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[Intervention Review]

Interventions for iatrogenic inferior alveolar and lingual nerve injury

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ABSTRACT

Background

Iatrogenic injury of the inferior alveolar or lingual nerve or both is a known complication of oral and maxillofacial surgery procedures. Injury to these two branches of the mandibular division of the trigeminal nerve may result in altered sensation associated with the ipsilateral lower lip or tongue or both and may include anaesthesia, paraesthesia, dysaesthesia, hyperalgesia, allodynia, hypoaesthesia and hyperaesthesia. Injury to the lingual nerve may also affect taste perception on the affected side of the tongue. The vast majority (approximately 90%) of these injuries are temporary in nature and resolve within eight weeks. However, if the injury persists beyond six months it is deemed to be permanent. Surgical, medical and psychological techniques have been used as a treatment for such injuries, though at present there is no consensus on the preferred intervention, or the timing of the intervention.

Objectives

To evaluate the effects of different interventions and timings of interventions to treat iatrogenic injury of the inferior alveolar or lingual nerves.

Search methods

We searched the following electronic databases: the Cochrane Oral Health Group's Trial Register (to 9 October 2013), the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2013, Issue 9), MEDLINE via OVID (1946 to 9 October 2013) and EMBASE via OVID (1980 to 9 October 2013). No language restrictions were placed on the language or date of publication when searching the electronic databases.

Selection criteria

Randomised controlled trials (RCTs) involving interventions to treat patients with neurosensory defect of the inferior alveolar or lingual nerve or both as a sequela of iatrogenic injury.

Data collection and analysis

We used the standard methodological procedures expected by The Cochrane Collaboration. We performed data extraction and assessment of the risk of bias independently and in duplicate. We contacted authors to clarify the inclusion criteria of the studies.

Interventions for iatrogenic inferior alveolar and lingual nerve injury (Review)

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Main results

Two studies assessed as at high risk of bias, reporting data from 26 analysed participants were included in this review. The age range of participants was from 17 to 55 years. Both trials investigated the effectiveness of low-level laser treatment compared to placebo laser therapy on inferior alveolar sensory deficit as a result of iatrogenic injury.

Patient-reported altered sensation was partially reported in one study and fully reported in another. Following treatment with laser therapy, there was some evidence of an improvement in the subjective assessment of neurosensory deficit in the lip and chin areas compared to placebo, though the estimates were imprecise: a difference in mean change in neurosensory deficit of the chin of 8.40 cm (95% confidence interval (CI) 3.67 to 13.13) and a difference in mean change in neurosensory deficit of the lip of 21.79 cm (95% CI 5.29 to 38.29). The overall quality of the evidence for this outcome was very low; the outcome data were fully reported in one small study of 13 patients, with differential drop-out in the control group, and patients suffered only partial loss of sensation. No studies reported on the effects of the intervention on the remaining primary outcomes of pain, difficulty eating or speaking or taste. No studies reported on quality of life or adverse events.

The overall quality of the evidence was very low as a result of limitations in the conduct and reporting of the studies, indirectness of the evidence and the imprecision of the results.

Authors' conclusions

There is clearly a need for randomised controlled clinical trials to investigate the effectiveness of surgical, medical and psychological interventions for iatrogenic inferior alveolar and lingual nerve injuries. Primary outcomes of this research should include: patient-focused morbidity measures including altered sensation and pain, pain, quantitative sensory testing and the effects of delayed treatment.

PLAIN LANGUAGE SUMMARY

Treatments for accidental damage during surgery to the nerves supplying sensation to the tongue, lower lip and chin

Review question

The main question addressed by this review is how effective are different treatments and what are the best timings for these treatments following accidental damage during surgery to the nerves that supply sensation to the tongue, lower lip and chin.

Background

The nerves (alveolar and lingual) supplying sensation to the tongue, lower lip and chin, may be injured as a result of surgical treatments to the mouth and face, including surgery to remove lower wisdom teeth. The vast majority (90%) of these injuries are temporary and get better within eight weeks. However if they last for longer than six months they are considered to be permanent. Damage to these nerves can lead to altered sensation in the region of the lower lip and chin, or tongue or both. Furthermore, damage to the nerve supplying the tongue may lead to altered taste perception. These injuries can affect people's quality of life leading to emotional problems, problems with socialising and disabilities. Accidental injury after surgery can also give rise to legal action.

There are many interventions or treatments available, surgical and non-surgical, that may enhance recovery, including improving sensation. They can be grouped as.

1. Surgical - a variety of procedures.
2. Laser treatment - low-level laser treatment has been used to treat partial loss of sensation.
3. Medical - treatment with drugs including antiepileptics, antidepressants and painkillers.
4. Counselling - including cognitive behavioural and relaxation therapy, changing behaviour and hypnosis.

Study characteristics

The Cochrane Oral Health Group carried out this review, and the evidence is current as of 9 October 2013. There are two studies included, both published in 1996, which compared low-level laser treatment to placebo or fake treatment for partial loss of sensation following surgery to the lower jaw. There were 15 participants in one study and 16 in the other, their ages ranging from 17 to 55 years. All had suffered accidental damage to nerves of the lower jaw and tongue causing some loss of sensation following surgery.

Key results

Low-level laser therapy was the only treatment to be evaluated in the included studies and this was compared to fake or placebo laser therapy. No studies were found that evaluated other surgical, medical or counselling treatments.

There was some evidence of an improvement when participants reported whether or not sensation was better in the lip and chin areas with low-level laser therapy. This is based on the results of a single, small study, so the results should be interpreted with caution.

No studies reported on the effects of the treatment on other outcomes such as pain, difficulty eating or speaking or taste. No studies reported on quality of life or harm.

Quality of the evidence

The overall quality of the evidence is very low as a result of limitations in the conduct and reporting of the two included studies and the low number of participants, and evidence from participants with only partial sensory loss.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Low-level laser treatment compared with placebo treatment for inferior alveolar and lingual nerve damage						
<p>Patient population: Patients with altered sensation due to inferior alveolar nerve injury Setting: Secondary care (dental hospital) Intervention: Low-level laser treatment (photon-plus GaAlAs diode laser; Rønvig Dental, Denmark: 70 mW output, continuous wavelength of 820 nm) Comparison: Placebo laser treatment</p>						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk ¹	Corresponding risk				
	Placebo treatment	Low-level laser treatment				
Pain.						This outcome was not reported in the included studies.
Sensation of the chin (spontaneous or evoked - anaesthesia/paraesthesia/dysaesthesia/hyperalgesia/allodynia) Patient-reported outcome: VAS scale 0 to 10 cm expressed as change (improvement)	The mean change in sensation in the placebo group was -0.68 cm	The mean change in sensation in the treatment group was 8.40 cm greater (95% CI 3.67 to 13.13) than in the placebo group		13 (1)	⊕○○○ very low ²	A positive change value indicates that neurosensory deficit was less post-treatment, i.e. an increase in subjective sensation The relative effect of the intervention is greater for the lip (13 patients analysed, MD 21.79, 95% CI 5.29 to 38.29) but imprecise
Difficulty eating.						This outcome was not reported in the included studies.

