postsurgical pain: Risk factors and prevention. Lancet. 2006; 367:1618.

17. Krause SJ, Backonja MM. Development of a neuropathic pain questionnaire. Clin J Pain. 2003; 19: 306-14.

18. Langley PC, Van Litsenburg C, Cappelleri JC, Carroll D. The burden associated with neuropathic pain in Western Europe. J Med Econ. 2013; 16: 85-95.

19. Maier C, Baron R, Tölle TR, Binder A, Birbaumer N, Birklein F *et al*. Quantitative sensory testing in the German Research Network on Neuropathic Pain (DFNS): Somatosensory abnormalities in 1236 patients with different neuropathic pain syndromes. Pain. 2010; 150: 439-50.

20. Martinez V, Ammar SB, Judet T, Bouhassira D, Chauvin M, Fletcher D. Risk factors predictive of chronic postsurgical neuropathic pain: The value of the iliac crest bone harvest model. Pain. 2012; 153:1478-83.

21. Merskey H, Bogduk H. Classification of chronic pain: Description of chronic pain syndromes and definitions of pain terms. Seattle, WA: IASP Press, 1994.

22. Monnazzi MS, Real-Gabrielli MF, Passeri LA, Gabrielli MA. Cutaneous sensibility impairment after mandibular sagittal split osteotomy: A prospective clinical study of the spontaneous recovery. J Oral Maxillofac Surg. 2012; 70: 696-702.
23. Okeson JP. The classification of orofacial pain. Oral Maxillofac Surg Clin North Am. 2008; 20: 133-44.

24. Park JW, Choung PH, Kho HS, Kim YK, Chung JW. A comparison of neurosensory alteration and recovery pattern among different types of orthognathic surgeries using current perception threshold. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011; 111: 24-33.

25. Phillips C, Essick G, Zuniga J, Turvey TA, BlakeyG 3rd. Qualitative descriptors used by patients following orthognathic surgery to portray altered sensation. J Oral Maxillofac Surg. 2006; 64: 1751-60.

26. Phillips C, Essick G, Preisser JS, Turvey TA, Tucker M, Lin D. Sensory retraining after orthognathic surgery: Effect on patients' perception of altered sensation. J Oral Maxillofac Surg. 2007; 65: 1162-73.

27. Popat H, Herdman W, Cronin P, Durning P. Management of chronic neuropathic pain following mandibular advancement surgery. Int J Oral Maxillofac Surg. 2012; 41: 1374-7.

28. Portenoy R. Development and testing of a neuropathic pain screening questionnaire.:ID pain. Curr Med Res Opin. 2006; 22: 1555-65.

29. Rasmussen PV, Sindrup SH, Jensen TS, Bach FW. Symptoms and signs in patients with suspected neuropathic pain. Pain. 2004; 110:461-9.

30. Renton T, Yilmaz Z. Managing iatrogenic trigeminal nerve injury: A case series and review of the literature. Int J Oral Maxillofac Surg. 2012; 41: 629-

31. Santos JG, Brito JO, De Andrade DC, Kaziyama VM, Ferreira KA, Souza I *et al*. Translation to Portuguese and validation of the Douleur Neuropathique 4 Questionnaire. J Pain. 2010; 11: 484-90.

32. Scholz J, Mannion RJ, Hord DE, Griffin RS, Rawal B, Zheng H *et al*. A novel tool for the assessment of pain: Validation in low back pain. PLoS Med. 2009; 6: e1000047.

33. Schuh-Hofer S, Wodarski R, Pfau DB, Caspani O, Magerl W, Kennedy JD, Treede RD *et al:* One night of total sleep deprivation promotes a state of generalized hyperalgesia—A surrogate pain model to study the relationship of insomnia and pain. Pain, 2013; 154: 1613-21.

34. Smith BH, Torrance N, Ferguson JA, Bennett MI, Serpell MG, Dunn KM. Towards a definition of refractory neuropathic pain for epidemiological research. An international Delphi survey of experts. BMC Neurol. 2012; 12: 29.

35. Szumita RP, Szumita PM, Just N. Understanding and managing patients with chronic pain. Oral Maxillofac Surg Clin N Am. 2010; 22: 481-94.

36. Takeuchi T, Furusawa K, Hirose I. Mechanism of transient mental nerve paraesthesia in sagittal split mandibular ramus osteotomy. Br J Oral Maxillofac Surg. 1994; 32: 105-8.

37. Treede RD, Jensen TS, Campbell JN, Cruccu G, Dostrovsky JO, Griffin JW *et al*. Neuropathic pain. Redefinition and a grading system for clinical and research purposes. Neurology. 2008; 70: 1630-5.

38. Unal-Cevik I, Sarioglu-Ay S, Evcik D. A comparison of the DN4 and LANSS questionnaires in the assessment of neuropathic pain: Validity and reliability of the Turkish version of DN4. J Pain. 2010; 11: 1129-35.

39. Yamamoto R, Nakamura A, Ohno K, Michi KI. Relationship of the mandibular canal to the lateral cortex of the mandibular ramus as a factor in the development of neurosensory disturbance after bilateral sagittal split osteotomy. J Oral Maxillofac Surg. 2001; 60: 490-5.

40. Zelman DC, Brandenburg NA, Gore M. Sleep impairment in patients with painful diabetic peripheral neuropathy. Clin J Pain. 2006; 22: 681-5.

