Int. J. Oral Maxillofac. Surg. 2017; xxx: xxx–xxx
https://doi.org/10.1016/j.ijom.2017.10.020, available online at https://www.sciencedirect.com

International Journal of Oral & Maxillofacial Surgery

Clinical Paper
Oral Surgery

Treatment modalities and risk factors associated with refractory neurosensory disturbances of the inferior alveolar nerve following oral surgery: a multicentre retrospective study

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Abstract. Little research has been conducted into hypoesthesia, and no studies have elucidated the risk factors for refractory hypoesthesia and compared treatment modalities. The purpose of this multicentre retrospective cohort study was to investigate the relationships between various risk factors, treatment modalities, and refractory hypoesthesia. Risk factors for refractory hypoesthesia after oral surgery were evaluated using univariate and multivariate analysis. To minimize the selection bias associated with a retrospective data analysis, a propensity score analysis was performed between the medication and non-medication groups (65 sites in each group). Moderate or severe hypoesthesia (odds ratio 13.42) and no or late administration of ATP/vitamin B12 (odds ratio 2.28) were significantly associated with refractory hypoesthesia. In the propensity score analysis, the incidence rate of refractory hypoesthesia in the medication group was lower than that in the non-medication group ($P < 0.001$). This study demonstrated the multivariate relationships between various risk factors, treatment modalities, and refractory hypoesthesia. Moderate or severe hypoesthesia and no or late administration of ATP/vitamin B12 were significantly associated with refractory hypoesthesia. Therefore, clinicians should consider these risk factors and initiate early oral administration of ATP/vitamin B12 in cases of hypoesthesia.

Key words: neurosensory deficit; extraction; treatment; hypoesthesia.

Accepted for publication 3 October 2017

0901-5027/000001+08

Neurosensory disturbances of the inferior alveolar nerve (IAN) are common complications of oral surgery. Some patients may tolerate mild and moderate hypoesthesia. However, severe hypoesthesia may be difficult to tolerate and often requires treatment. The quality of life of patients with severe hypoesthesia can be significantly impaired. Therefore, this complication often leaves the patient dissatisfied with the surgery.

Neurosensory disturbance after lower third molar extraction occurs in 0.3–8.4% of cases[1–3]. Most cases of hypoesthesia are temporary, and the incidence of refractory hypoesthesia is generally <1%[4]. However, Cheung et al. reported that one-third of neurosensory deficits after lower third molar extractions may be permanent[5]. In a study of 2528 mandibular third molar extractions by Hasegawa et al., temporary hypoesthesia occurred in 1.5% of cases and refractory hypoesthesia (>6 months) occurred in 0.6% of cases[4]. Risk factors were the absence or diversion of the white line of the inferior alveolar canal on panoramic radiographs and excessive haemorrhage during extraction[4].

Many studies have demonstrated the incidence rate and risk factors of neurosensory disturbance (temporary hypoesthesia) after mandibular third molar extractions[4,6,7]. Various treatments have been reported, but their effects have been variable and controversial[2,8–11]. Few investigators have studied treatment modalities and sequential changes in hypoesthesia[2,9], and no studies have elucidated the risk factors for refractory hypoesthesia and compared treatment modalities. A study by Akashi et al. indicated current problems in the diagnosis and treatment of neurosensory complications after mandibular third molar extraction, and discussed the appropriate management of these complications[10]. It is hypothesized that some risk factors are linked to refractory hypoesthesia after oral surgery. The multivariate relationships between various risk factors, treatment modalities, and refractory hypoesthesia were investigated in this study.

Methods

This was a non-randomized, multicentre retrospective cohort study. This multicentre validation study included pooled individual patient data from seven institutions belonging to the Japanese Study Group of Cooperative Dentistry with Medicine (JCDM). The study subjects were patients who had undergone oral surgeries between January 2010 and December 2015 at the following institutes: Department of Oral and Maxillofacial Surgery, Kobe University Graduate School of Medicine; Department of Dentistry and Oral Surgery, Shinshu University School of Medicine; Department of Oral and Maxillofacial Surgery, Nara Medical University; Department of Clinical Oral Oncology, Nagasaki University Graduate School of Biomedical Sciences; Department of Oral and Maxillofacial Surgery, Nagoya City University Graduate School of Medical Sciences; Department of Oral and Maxillofacial Surgery, Wakayama Medical University; and Department of Dentistry and Oral Surgery, Kansai Medical University. Subjects were drawn from patients who had experienced postoperative hypoesthesia of the lower lip after receiving oral surgery at these institutions.