Difficulty speaking.			This outcome was not reported in the included studies.
Taste.			This outcome was not reported in the included studies.
Adverse events.			This outcome was not reported in the included studies.

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **MD:** mean difference; **VAS:** visual analogue scale.

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹ The basis for the assumed risk was the mean of the control group in the single included study.

² One, small trial assessed at high risk of bias. Imprecision of effect estimate and limited applicability as the trial included a small number of patients with only partial sensory loss.

BACKGROUND

The lingual and inferior alveolar nerves are branches of the third, or mandibular division, of the trigeminal nerve. The lingual nerve provides innervation to the ipsilateral anterior two-thirds of the tongue and the lingual mandibular gingivae, while the inferior alveolar nerve supplies sensation to the ipsilateral lower lip, buccal mandibular gingivae and teeth. The anatomical position of these nerves places them at increased risk of injury during certain surgical procedures. Iatrogenic injury of the inferior alveolar or lingual nerve is a relatively rare but serious sequelae of oral and maxillofacial surgery procedures. The aetiology of injuries to these nerves includes: dental local anaesthetic injection, third lower molar surgery, dental implant placement or removal, endodontic therapy, trauma, ablative surgery, orthognathic surgery, intubation, and submandibular gland surgery.

Description of the condition

Injury to the inferior alveolar nerve can result in impaired sensation to the area innervated by the damaged nerve, including altered sensation associated with the ipsilateral lower lip, chin, buccal mandibular gingivae and dentition. Damage to the lingual nerve may cause unilateral sensory deficit of the anterior two-thirds of the tongue and the lingual mandibular gingivae.

The impaired sensation can be classified as (www.iasp-pain.org).

- Paraesthesia - An abnormal sensation, whether spontaneous or evoked.
- Anaesthesia - Complete absence of perception of stimuli including touch.
- Dysaesthesia - An unpleasant abnormal sensation, whether spontaneous or evoked.
- Hyperalgesia - Increased pain from a stimulus that normally provokes pain.
- Allodynia - Pain due to a stimulus that does not normally provoke pain.
- Hypoaesthesia - Decreased sensitivity to stimulation, excluding the special senses.
- Hyperaesthesia - Increased sensitivity to stimulation, excluding the special senses.

The injury to the lingual nerve may also affect taste perception on the same side.

- Ageusia - Loss of taste perception.
- Dysgeusia - Altered taste perception.

The vast majority (approximately 90%) of these injuries are temporary in nature and resolve within eight weeks ([Blackburn 1990](#); [Mason 1988](#); [Pogrel 2001](#)). However, if the injury persists beyond six months it is deemed to be permanent ([Rood 1990](#)). Neurosensory disturbances arising from damage to the inferior alveolar or lingual nerve can cause significant distress; patients often complain

of a lower quality of life, psychological discomfort, and social disability and handicap ([Lam 2003](#); [Meyer 2001](#)). Iatrogenic injuries are also a prevalent medico-legal issue.

Description of the intervention

This review is based on a Cochrane protocol 'Interventions for iatrogenic inferior alveolar nerve injury' (New Reference). There are a number of reported interventions for the treatment of iatrogenic nerve injury; they can be categorised as follows.

(1) Surgical intervention.

- External neurolysis: This is a technique that involves releasing the nerve from its connective tissue bed and removing any restrictive fibrous/scar tissue or bone. Injury to the surrounding tissue may result in scar tissue formation which may cause compression/constriction of the nerve and block nerve transmission, or in some cases prevent nerve recovery ([Greenwood 2005](#); [Joshi 2002](#)).

- Internal neurolysis: This is a technique that aims to examine and release the nerve fascicles from epineural fibrosis. It is indicated where there is evidence of nerve fibrosis and associated changes in the appearance of the nerve. This procedure is not recommended by some surgeons as it may lead to further scar tissue formation ([Ziccardi 2007](#)).

- Neuroorrhaphy: This method is also called coaptation or direct anastomosis. It is indicated where the nerve is transected and its two ends can be sutured together without tension. Usually, defects of less than 1 cm can be repaired by direct suture. Immediate repair using this method is advocated when a nerve transection is witnessed ([Tay 2008](#)). The repair is by approximation of the two ends and application of epineural sutures.

- Neuroma excision: The formation of a neuroma is the result of disorganised axonal regeneration or sprouting at the injury site in an attempt to reach the distal stump. The aetiology of this injury may include not only section of the nerve but also crushing, laceration, stretching, and the pathological effects of objects such as root tips, endodontic medicaments, implants etc ([Chau 1989](#); [Gregg 1990](#)). It may be in the form of an amputation neuroma, lateral neuroma or neuroma in continuity. The nerve fibres within a neuroma may show abnormal spontaneous activity or mechanical sensitivity resulting in the development of sensory disorders such as dysaesthesia ([Devor 1994](#)). The surgical treatment of choice is excision of the neuroma, followed by direct apposition and suturing, or grafting depending on whether the nerve stumps can be approximated without tension.

- Autologous nerve grafting: This method allows for bridging of a defect between nerve stumps in cases where the post-injury defect does not allow for direct approximation of the neural ends without tension. The donor tissue for such interpositional grafts is usually the sural nerve, greater auricular nerve or medial

antebrachial nerve (Eppley 1991; Jones 1992; Wessberg 1982). However, autologous nerve graft techniques involve unavoidable donor site morbidity. Alternatively, denatured skeletal muscle autografts can be used (Rath 2002).

- Tubulization: In cases where post-injury defects do not allow for direct apposition, a hollow conduit structure can also be used that allows nerve regeneration to occur. Autologous as well as alloplastic materials can be used. Pogrel 2001 advocates the use of saphenous vein for repair of the lingual nerve and facial vein for inferior alveolar nerve repair. Alloplastic conduits for reconstruction of lingual and inferior alveolar nerve defects include: polyglycolic acid (PGA) bioabsorbable tubes (Crawley 1992), PGA-collagen tubes (Seo 2008), collagen tubes (NeuraGen) (Farole 2008), and Gore-Tex tubes (Pitta 2001; Pogrel 1998). However, there is general agreement that more studies in the field are necessary.

(2) Laser treatment.

Low-level laser therapy has been used for the treatment of partial sensory loss in patients suffering from iatrogenic injuries to the inferior alveolar nerve (Khullar 1996a; Khullar 1996b). The application of the laser treatment before and after surgical procedures including sagittal split osteotomies has been shown to speed up the recovery process (Miloró 2000).

(3) Medical treatment.

