REVIEW ARTICLE

Paresthesia as a Result of Endodontic Sealer Extrusion: A Systematic Review

Genovefa Tsompani[1], Menelaos Anastasopoulos[2], Zafeiria Mavrogiannidou[3], Androniki Nasta[4]

Abstract

Aim: The aim of this systematic review is to accumulate the available evidence on management approaches as well as factors resulting in the development of paresthesia due to sealer extrusion.

Materials and methods: A literature search was conducted in MEDLINE, EMBASE, and Web of Science and Cochrane Central Register of Controlled Trials up to March 2022, accompanied by a manual search of journals, textbooks, and grey literature. Inclusion criteria were studies on adult patients experiencing paresthesia related to sealer extrusion. The quality of included studies was appraised using a custom set of criteria.

Results: A total of 102 publications were identified, and 9 of them fulfilled the inclusion criteria. All of the included studies were case reports describing a total of 10 patients. The predetermined data were independently extracted and evaluated by four reviewers.

Conclusion: Because of the low amount and quality of available evidence, conclusions on the factors resulting in paresthesia due to sealer extrusion cannot be drawn. The management approach remains empirical. The need for prospective studies is highlighted. The future case reports in endodontics ought to be reported in a uniform and methodological way.

Clinical significance: Paresthesia as a result of endodontic sealer extrusion is an alarming complication of endodontic treatment that general dentists need to be aware of. Although worrying, for both clinician and patient, it is a manageable complication and early diagnosis is important; thus, dentists need to be educated on this topic.

Keywords: Endodontic therapy, Paresthesia, Sealer extrusion, Systematic review.

The Journal of Contemporary Dental Practice (2022): 10.5005/jp-journals-10024-3339

Introduction

The purpose of endodontic treatment is the removal of vital or necrotic pulp tissue, canal cleaning, and subsequent filling of the root canal space.[1] During the obturation stage, gutta-percha combined with the sealer aim to provide a three-dimensional hermetic seal against fluids and microorganisms. Sealers act as luting agents, simultaneously filling the available root canal space and enhancing the sealing ability of the filling material.[2–4] As in every part of dental procedures, complications may emerge. Perforation of the mandibular canal due to over-instrumentation can result in extrusion of sealers and other materials.[5]

Nerve injury is a rare but serious complication that can occur in different stages of endodontic treatment.[6–12] Paresthesia is a neurosensitivity disorder which is expressed as numbness of the affected area, along with a tingling or burning sensation.[13] Although an infrequent complication, studies have demonstrated that it can be a result of errors during endodontic treatment such as the extrusion of sealer material.[14,15]

Clinicians rely on the best available evidence to make judicious decisions and provide preeminent care to patients.[16] The topic of endodontic related paresthesia has already been addressed in the past. This is the first review to systematically approach the topic of paresthesia as a result of endodontic sealer extrusion. The aim of this systematic review is to summarize the available data regarding the factors leading to the development of paresthesia as a result of endodontic sealer extrusion, and its management approaches. Since early diagnosis is of vital importance for the outcome of the treatment of paresthesia, it is important to methodologically gather all the available evidence on this topic and assess them via a systematic review.

[1–4]Department of Preventive Dentistry, Periodontology and Implant Biology, School of Dentistry, Aristotle University of Thessaloniki, Thessaloniki, Greece

Corresponding Author: Menelaos Anastasopoulos, Department of Preventive Dentistry, Periodontology and implant Biology, School of Dentistry, Aristotle University of Thessaloniki, Thessaloniki, Greece, Phone: +306987967892, e-mail: mene.anastas@gmail.com

How to cite this article: Tsompani G, Anastasopoulos M, Mavrogiannidou Z, *et al*. Paresthesia as a Result of Endodontic Sealer Extrusion: A Systematic Review. J Contemp Dent Pract 2022;23(5): 558–565.

Source of support: Nil

Conflict of interest: None

Materials and Methods

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[17] A protocol agreed by all authors was developed in advance according to the PRISMA-P guidelines.[18]

Review Questions

The following two focused questions were formed and addressed:

- In adult patients, experiencing paresthesia related to the extrusion of endodontic sealer, what are the factors affecting the development of paresthesia?

- In adult patients, experiencing paresthesia related to the extrusion of endodontic sealer, what are the management approaches to reduce/resolve the symptoms?