CONCLUSÃO

A dor neuropática após osteotomia sagital dos ramos mandibulares é uma complicação infrequente, apresentando prevalência de 0.42%, com maior ocorrência em mulheres acima de 40 anos de idade com histórico de depressão.

REFERÊNCIAS[1]

1. Bouhassira D, Attal N, Alchaar H, Boureau F, Brochet B, Bruxelle J *et al*. Comparison of pain syndromes associated with nervous or somatic lesions and development of a new neuropathic pain questionnaire (DN4). Pain. 2005; 114: 29-36.

2. Cruccu G, Anand P, Attal N, Garcia-Larrea L, Haanpää M, Jørum E *et al*. EFNS guidelines on neuropathic pain assessment. Eur J Pain. 2004; 11: 143-62.

3. Cruccu G, Sommer C, Anand P, Attal N, Baron R, Garcia-Larrea L *et al*. EFNS guidelines on neuropathic pain assessment: revised 2009. Eur J Pain. 2010; 17: 1010-18.

4. Dworkin RH, Backonja M, Rowbotham MC, Allen RR, Argoff CR, Bennett GJ *et al.* Advances in Neuropathic Pain. Diagnosis, mechanisms, and treatments recommendations. Arch Neurol. 2003; 60: 1524-34.

5. Dworkin RH, Jensen MP, Gammaitoni AR, Olaleye DO, Galer BS. Symptom profiles differ in patients with neuropathic versus non-neuropathic pain. J Pain. 2007; 8: 118-26.

6. Finnerup NB, Otto M, McQuay HJ, Jensen TS, Sindrup SH. Algorithm for neuropathic pain treatment: an evidence based proposal. Pain. 2005; 118: 289-305.

---

[1] De acordo com a norma da Unicamp/FOP baseada na norma do International Committee of Medical Journal Editors – Grupo de Vancouver. Abreviatura dos periódicos em conformidade com o Medline.

7. Finnerup NB, SindrupSH, Jensen TS. The evidence for pharmacological treatment of neuropathic pain. Pain. 2010; 150: 573-81.

8. Guastella V, Mick G, Soriano C, Valle L, Escande V, Dubray C, Eschalier A. A prospective study of neuropathic pain induced by thoracotomy: Incidence, clinical description, and diagnosis. Pain. 2011; 152: 74-81.

9. Jääskeläinen SK, Teerijoki-Oksa T, Virtanen A, Tenovuo O, Forssell H. Sensory regeneration following intraoperatively verified trigeminal nerve injury. Neurology. 2004; 62: 1951-7.

10. Johnson MI. The physiology of the sensory dimensions of clinical pain. Physiotherapy. 1997; 83: 526-36.

11. Kehlet H, Jensen TS, Woolf C. Persistent postsurgical pain: Risk factors and prevention. Lancet. 2006; 367:1618.

12. Merskey H, Bogduk H. Classification of chronic pain: Description of chronic pain syndromes and definitions of pain terms. Seattle, WA: IASP Press, 1994.

13. Okeson JP. Introduction to orofacial pain. In: Orofacial pain. Guidelines for assessment, diagnosis, and management. 1996; Chicago.

14. Okeson JP. The classification of orofacial pain. Oral Maxillofac Surg Clin North Am. 2008; 20: 133-44.

15. Phillips C, Essick G, Zuniga J, Turvey TA, BlakeyG 3rd. Qualitative descriptors used by patients following orthognathic surgery to portray altered sensation. J Oral Maxillofac Surg. 2006; 64: 1751-60.

16. Popat H, Herdman W, Cronin P, Durning P. Management of chronic neuropathic pain following mandibular advancement surgery. Int J Oral Maxillofac Surg. 2012; 41: 1374-7.

17. Rasmussen PV, Sindrup SH, Jensen TS, Bach FW. Symptoms and signs in patients with suspected neuropathic pain. Pain. 2004; 110:461-9.

18. Szumita RP, Szumita PM, Just N. Understanding and managing patients with chronic pain. Oral Maxillofac Surg Clin N Am. 2010; 22: 481-94.

19. Treede RD, Jensen TS, Campbell JN, Cruccu G, Dostrovsky JO, Griffin JW *et al*. Neuropathic pain. Redefinition and a grading system for clinical and research purposes. Neurology. 2008; 70: 1630-5.

ANEXO

Anexo 1

K · F · R · I
KAISER FOUNDATION
RESEARCH INSTITUTE

THIS IS YOUR OFFICIAL COMMUNICATION FROM THE KPNC IRB REGARDING YOUR RECENT SUBMISSION.

July 20, 2012

Felice O'Ryan, DDS
Principal Investigator
Oakland

Re: Prevalence of Neuropathic Pain Following Sagittal Ramus Osteotomies of the Mandible

IRB Expiration Date: **July 17, 2013**

Dear Dr. O'Ryan:

Thank you for your submission to the Kaiser Permanente Northern California (KPNC) Institutional Review Board (IRB).

On July 18, 2012, a designated member of the IRB conducted an expedited review and **approved** your new study (initial application) for one year.

In addition, the following determinations were made:

- The requirement that informed consent be obtained from study participants was waived.
- The requirement that Privacy Rule authorization be obtained from study participants was waived.

Please review the attached documents entitled *Important Information about Your IRB Approval* and *HIPAA Privacy Rule Instructions*.

Sincerely,

Michael Shaffer, CIP
Team Lead, KPNC Health Services IRB
Michael.M.Shaffer@kp.org

CN-12FO'Ry-02-H Expedited (7)