Injury to a peripheral nerve may result in changes within the central nervous system. Dysfunction of the peripheral and central neurons may lead to the development of neuropathic pain. The pharmacological treatment of this condition is based on the following medications: antiepileptics, antidepressants and analgesics (Clark 2008; Heir 2008). These drugs can be administered via enteral and topical routes.

(4) Counselling.

This group of interventions includes psychological treatment and sensory re-education methods (Meyer 2001). These may employ the following techniques: cognitive behavioural therapy, relaxation therapy, behaviour modification, electromyographic biofeedback, and hypnosis (Dworkin 1997, Feinmann 2004).

How the intervention might work

The aim for any intervention for the treatment of peripheral sensory nerve injury is to improve the neurosensory perception and therefore the quality of life of the patient. However, although many attempts have been made to improve results, these have had limited success, outcomes to date have been variable, and full recovery is extremely difficult to achieve. Ultimately any intervention should aim to reduce morbidity and improve the patient's quality of life.

Why it is important to do this review

At present, there appears to be no consensus on the type of intervention (surgical, medical, psychological), or the timing of intervention for the treatment of iatrogenic alveolar and lingual nerve injury. Given the morbidity and significant psychological distress arising from such injuries it is important to establish the effects of the available interventions.

OBJECTIVES

To evaluate the effects of different interventions and timings of interventions to treat iatrogenic injury of the inferior alveolar or lingual nerves.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised controlled trials (RCTs) comparing interventions for the treatment of iatrogenic inferior alveolar or lingual nerve injury. We planned to include trials comparing an active intervention to no treatment and trials that directly compared active interventions. We planned to include trials of interventions at any time point.

Types of participants

Patients of any age in any setting requiring intervention for iatrogenic injury to the inferior alveolar or lingual nerve.

Types of interventions

Comparisons of different active interventions (at all reported time points), or comparisons of different interventions with no treatment. We also planned to include trials of the same intervention delivered at different time points. For the purpose of analysis we have categorised the treatments as follows.

- Surgical: exploration and external neurolysis, internal neurolysis, neuroorrhaphy, neuroma excision, tubulization, grafting, laser.
- Medical: systemic medications (analgesics, antidepressants, antiepileptics, steroids), topical agents (analgesics, anaesthetics).
- Psychological: counselling, acupuncture, cognitive behavioural therapy, relaxation therapy, behaviour modification, electromyographic biofeedback, hypnosis, re-education.

Types of outcome measures

Primary outcome measures

- Pain.
- Patient-reported altered sensation (spontaneous or evoked - anaesthesia/paraesthesia/dysaesthesia/hyperalgesia/allodynia).
- Difficulty eating.
- Difficulty speaking.
- Taste.

Secondary outcome measures

- Quality of life/patient satisfaction.
- Adverse events.
- Mechanosensory (pin prick/two-point/light touch/pressure thresholds/pain thresholds/thermal thresholds).
- Thermosensory.
- Somatosensory evoked potentials.

The primary outcomes were chosen to reflect the importance of patient-reported outcomes.

Where outcomes were deemed to be measuring the same concept but measured in different ways (e.g. using different measurement scales), we planned to combine the outcomes, using statistical measures (e.g. standardised mean difference) where appropriate. If outcomes are measured at multiple time points we planned to categorise the time of measurement as closest to < 3 months, < = 6 months and > 6 months post-operative.

Search methods for identification of studies

Detailed search strategies were developed for each database searched. No restrictions were placed on the language of publication when the electronic databases were searched. These were based on the search strategy developed for MEDLINE (OVID) but revised appropriately for each database. The search strategy combined the subject search with the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE, as published in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011), chapter 6.4.11.1. The search strategy used a combination of controlled vocabulary and free text terms. Searches were undertaken in October 2013.

Electronic searches

We searched the following electronic databases:

- the Cochrane Oral Health Group's Trial Register (to 9 October 2013) (Appendix 1);
- the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2013, Issue 9) (Appendix 2);
- MEDLINE via OVID (1946 to 9 October 2013) (Appendix 3);

- EMBASE via OVID (1980 to 9 October 2013) (Appendix 4).

Searching other resources

The bibliographies of identified RCTs and review articles were checked for additional studies.

Handsearching

Handsearching was performed by staff at the Cochrane Oral Health Group using specially selected journals. The list of the dental journals handsearched by the Cochrane Oral Health Group can be found on the following website (www.ohg.cochrane.org/handsearching.html). The following journals were identified as being important to be handsearched for this review: *British Journal of Oral and Maxillofacial Surgery*, *International Journal of Oral and Maxillofacial Surgery*, *Journal of the American Dental Association*, *Journal of Dental Research*, *Journal of Oral and Maxillofacial Surgery*, *Oral Surgery Oral Medicine Oral Pathology Oral Radiology and Endodontics*, *Journal of the American Dental Association*, *Australian Dental Journal*, *British Dental Journal*, *Journal of Orofacial Pain*, and *European Journal of Oral Sciences*.

Unpublished studies

The ClinicalTrials.gov and [WHO International Clinical Trials Registry Platform](http://WHOInternationalClinicalTrialsRegistryPlatform) were searched in October 2013 for ongoing studies. Personal contacts were also used to identify unpublished RCTs.

Data collection and analysis

Selection of studies

Three review authors scanned independently the titles and abstracts (where available) of all reports identified by the search strategy. For studies that appeared to meet the inclusion criteria or for which there was insufficient information in the title or abstract to make a clear decision, the full report was obtained. These were assessed independently by at least two review authors to establish whether the studies were eligible for inclusion. Disagreements were resolved by discussion. Where resolution was not possible, we planned to consult a third review author but this was not necessary. Any studies rejected at this or subsequent stages were recorded in the [Characteristics of excluded studies](#) table, and the reason for exclusion recorded.

Data extraction and management

Three review authors extracted data independently using a specially designed and piloted data extraction form. Any disagreement or points that required clarification were discussed and resolved through discussion. It was agreed that trial authors would be contacted for clarification of missing or ambiguous information/data if required.

For each trial the following data were recorded.

- Year of publication, country of origin and source of study funding.
- Study design.
- Details of the participants including demographic characteristics, source of recruitment and criteria for inclusion.
- Details of the type and timing of the intervention and comparator.
- Details of the outcomes reported, including method and timing of assessment.

Where summary outcome data were not fully reported we planned

to use information from effect estimates, confidence intervals and test statistics wherever possible.

Assessment of risk of bias in included studies

The assessment of risk of bias of the included trials was undertaken independently and in duplicate by the review authors as part of the data extraction process. We used the recommended approach for assessing risk of bias in studies included in Cochrane reviews (Higgins 2011). We assessed each study on six specific domains (namely sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting and other sources of bias) and assigned a risk of bias of low, high or unclear for each domain. For the blinding domain we assessed separately the risk of bias from blinding of participants/personnel and outcome assessors.

After carrying out the risk of bias assessments, included studies were categorised as illustrated in Additional Table 1.

We completed a risk of bias table for each included study and presented the results graphically (Figure 1).