Literature Search

The MEDLINE, EMBASE, and Web of Science databases along with Cochrane Central Register of Controlled Trials were searched up to January 2022 to identify eligible studies. The search algorithm used was "[endodontic or (root canal) AND paresthesia AND (overfilling or extrusion)]". All issues of International Endodontic Journal, Journal of Endodontics, Australian Endodontic Journal and ENDO-Endodontic Practice Today were hand-searched for additional publications. In addition, the textbooks of "Endodontics," "Cohen's Pathways of the Pulp," and "Problem Solving in Endodontics" were scrutinized for potential studies. Grey literature was searched using GreyNet International (http://www.greynet.org) and Grey Literature Report (http://www.greylit.org). References of all articles were hand-searched to include any relevant publications. No restrictions regarding the language or publication date were applied. A follow-up search was conducted using the same keywords in March 2022 for the inclusion of additional articles.

Study Selection

Four reviewers (GT, MA, ZM, and AN) independently performed the study selection, by assessing the eligibility of the literature search results based on their titles and abstracts on the first stage, and full-text on the second stage. To avoid disregarding relevant publications, any articles providing limited information were included in the full-text analysis. Any potential disagreement was resolved with discussion.

Inclusion Criteria

Inclusion criteria included clinical studies, case reports, and case series on paresthesia as a result of extrusion of endodontic sealers in humans. Animal studies, *in vitro* studies, *ex vivo* studies, studies reporting the extrusion of root filling material along with sealer materials were not eligible for inclusion.

Quality Appraisal

A personalized set of criteria (Table 1) was developed to methodologically evaluate the quality of the included studies. This set was based on the consensus-based clinical case reporting guideline development (CARE) guidelines and previously suggested criteria for the evaluation of case reports.[19–21] The four reviewers independently appraised the included studies, and any disagreement was resolved with discussion.

Data Extraction

A standardized pre-decided form was used for the extraction of data from the studies. A list of the predetermined data extracted is presented in Table 2. The data extraction was performed independently by the four reviewers. Cases of disagreement were discussed by the reviewers until consensus was reached.

Table 1: Critical appraisal requirements

Selection bias
1. Is the selection method of patients clear to the extent that other patients with similar presentation may have not been reported?
Demographic information and medical history
2. Is the age and gender reported?
3. Is the medical history reported?
Information on endodontic treatment procedure
4. Involved tooth
5. Endodontic diagnosis of involved tooth
6. Information on the Endodontic procedure (materials used in detail, setting such as the use of rubber dam)
7. Description of the specific endodontic sealer used
Symptoms and diagnosis
8. Detailed description of diagnostic process (including radiographic examination)
9. Adequate report of patient symptoms
Management
10. Adequate description of the management, including a follow-up timeline

Table 2: Data to be extracted from included studies

1. Gender
2. Age
3. Medical history
Information of endodontic procedure
4. Involved tooth
5. Endodontic diagnosis
6. Sealer material used
7. Iatrogenic errors
8. The way the sealer material was introduced in the root canal
Diagnosis
9. Radiographic examination
10. Affected area
11. Symptoms reported
Management
12. Treatment option chosen and description of intervention
13. Follow-up timeline
14. Were the symptoms resolved?
Conflict of interest

Review Results

An overview of the selection process is presented in Flowchart 1. The literature search yielded 102 publications. After removing the duplicates (n = 41), 61 unique articles were identified for evaluation of titles and abstracts. Of those, 23 were eligible for full-text analysis. After the full-text analysis, nine publications fulfilled the inclusion criteria and were subsequently included in the review.[22–28] The list of excluded publications (n = 14) along with the reasons for exclusion is presented at Table 3. The included studies were case reports describing a total of 10 cases. Their publication date ranged from 1982 to 2020. Cohen's kappa was calculated to be 0.94 in the first stage and 0.96 in the second stage. A summary of the included case reports along with the extracted data is shown