Patients with hypoesthesia caused by inflammatory diseases, nerve excision in cancer surgery, mandibular fracture, or orthognathic surgery were excluded. Therefore, the procedures included in this study were enucleation of cysts or benign lesions, tooth extraction, and the removal of foreign material. The primary endpoint was hypoesthesia that was still present at 6 months after surgery (refractory hypoesthesia). Cases in which the condition was unclear at 6 months after surgery were excluded. Cases in which the follow-up was completed at less than 6 months after surgery and hypoesthesia was still present were also excluded. This study was approved by the Institutional Review Board of Kobe University Graduate School of Medicine and by the institutional review boards of the respective hospitals.

Before surgery, each patient was informed about hypoesthesia and other surgery-associated risks, and gave their consent for treatment. Postoperative hypoesthesia of the lower lip was examined at 2 weeks and 1, 3, 6, and 12 months after surgery. The possibility of any impairment of labial and chin sensation was investigated by subjective symptoms, a two-point discrimination test, and light touch sensation. The two-point discrimination test was applied with blunt-tipped calipers to provoke a static stimulus. The inter-probe distance was then decreased in 2-mm increments from 20 mm apart, and patients were asked whether they sensed one or two points[12]. Light touch sensation was checked with a cotton pellet lightly touching the area of hypoesthesia[9,13–15]. A neurological examination assessed the degree of hypoesthesia and involved the use of questionnaires and a visual analogue scale (VAS)[16] graded from 0 (no sensitivity, i.e. anaesthesia) to 10 (completely normal sensitivity). Responses were classified as follows: 0–3, severe hypoesthesia; 4–6, moderate hypoesthesia; and 7–9, mild hypoesthesia.

Information was collected from all patients about a range of variables. Panoramic radiograph and computed tomography (CT) findings were categorized into three types: in type 1, the surgical site (for enucleation of cysts or benign lesions, tooth extraction, or the removal of foreign material) was separate from the IAN; in type 2, the surgical site impinged on the nerve; in type 3, the nerve was superimposed on the surgical site. Steroid use was noted, including the use of hydrocortisone, methylprednisolone, dexamethasone, and prednisolone. The oral administration of mecobalamin (vitamin B12) (Methycobal, 1500 μg/day; Eisai Co. Ltd, Tokyo, Japan) and adenosine triphosphate (ATP) (Adetphos, 180 mg/day; Kowa Co. Ltd, Tokyo, Japan) during the perioperative period was recorded, together with the duration and timing of administration. Other details recorded included whether the patient underwent a stellate ganglion block (SGB), including non-invasive SGB application using light irradiation (SG-LI), and the presence or absence of dysesthesia (painful sensation triggered by non-noxious stimuli). Details of these characteristics, as well as the demographic characteristics of the patients included, are listed in Table 1. Patients who did not consent to SGB received only observation or continued medication.

The timing of medication (oral ATP/vitamin B12) as an indicator of possible refractory hypoesthesia events was evaluated using a receiver operating characteristics (ROC) curve. The ROC curve was used to determine the cut-off values for clinical tests. The cut-off for increased risk of refractory hypoesthesia was 2 days based on the result of the ROC curve analysis, although this result was of low accuracy. Therefore, the patients were divided into two groups: the medication group (starting on day 0 or 1 postoperative) and the non-medication group (no medication or medication starting on day 2 or later postoperative).

When the data were introduced into a multiple logistic regression model, the patients were also divided according to the VAS grade (mild vs. moderate and severe hypoesthesia), the site of surgery (lower third molar vs. others), the extent of the surgical site (single tooth vs. multiple teeth), surgical procedure (tooth extraction only vs. others), and panoramic

Please cite this article in press as: Hasegawa T, et al. Treatment modalities and risk factors associated with refractory neurosensory disturbances of the inferior alveolar nerve following oral surgery: a multicentre retrospective study, *Int J Oral Maxillofac Surg* (2018),