Figure 1. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Khullar 1996a	?	?	+	+	+	-	+
Khullar 1996b	?	?	+	+	-	+	+

Measures of treatment effect

For dichotomous outcomes, the estimate of effect of an intervention was planned to be expressed as risk ratios together with 95% confidence intervals (CIs); mean differences and 95% CIs for continuous outcomes measured on the same scale and standardised mean differences and 95% CIs for continuous outcomes measured on different scales. For ease of interpretation we planned to re-express the standardised mean difference on a known scale.

Dealing with missing data

Where information about the study design or outcome measures was unclear or missing, we contacted authors of the studies in order to obtain further information about the trial.

Assessment of heterogeneity

We planned to assess clinical heterogeneity through examining the types of participants and interventions for all outcomes in each study. We planned to assess statistical heterogeneity through Cochran's test of heterogeneity and the I^2 statistic. Only if there were studies of similar comparisons reporting the same outcome

measures would meta-analyses have been carried out.

Data synthesis

Data synthesis was planned using risk ratios for dichotomous data and mean differences or standardised mean differences for continuous data, together with 95% CIs. Each intervention would be categorised according to surgery, medical or psychological as per [Types of interventions](#) section. Where the information was limited we planned to use a fixed-effect model to pool the data; we would use a random-effects model with a larger number of studies of the same comparison.

For each comparison, we considered whether pooling of results through a meta-analysis was appropriate, based on clinical and methodological characteristics of the studies. Where there was heterogeneity that could not readily be explained we would consider a random-effects model. With this approach, the confidence intervals for the average intervention effect would be wider than those obtained with a fixed-effect approach, leading to a more conservative interpretation. When information is limited, either because there are few studies or if the studies are small, a random-effects analysis would provide poor estimates of the width of the distribution of intervention effects and in such instances we would provide a narrative report of the results.

Subgroup analysis and investigation of heterogeneity

Subgroup analyses were to be undertaken in respect of the experience of surgeon (junior/senior) and the timing of the intervention (< 3 months, < = 6 months and > 6 months post-operative).

Sensitivity analysis

We planned to undertake sensitivity analyses to examine the effect of blinded outcome assessment on the overall estimates of effect for each intervention.

Presentation of main results

A summary of findings table was developed for the primary outcomes of this review using GRADEProfiler software. The quality of the body of evidence was assessed with reference to the overall risk of bias of the included studies, the directness of the evidence, the inconsistency of the results, the precision of the estimates, the risk of publication bias, the magnitude of effect and whether or not there was evidence of a dose response. The quality of the body of evidence for each of the primary outcomes was categorised as high, moderate, low or very low.

RESULTS

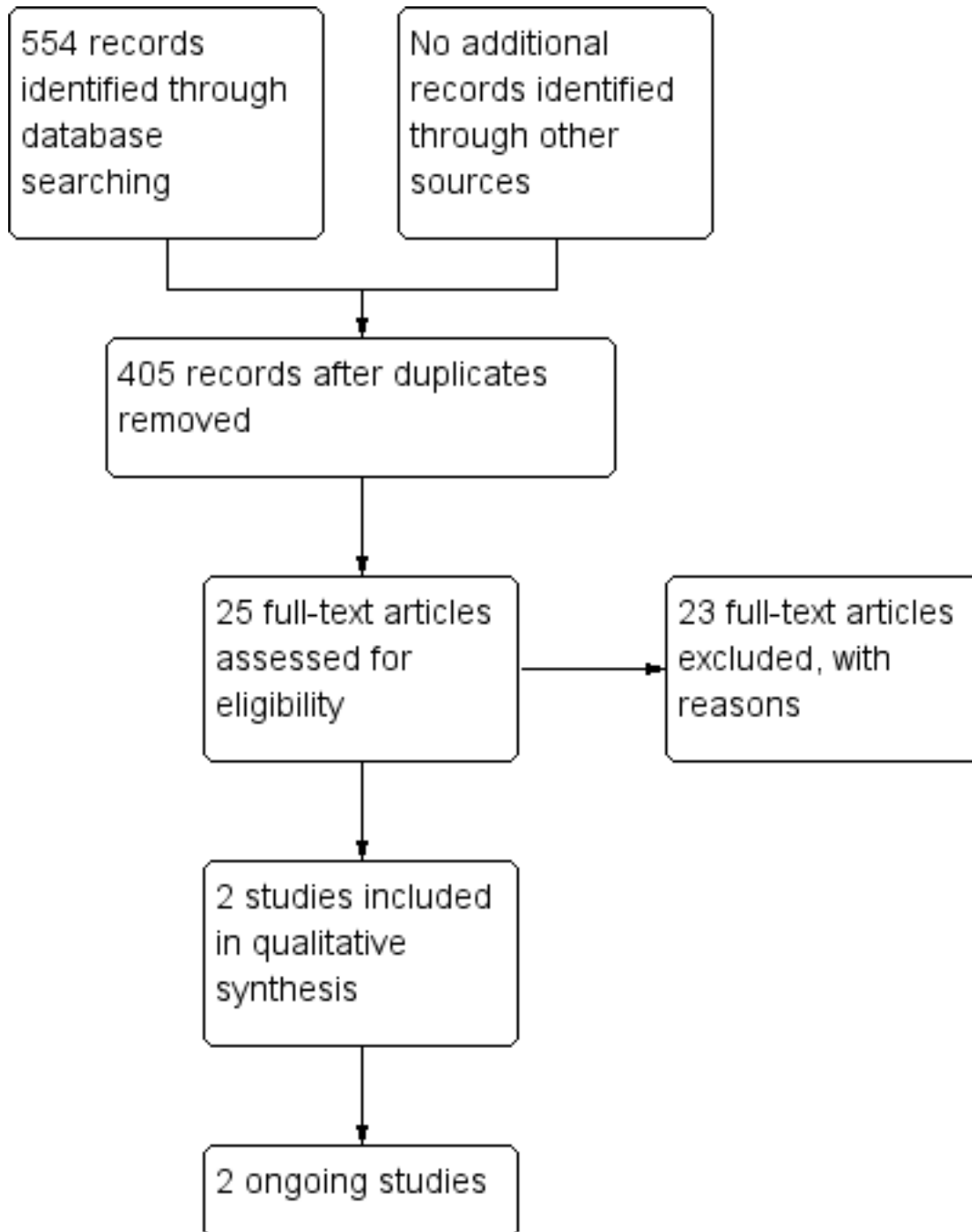
Description of studies

Results of the search

The electronic search identified a total of 554 publications of which 405 remained after removing duplicates. Two review authors independently screened the titles and abstracts (where available) for eligibility. 25 publications were considered potentially eligible and full text copies were obtained. Of this number, 23 studies were considered ineligible for inclusion as they were not randomised controlled trials (RCTs).