Flowchart 1: Selection process

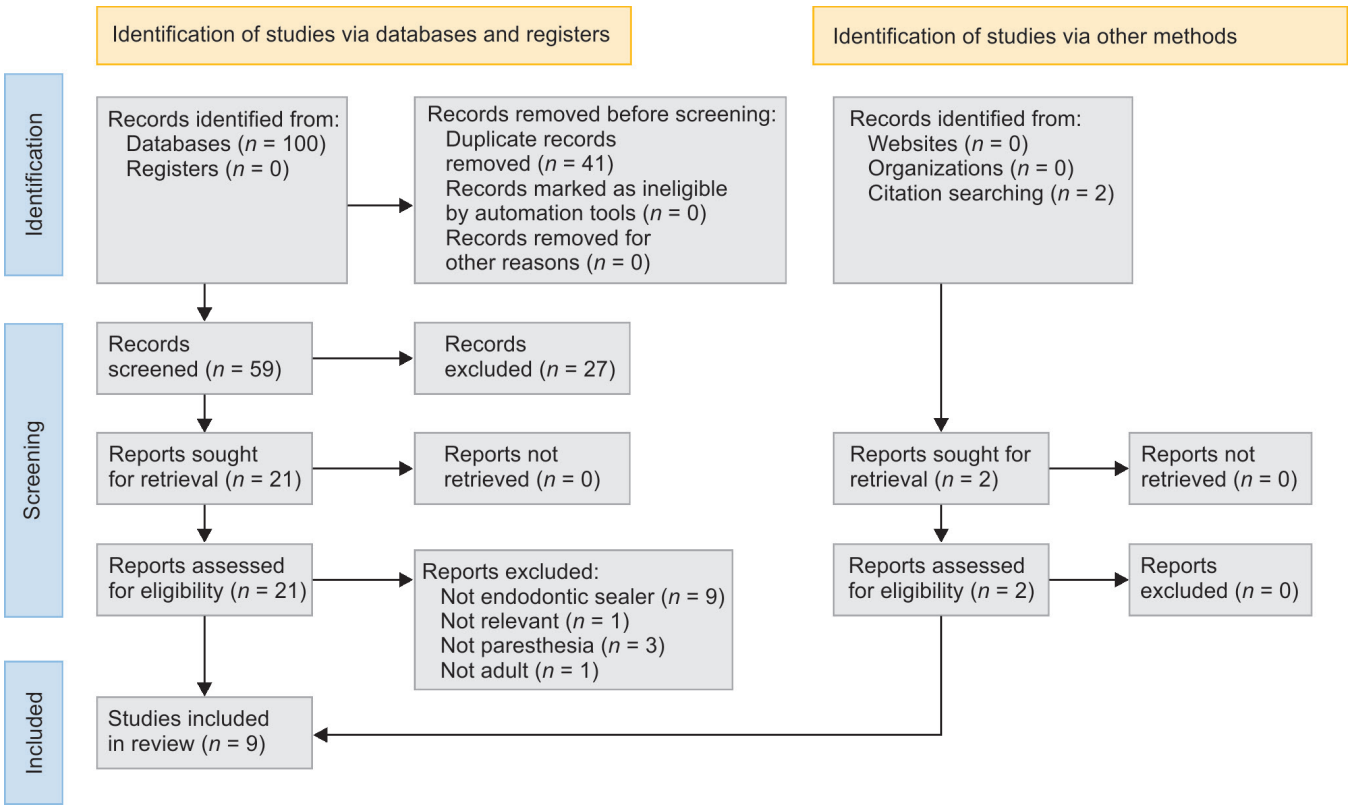

Table 3: Excluded publications with reason for exclusion

Author	*Reason for exclusion*
Grotz KA, Al-Nawas B, de Aguiar EG, et al. Treatment of injuries to the inferior alveolar nerve after endodontic procedures. Clin Oral Investig 1998;2(2):73–76. DOI: 10.1007/s007840050048.	Not endodontic sealer
Ngeow WC. Is there a "safety zone" in the mandibular premolar region where damage to the mental nerve can be avoided if periapical extrusion occurs? J Can Dent Assoc. 2010;76:a61. PMID: 20579448.	Not relevant
Byun SH, Kim SS, Chung HJ, et al. Surgical management of damaged inferior alveolar nerve caused by endodontic overfilling of calcium hydroxide paste. Int Endod J 2016;49(11):1020–1029. DOI: 10.1111/iej.12560.	Not paresthesia
Coskunses FM, Sinanoglu A, Helvacioglu-Yigit D, et al. The extrusion of root canal cement containing paraformaldehyde into the inferior alveolar nerve canal resulting in infection and numbness. Int Endod J 2016;49(6):610–617. DOI: 10.1111/iej.12510.	Not paresthesia
Olsen JJ, Thorn JJ, Korsgaard N, et al. Nerve lesions following apical extrusion of non-setting calcium hydroxide: a systematic case review and report of two cases. J Craniomaxillofac Surg 2014;42(6):757–762. DOI: 10.1016/j.jcms.2013.11.007.	Not endodontic sealer
Rosen E, Goldberger T, Taschieri S, et al. The prognosis of altered sensation after extrusion of root canal filling materials: a systematic review of the literature. J Endod 2016;42(6):873–879. DOI: 10.1016/j.joen.2016.03.018.	Not endodontic sealer
Bastien AV, Adnot J, Moizan H, et al. Secondary surgical decompression of the inferior alveolar nerve after overfilling of endodontic sealer into the mandibular canal: case report and literature review. J Stomatol Oral Maxillofac Surg 2017;118(6):389–392. DOI: 10.1016/j.jormas.2017.09.001.	Not paresthesia
Kudoh K, Takaishi K, Kudoh T, et al. Inferior alveolar nerve paresthesia caused by the extrusion of calcium hydroxide-based paste into the mandibular canal: a case report, J Oral Maxillofac Surg Med Pathol 2020;32(5):366–369. DOI: 10.1016/j.ajoms.2020.05.005.	Not endodontic sealer
Shin Y, Roh BD, Kim Y, et al. Accidental injury of the inferior alveolar nerve due to the extrusion of calcium hydroxide in endodontic treatment: a case report. Restor Dent Endod 2016;41(1):63–67. DOI: 10.5395/rde.2016.41.1.63.	Not endodontic sealer