No additional eligible trials were found as a result of handsearching, contact with authors or searching references lists of relevant publications. Two ongoing studies were identified. ([Figure 2](#)).

Figure 2. Study flow diagram.



Included studies

Two RCTs were included in this review, one conducted in Norway (Khullar 1996a) and the other in Sweden (Khullar 1996b). Both trials used a parallel study design and compared the effect of surgical intervention (low-level laser treatment) versus placebo. A total of 31 patients were randomised across the two trials and 26 patients were evaluated. Information about the trials is provided in the [Characteristics of included studies](#) section. No studies evaluated medical or psychological interventions.

Excluded studies

23 studies were excluded from the review as they were not RCTs (for reference see [Characteristics of excluded studies](#) table).

Risk of bias in included studies

The overall risk of bias assessments for the two included studies are shown in [Figure 1](#). Both studies were assessed as at high risk of bias overall, arising from selective outcome reporting (Khullar 1996a) and incomplete outcome data (Khullar 1996b).

Allocation

No information was provided about allocation concealment or sequence generation in either included study (Khullar 1996a; Khullar 1996b). We classified both trials as being at unclear risk of selection bias.

Blinding

We assessed both studies at low risk of performance bias and detection bias (Khullar 1996a; Khullar 1996b).

Incomplete outcome data

Post-randomisation exclusions were minimal and evenly distributed across the intervention and comparator groups in one trial (Khullar 1996a) which we assessed as at low risk of attrition bias, but were significant and unevenly distributed (all exclusions in the placebo arm) in the other trial (Khullar 1996b), which we assessed as at high risk of attrition bias.

Selective reporting

Subjective rating of sensory function was incompletely reported (text in the abstract only) in one study which we assessed as at high risk of reporting bias (Khullar 1996a), while all outcome data were fully reported in the second (Khullar 1996b).

Other potential sources of bias

Both studies appeared to be free of other sources of bias.

Effects of interventions

See: [Summary of findings for the main comparison](#)

The only intervention to be evaluated in the included studies was surgery (low-level laser) and this was compared to placebo laser. No studies evaluated medical or psychological interventions.

Surgical intervention (low-level laser) compared to placebo (placebo laser)

Two, two-arm, parallel group trials (Khullar 1996a; Khullar 1996b) compared the effect of surgical intervention (low-level laser treatment) versus placebo (placebo laser) for the treatment of inferior alveolar nerve injury. A total of 31 patients were randomised across the two trials. Of the primary outcome measures for evaluation in this review, only subjective rated altered sensation was reported in the included studies. One study with 13 analysed patients reported patient's subjective assessment of the degree of sensory deficit on a 10 cm visual analogue scale (VAS) (Khullar 1996b). There was some evidence of an effect, with the laser group reporting an improvement in subjective assessment of neurosensory deficit (i.e. a reduction in degree of sensory deficit), as measured by the VAS scale. This was observed for both sites of measurement: the chin (mean difference (MD) 8.40; 95% confidence interval (CI) 3.67 to 13.13) and the lip (MD 21.79; 95% CI 5.29 to 38.29). The confidence intervals were relatively wide, indicating imprecision of the estimate of effect. In the second study (Khullar 1996a) a subjective improvement in sensory function for the laser group was reported in abstract but no details of this outcome were reported in the methods or results section of the paper. The overall quality of evidence for this outcome was assessed as very low ([Summary of findings for the main comparison](#)).

No studies reported on pain, difficulty eating or speaking or taste. Of the secondary outcome measures for evaluation in this review, only mechanosensory and thermosensory outcomes were reported (two studies, 26 patients analysed).

- Mechanosensory perception was tested using Semmes Weinstein monofilaments (North Coast Medi-Tek, San Jose, California, USA). Khullar 1996a reported a statistically significant difference in the change in load (g) necessary to elicit a sensation between the treatment and placebo groups (13 patients analysed, MD 1.07; 95% CI 0.17 to 1.97) in favour of the treatment group. This finding was not observed in the second study (Khullar 1996b); on average, there was a greater reduction in load (g) necessary to elicit a sensation for patients

with neurosensory deficit of the lip and chin in the treatment group than the control group. These results were not statistically significant however, the range of effects within the confidence intervals included no intervention effect and a beneficial effect of the intervention (13 patients analysed with neurosensory deficit of the chin, MD 0.54; 95% CI -0.12 to 1.19; 10 patients analysed with neurosensory deficit of the lip, MD 0.50; 95% CI -0.33 to 1.32).

- Both studies reported no significant changes in thermal perception with treatment (Khullar 1996a; Khullar 1996b); there was no evidence of an improvement in thermal perception with the low-level laser compared to placebo laser (12 patients analysed, MD 1.79; 95% CI -2.04 to 5.62; 13 patients analysed, MD 3.21; 95% CI -1.67 to 8.09). In the second study “normal pre-treatment values were excluded from statistical analysis” which meant that results are available only for the site of left chin and not for the sites of right chin, left and right lip.

No studies reported on quality of life, somatosensory evoked potentials, or adverse events.

DISCUSSION

Summary of main result

Despite the large number of studies detailing different interventions for the treatment of iatrogenic trigeminal nerve injury, we found only two, small, low quality randomised controlled trials of laser therapy which were eligible for inclusion in this review. Surgical and non-surgical methods have been reported as beneficial in some circumstances for the improvement of neurosensory deficit. However, such methods have yet to be fully evaluated in randomised controlled trials, and at present, no firm conclusions can be drawn as to whether any of these methods provide beneficial results. There is also a lack of trials directly comparing these methods or addressing the issue of optimal timing for carrying out the procedure. There are two ongoing studies (Chiang Shing Huang and Yu-Fang Liao). Despite the fact that they are both active randomised controlled trials, they are currently not recruiting participants.

Overall completeness and applicability of evidence

It has not been possible to fully achieve the objectives of this review as there is a lack of trials meeting the inclusion criteria. The number of included studies was low (two), and these only compared one type of intervention (laser treatment) against a placebo; crucially, the total number of participants randomised (31) was too few to fully address the efficacy of the intervention.

There were no studies evaluating the effects of other surgical interventions, or medical or psychological interventions. The included studies reported on only one (altered sensation) of the five patient-reported primary outcomes for evaluation in this review.

Quality of the evidence

These trials (Khullar 1996a; Khullar 1996b) cannot be considered as a valuable source of information on how to manage iatrogenic trigeminal nerve injury. The overall quality of the evidence was very low, a judgement based on limitations in the implementation and reporting of the trials and the imprecision of the results for the outcomes where reported, directness of the evidence (a small group of patients with only partial sensory loss). There is insufficient evidence that low-level laser therapy leads to improved or quicker neurosensory recovery and thus contributes to improvement of patients' quality of life.

Agreements and disagreements with other studies or reviews

This review includes only laser treatment for iatrogenic inferior alveolar nerve injury due to a lack of randomised controlled trials for other interventions. Nevertheless Miloro 2000 also reports positive results using low-level laser for sensation recovery after nerve damage.

AUTHORS' CONCLUSIONS

Implications for practice

There is a lack of evidence to support or refute the effects of the surgical, medical and psychological interventions in the treatment of inferior alveolar or lingual nerve injury, and very low quality evidence to support the effects of laser therapy on patient-reported altered sensation. Despite the lack of evidence, we should not abandon the development of early referral criteria from general practitioners to specialist centres. All front-line healthcare staff should be educated and trained in this area to increase and improve awareness, and to recognise and provide support for people with these injuries. This training should emphasize the competence of the surgeon, methods to help avoid iatrogenic nerve injury, and the effect these injuries can have on a patient's quality of life.

Implications for research

There is a need for randomised controlled clinical trials to investigate the effectiveness of surgical, medical and psychological interventions for iatrogenic inferior alveolar and lingual nerve injuries.

These trials should be conducted in specialist centres seeing large numbers of patients presenting with inferior alveolar or lingual nerve injury. Primary outcomes of such research should include: patient-focused morbidity measures, altered sensation, pain, quantitative sensory testing and the effects of delayed treatment. Improved partnership between local general practitioners in the primary care setting and secondary specialist healthcare organisations may be the first crucial step in the development of such trials in this area.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Khullar 1996a

Methods	Randomised placebo-controlled trial, parallel groups.
Participants	A total of 15 patients requiring intervention due to post-surgical inferior alveolar nerve sensory abnormalities lasting longer than 6 months were recruited to the study. The 13 patients who were evaluated in the study suffered from neurosensory deficit subsequent to removal of mandibular wisdom teeth or mandibular fracture or mandibular sagittal split osteotomy. Mean age 36.7 years (SD 11.1 years range 17 to 53 years)
Interventions	Patients in the treatment group (n = 6 evaluated) received 20 sessions of a low-level laser treatment (photon-plus GaAlAs diode laser; Rønvig Dental, Denmark). 70 mW output in a continuous wavelength of 820 nm; spot of 0.13 cm ² ; incident power density 550 mW/cm ² , applied in the area of distribution of the inferior alveolar nerve. Patients in the placebo group (n = 7 evaluated) received placebo laser treatment Treatment was completed in 20 sessions over a period of between 39 and 69 days
Outcomes	Nerve damage as assessed by mechanosensory and thermosensory testing
Notes	The patients participating in the study suffered only partial loss of sensation and had a normal response to heat pain. Only mechanosensory and thermosensory testing was conducted. None of the primary outcome measures we identified for this review were evaluated in the trial. Many patients showed a reduction in the area of reduced mechanopereception, but it was not possible to measure this accurately Small sample size.

Risk of bias

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly divided..." Comment: No information given about the method of sequence generation
Allocation concealment (selection bias)	Unclear risk	No information given about the method of allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "treatment was conducted blind." Comment: Assume as placebo comparator that participants were blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "double-blind." Comment: Assume that the outcome assessor was blinded.

Khullar 1996a (Continued)

Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "One patient in each group failed to complete treatment because of personal reasons." Comment: Drop-out low overall (1/7 laser, 1/8 placebo) and similar proportions across groups. Reasons for drop-outs the same
Selective reporting (reporting bias)	High risk	Individual data reported for outcome of nerve damage but subjective improvement in sensory function for intervention group reported in abstract but not appearing in methods or results section. Patient's subjective sensory assessment not fully reported
Other bias	Low risk	Study appears to be free of other sources of bias.

Khullar 1996b

Methods	Randomised placebo-controlled trial, parallel groups.
Participants	A total of 16 patients were recruited and randomised. The 13 patients evaluated (aged 20-55 years) had undergone sagittal split ramus osteotomy and passed the final check-up 2 years after surgery, but had suffered neurosensory deficit from injury to the inferior alveolar nerve. Patients who had received damage to the inferior alveolar nerve during the split procedure or who had the nerve dissected from the lateral ramus fragment were excluded from the study. Mean age 35.7 years (range 20 to 55 years), 4 male 9 female
Interventions	Patients in the treatment group (n = 8 evaluated) received 20 sessions of a low-level laser treatment (4x6 J per treatment: photon-plus GaAlAs diode laser; Rønvig Dental, Denmark). 70 mW output in a continuous wavelength of 820 nm; spot of 0.13 cm ² ; incident power density 550 mW/cm ² , applied in the area of distribution of the inferior alveolar nerve The placebo group (n = 5 evaluated) received placebo treatment The treatment was conducted in 20 sessions over a period of between 20 and 63 days (mean 31 days)
Outcomes	Patient's subjective assessment on VAS, nerve damage as assessed by mechanosensory and thermosensory testing
Notes	The patients participating in the study suffered only partial loss of sensation and had a normal response to heat pain. Small sample size

Risk of bias

Risk of bias

Bias	Authors' judgement	Support for judgement
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Khullar 1996b (Continued)

Random sequence generation (selection bias)	Unclear risk	Quote: “randomly divided...” Comment: No information given about the method of sequence generation
Allocation concealment (selection bias)	Unclear risk	No information given about the method of allocation used.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: “The LLL treatments and recording of data were performed by a second doctor not involved in the surgery. Analysis of the data was performed by a third doctor.” ... “conducted blind.” Comment: Assume as placebo comparator that participants were blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	As above. Data recording and analysis of data were performed by different investigators not involved in the study
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: “the study consisted of 16 patients, three of whom dropped out for personal reasons and all of whom were in the placebo group.” Comment: Drop-outs in placebo group only and significant proportion (3/8)
Selective reporting (reporting bias)	Low risk	Primary and secondary outcomes were fully reported.
Other bias	Low risk	Study appears to be free of other sources of bias.

SD = standard deviation; VAS = visual analogue scale.

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Blackburn 1992	Found not to be randomised controlled trial.
Cornelius 1997	Found not to be randomised controlled trial.
Crawley 1992	Found not to be randomised controlled trial.

(Continued)

Farole 2008	Found not to be randomised controlled trial.
Greenwood 2005	Found not to be randomised controlled trial.
Grötz 1998	Found not to be randomised controlled trial.
Hillerup 1994	Found not to be randomised controlled trial.
Hillerup 2007	Found not to be randomised controlled trial.
Hillerup 2008	Found not to be randomised controlled trial.
Joshi 2002	Found not to be randomised controlled trial.
Miloro 2000	Found not to be randomised controlled trial.
Mozsary 1984	Found not to be randomised controlled trial.
Pitta 2001	Found not to be randomised controlled trial.
Pogrel 1998	Found not to be randomised controlled trial.
Pogrel 2001	Found not to be randomised controlled trial.
Robinson 1996	Found not to be randomised controlled trial.
Rutner 2005	Found not to be randomised controlled trial.
Schultes 2000	Found not to be randomised controlled trial.
Seo 2008	Found not to be randomised controlled trial.
Strauss 2006	Found not to be randomised controlled trial.
Susarla 2007	Found not to be randomised controlled trial.
Tay 2008	Found not to be randomised controlled trial.
Zuniga 1997	Found not to be randomised controlled trial.