Ahlgren FK, Johannessen AC, Hellem S. Displaced calcium hydroxide paste causing inferior alveolar nerve paraesthesia: report of a case. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2003;96(6):734–737. DOI: 10.1016/j.tripleo.2003.08.018.	Not endodontic sealer
Fonsêca MJ, Palmier RN, Amaral–Silva GK, et al. Massive extrusion of calcium hydroxide paste containing barium sulphate during endodontic treatment. Aust Endod J 2020;46(2):257–262. DOI: 10.1111/aej.12382.	Not endodontic sealer
Grossman LI. Paresthesia from N2 or N2 substitute. Report of a case. Oral Surg Oral Med Oral Pathol 1978;45(1): 114–115. DOI: 10.1016/0030-4220(78)90233-5.	Not adult
Gluskin AH, Lai G, Peters CI, et al. The double-edged sword of calcium hydroxide in endodontics: precautions and preventive strategies for extrusion injuries into neurovascular anatomy. J Am Dent Assoc 2020;151(5):317–326. DOI: 10.1016/j.adaj.2020.01.026.	Not relevant
Gambarini G, Plotino G, Grande NM, et al. Differential diagnosis of endodontic-related inferior alveolar nerve paraesthesia with cone beam computed tomography: a case report. Int Endod J 2011;44(2):176–181. DOI: 10.1111/j.1365-2591.2010.01816.x.	Not endodontic sealer

in Table 4. Due to the lack of prospective studies, only case reports were available and thus included in this study.

Quality Appraisal

The criteria of the quality assessment checklist were not fully met by any of the included studies. A summary of the quality appraisal checklist is presented at Table 5. No study clarified whether all the available cases to the author were reported. All studies provided the demographic information regarding the age and gender of patients. Two studies failed to report the patients' medical history. All studies reported the teeth involved; however, only four studies reported the diagnosis of the teeth prior to endodontic treatment. The root canal treatment was described in adequate detail in four studies, and the endodontic sealer material extruded was reported in eight studies. All studies described the diagnostic process, patient symptoms, management and follow-up until the disappearance or decrease of the symptoms sufficiently.

Demographic Information and History

A total of 10 patients were included in this systematic review, all of them were women. Their age ranged 23–45 years. When reported, the patient medical history was uneventful.

Involved Tooth

In all included cases, the teeth involved were permanent mandibular posterior teeth (n = 10). The most commonly reported involved tooth was the left mandibular second molar (n = 2) along with the right mandibular second molar (n = 2), and right mandibular first molar (n = 2), followed by the right mandibular second premolar (n = 1), right mandibular first premolar (n = 1), left mandibular second premolar (n = 1), and left mandibular first molar (n = 1). The endodontic diagnosis of the involved teeth was reported only in four studies to be apical periodontitis subsequent to caries (n = 3) and crown fracture along with deep caries (n = 1).