Characteristics of ongoing studies [ordered by study ID]

Chiung Shing Huang

Trial name or title	Sensory retraining exercise facilitates sensory recovery after bilateral sagittal split osteotomy - a randomised controlled trial
Methods	Randomised controlled trial.
Participants	<p>Inclusion criteria.</p> <ul style="list-style-type: none"> • Taiwanese adults (18-40 years old). • Developmental dentofacial disharmony (Class III). • Patients received orthognathic surgery (BSSO alone or with maxillary procedure). <p>Exclusion criteria.</p> <ul style="list-style-type: none"> • Medical condition associated with systemic neuropathy. • Unwilling to sign informed consent. • Congenital anomaly or acute trauma affecting the face. • Previous facial surgery. • Positive pain sensation at first week of post-surgery. • Altered sensation before orthognathic surgery as numbness or unusual feeling. • Cleft lip and palate.
Interventions	<p>Behavioural: sensory retraining protocol:</p> <ol style="list-style-type: none"> 1. within 1 month after the surgery: facial massage and physical stimulation over lower face and lip, 4 times (20 minutes each time) a day; 2. 1 to 3 months after the surgery: brush and physical stimulation over lower face and lip, 4 times (20 minutes each time) a day; 3. 3 to 6 months after the surgery: brush, pin and physical stimulation over lower face and lip, 4 times (20 minutes each time) a day. <p>Other name: sensory retraining.</p>
Outcomes	<p>Sensory function test (Time frame: 1 year after surgery) (designated as safety issue: no)</p> <p>The sensory function evaluation include objective and subjective examinations as the followings</p> <ul style="list-style-type: none"> • Questionnaire. • Visual analogue scale (VAS). • 2-point discrimination (2PD). • Pain detection threshold (PD) tests. • Touch sensory threshold.
Starting date	April 2012.
Contact information	Chiung Shing Huang, PhD, DDS; Chang Gung Memorial Hospital.
Notes	This study is ongoing, but not recruiting participants.

Yu-Fang Liao

Trial name or title	Inferior alveolar nerve injury after bilateral sagittal split osteotomy in oral clefts
Methods	Observational model: case control. Time perspective: prospective.
Participants	Inclusion criteria. <ul style="list-style-type: none">• Patients with non-syndromic cleft lip and palate (age, > 16 for females, > 18 for males), who will undergo Dal Pont type BSSO as a part of the correction of their dentofacial deformities, from Chang Gung Craniofacial Center, Taoyuan. Exclusion criteria. <ul style="list-style-type: none">• Patients with history of previous BSSO or mandibular fracture.• Patients with craniofacial anomaly.• Patients with inferior alveolar nerve disturbances before BSSO.• Patients with inferior alveolar nerve being cut or drilled at BSSO.• Patients who are non-compliant with test or test schedule.• Patients who are reluctant to sign informed consent.
Interventions	<ol style="list-style-type: none">1. Determine the incidence of inferior alveolar nerve injury after BSSO.2. Identify the risk factors associated with such injuries.3. Understand the consequences of such injuries including the degree of neurologic recovery by performing a prospective, longitudinal study.
Outcomes	Assessment of changes in neurosensory function (Time frame: before surgery and 12 months after surgery) (Designated as safety issue: no) <ol style="list-style-type: none">1. Subjective assessment.2. Objective assessment: (1) 2-point (2-PD) discrimination, (2) light touch (LT) detection, (3) sharp-and-blunt nociception test.
Starting date	June 2013.
Contact information	Yu-Fang Liao, PhD; Department of Craniofacial Orthodontics, Chang Gung Memorial Hospital
Notes	This study is not yet open for participant recruitment. May not be randomised controlled trial.

BSSO = bilateral sagittal split osteotomy.

DATA AND ANALYSES

This review has no analyses.

ADDITIONAL TABLES

Table 1. Risk of bias categories and description

Risk of bias	Interpretation	Within a study	Across studies
Low risk of bias	Plausible bias unlikely to seriously alter the results	Low risk of bias for all key domains	Most information is from studies at low risk of bias
Unclear risk of bias	Plausible bias that raises some doubt about the results	Unclear risk of bias for one or more key domains	Most information is from studies at low or unclear risk of bias
High risk of bias	Plausible bias that seriously weakens confidence in the results	High risk of bias for one or more key domains	The proportion of information from studies at high risk of bias is sufficient to affect the interpretation of results

APPENDICES

Appendix I. Cochrane Oral Health Group's Trials Register search strategy

The search strategy for the Cochrane Oral Health Group's Trials Register has been amended for the Cochrane Register of Studies:

#1 ((“inferior dental nerve*” or “inferior alveolar nerve*” or “mandibular nerve*” or “trigeminal nerve*” or “lingual nerve*” or “lingual dental nerve*”) AND (INREGISTER)

#2 (“sensory disturbance*” or “taste disorder*” or “neurosensory deficit*” or “somatosensory disorder*” or hyperalgesia or hypoaesthesia or paraesthesia or hyposthesia or paraesthesia or injur* or damag* or contus* or section* or trauma* or lesion* or morbid*) AND (INREGISTER)

#3 ((repair* or surg* or anastamos* or graft* or medical* or analgesi* or antidepressant* or anti-depressant* or antiepileptic* or anti-epileptic*)) AND (INREGISTER)

#4 (#1 and #2 and #3) AND (INREGISTER)

The original version of this review used the following search strategy for the ProCite software:

((“inferior dental nerve*” or “inferior alveolar nerve*” or “mandibular nerve*” or “trigeminal nerve*” or “lingual nerve*” or “lingual dental nerve*”) AND (“sensory disturbance*” or “taste disorder*” or “neurosensory deficit*” or “somatosensory disorder*” or hyperalgesia or hypaesthesia or paresthesia or hypesthesia or paraesthesia or inju* or damage* or contus* or section* or trauma* or lesion* or morbid*) AND (repair* or surg* or anastamos* or graft* or medical* or analgesi* or antidepressant* or anti-depressant* or antiepileptic* or anti-epileptic*))

Appendix 2. CENTRAL search strategy

- #1 (inferior next dental next nerve* in All Text or inferior next alveolar next nerve* in All Text or mandibular next nerve* in All Text or trigeminal next nerve* in All Text)
- #2 “inferior alveolar nerve” in All Text
- #3 (lingual next dental next nerve* in All Text or lingual next nerve* in All Text)
- #4 MeSH descriptor Mandibular nerve this term only
- #5 MeSH descriptor Lingual Nerve this term only
- #6 (#1 or #2 or #3 or #4 or #5)
- #7 sensory next disturbance in All Text
- #8 MeSH descriptor Somatosensory disorders explode all trees
- #9 MeSH descriptor Taste disorders this term only
- #10 (hyperalgesia in All Text or hypesthesia in All Text or paresthesia in All Text or hypaesthesia in All Text or paraesthesia in All Text or “taste disorder*” in All Text)
- #11 (injur* in All Text or damage* in All Text or contus* in All Text or section* in All Text or trauma* in All Text or lesion* in All Text or morbid* in All Text or neurosensory next deficit* in All Text)
- #12 (#7 or #8 or #9 or #10 or #11)
- #13 (#6 and #12)
- #14 (repair* in All Text or surg* in All Text or anastamos* in All Text or graft* in All Text)
- #15 MeSH descriptor Neurosurgical procedures this term only
- #16 neurolysis in All Text
- #17 (medical* in All Text or analgesi* in All Text or antidepressant* in All Text or anti-depressant* in All Text or antiepileptic* in All Text or anti-epileptic* in All Text)
- #18 (#14 or #15 or #16 or #17)
- #19 (#13 and #18)

Appendix 3. MEDLINE via OVID search strategy

- 1. ((inferior adj dental adj nerve\$) or (inferior adj alveolar adj nerve\$) or (mandibular adj nerve\$) or (trigeminal adj nerve\$)).mp.
- 2. “inferior alveolar nerve\$”.mp.
- 3. (lingual adj dental adj nerve\$) or (“lingual adj nerve\$”).mp.
- 4. MANDIBULAR NERVE/
- 5. INFERIOR ALVEOLAR NERVE/
- 6. LINGUAL NERVE/
- 7. or/1-6
- 8. (sensory adj disturbance).mp.
- 9. exp SOMATOSENSORY DISORDERS/
- 10. TASTE DISORDERS/
- 11. (hyperalgesia or hypesthesia or paresthesia or hypaesthesia or paraesthesia or “taste disorder”).mp.
- 12. (injur\$ or damage\$ or contus\$ or section\$ or trauma\$ or lesion\$ or morbid\$ or (neurosensory adj deficit)).mp.
- 13. or/8-12
- 14. 7 and 13
- 15. (repair\$ or surg\$ or anastamos\$ or graft\$).mp.
- 16. NEUROSURGICAL PROCEDURES/
- 17. neurolysis.mp.
- 18. (medical\$ or analgesi\$ or antidepressant\$ or anti-depressant\$ or antiepileptic\$ or anti-epileptic\$).mp.
- 19. or/15-18
- 20. 14 and 19

Appendix 4. EMBASE via OVID search strategy

1. ((inferior adj dental adj nerve\$) or (inferior adj alveolar adj nerve\$) or (mandibular adj nerve\$) or (trigeminal adj nerve\$)).mp.
2. "inferior alveolar nerve\$.mp.
3. (lingual adj dental adj nerve\$) or ("lingual adj nerve\$").mp.
4. MANDIBULAR NERVE/
5. INFERIOR ALVEOLAR NERVE/
6. LINGUAL NERVE/
7. or/1-6
8. (sensory adj disturbance).mp.
9. exp SOMATOSENSORY DISORDERS/
10. TASTE DISORDERS/
11. (hyperalgesia or hypesthesia or paresthesia or hypaesthesia or paraesthesia or "taste disorder").mp.
12. (injur\$ or damage\$ or contus\$ or section\$ or trauma\$ or lesion\$ or morbid\$ or (neurosensory adj deficit)).mp.
13. or/8-12
14. 7 and 13
15. (repair\$ or surg\$ or anastamos\$ or graft\$).mp.
16. NEUROSURGICAL PROCEDURES/
17. neurolysis.mp.
18. (medical\$ or analgesi\$ or antidepressant\$ or anti-depressant\$ or antiepileptic\$ or anti-epileptic\$).mp.
19. or/15-18
20. 14 and 19

The above subject search was linked to the Cochrane Oral Health Group filter for identifying randomised controlled trials in EMBASE via OVID:

1. random\$.ti,ab.
2. factorial\$.ti,ab.
3. (crossover\$ or cross over\$ or cross-over\$).ti,ab.
4. placebo\$.ti,ab.
5. (doubl\$ adj blind\$).ti,ab.
6. (singl\$ adj blind\$).ti,ab.
7. assign\$.ti,ab.
8. allocat\$.ti,ab.
9. volunteer\$.ti,ab.
10. CROSSOVER PROCEDURE.sh.
11. DOUBLE-BLIND PROCEDURE.sh.
12. RANDOMIZED CONTROLLED TRIAL.sh.
13. SINGLE BLIND PROCEDURE.sh.
14. or/1-13
15. ANIMAL/ or NONHUMAN/ or ANIMAL EXPERIMENT/
16. HUMAN/
17. 16 and 15
18. 15 not 17
19. 14 not 18

HISTORY

Protocol first published: Issue 2, 2005

Review first published: Issue 4, 2014

Date	Event	Description
5 September 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

Conceiving, designing and co-ordination of the review (Tara Renton (TR), Paul Coulthard (PC)).

Developing the search strategy and undertaking the searches (PC, Evgeny Kushnerev (EK)).

Screening search results and retrieval of papers against inclusion criteria (PC, EK, Tanya Walsh (TW)).

Appraising quality and extracting data from papers (PC, EK, Julian M Yates (JMY), TW).

Writing to authors for additional information (EK, JMY).

Data management for the review and entering data into RevMan (PC, EK, TW).

Analysis and interpretation of data (PC, EK, JMY, Neil Patel (NP), Edmund Bailey (EB), TW).

Writing the review (PC, EK, TW).

Providing general advice on the review and proofreading (PC, TR, JMY, NP, EB, TW).

Performing previous work that was the foundation of current study (TR, PC).

DECLARATIONS OF INTEREST

Paul Coulthard, Evgeny Kushnerev, Julian M Yates, Tanya Walsh, Neil Patel, Edmund Bailey, Tara F Renton: no interests to declare.

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Disclaimer:

The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the NIHR, NHS or the Department of Health.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We wrote two separate protocols describing interventions for iatrogenic inferior alveolar nerve injury (0094) and interventions for iatrogenic lingual nerve injury (0093). These were almost identical and therefore the protocols were merged into a single protocol 'Interventions for iatrogenic inferior alveolar and lingual nerve injury' (0094) in 2009. The new search strategy has been developed for this review since the original protocols were written.

The primary outcome of 'altered sensation' in the protocol has been changed to 'patient-reported altered sensation' for the review.

INDEX TERMS

Medical Subject Headings (MeSH)

*Iatrogenic Disease; Lingual Nerve Injuries [*radiotherapy]; Low-Level Light Therapy [*methods]; Randomized Controlled Trials as Topic; Somatosensory Disorders [etiology; *radiotherapy]; Time Factors; Trigeminal Nerve Injuries [*radiotherapy]

MeSH check words

Humans