Endodontic Procedure

The endodontic procedure characteristics reported in studies were as follows: Anesthesia (n = 4), irrigation (n = 4), establishment of apical patency (n = 3), use of rubber dam (n = 3), use of apex locator for root length (n = 3), condensation technique (n = 3), file used (n = 2), use of step-back technique (n = 1), and radiographic imaging for root length (n = 1). Eight of the included studies reported the sealer material used in endodontic treatment. The most frequent was epoxy resin-based sealer (n = 5), followed by zinc oxide–eugenol-based sealers (n = 3) and mineral trioxide aggregate (MTA) (n = 1). One study failed to identify the sealer material. The endodontic sealer was introduced using either a lentulo spiral (n = 3), a manual instrument (n = 2) or the sealer's intraoral adjustable tip (n = 1). Four studies failed to report how the sealer was placed during the procedure. No iatrogenic errors were described in any of the studies.

Diagnosis

The diagnosis of paresthesia was formed using the patient's reported symptoms, as well as radiographic imaging in all studies. Only five studies explored the area affected by the paresthesia and reported it in detail. Five cases reported using tactile exploration for the diagnosis. The most common symptom reported in the studies was numbness (n = 7), followed by paresthesia (n = 3), pain (n = 3), tingling sensation (n = 2), pain in treated tooth (n = 2), lack of temperature sensation (n = 1), purulent drainage (n = 1), itching sensation (n = 1), and burning sensation increasing at night and when the affected area is touched (n = 1). In only one study, the patient reported acute pain during the root canal treatment.

Management and Follow-up

Management mainly involved patient monitoring through follow-up visits (n = 4) and medication combined with follow-up visits (n = 4). One study reported prescribing antibiotics and analgesics, offering no improvement of the symptoms, ultimately leading to extraction of the involved tooth and surgical removal of the material. Another study described the extraction of the involved tooth along with the prescription of antibiotics and ibuprofen, with no improvement observed, resulting in the surgical removal of the material. Among the studies approaching the management with medication, in one study, 500-mg naproxen non-steroidal anti-inflammatory drug (NSAID) was prescribed for 5 days. The combined use of 20-mg prednisone every 12 hours for 5 days and 1 pill Citoneurin (Merck, São Paulo, Brazil; 100-mg B1, 100-mg B6, 5,000-µg B12) every 8 hours for 2 weeks were reported in another study. Two studies reported prescribing 1 mg/kg per day prednisone for 1 week along with 150-mg pregabalin per day until the symptoms reported were resolved. The symptoms were resolved fully in six cases. The two studies using prednisolone combined with pregabalin reported disappearance of the symptoms in 1 month and 6 weeks, respectively. The study using naproxen reported the resolution of symptoms in two months, while a study managing the paresthesia with monitoring through follow-up reported 12 months. The two cases managing the paresthesia with surgical removal of the material described the disappearance of symptoms in 4 and 9 months, respectively. Of the cases not resolved, all reported a decrease in paresthesia in

Table 4: Overview of results

Study	*Gender/ age*	*Medical history*	*Tooth/ diagnosis*	*Sealer material*	*Material introduction*	*Iatrogenic errors*	*Radiographic examination*	*Affected area*	*Symptoms*	*Treatment*	*Follow-up*	*Resolved?*	*Conflict of interest reported?*
González–Martín et al., 2010	F/32	Clean	#37/Apical periodontitis subsequent to caries	Epoxy resin-based	Manual instrument	N/A	Yes	Yes	Numbness, tingling sensation	Follow-up	7 months, 3 years	No	N/A
Alves et al., 2020	F/23	N/A	#47/Fracture, deep caries	MTA	N/A	N/A	Yes	Yes	Numbness, lack of temperature sensation	Medication	1 week, 1 month, 3 months, 6 months, 1 year	No	Yes
López–López et al., 2012	F/37	Clean	#37/Apical periodontitis subsequent to caries	Epoxy resin-based	Manual Instrument	N/A	Yes	Yes	Pain in treated tooth, numbness, tingling sensation	Medication	1 week, 2 weeks, 1 month	Yes	N/A
Alonso–Ezpeleta et al., 2014	F/36	N/A	#45/ Apical periodontitis subsequent to caries	Epoxy resin-based	Intraoral adjustable tip	N/A	Yes	Yes	Pain in treated tooth, numbness	Medication	1 week, 3 months, 6 months	Yes	Yes
Escoda–Francoli et al., 2007	F/41	Clean	#46/ N/A	N/A	N/A	N/A	Yes	No	Pain, purulent drainage, paresthesia	Surgical removal of material	4 months, 9 months	Yes	N/A
Froes et al., 2009	F/42	Clean	#47/ N/A	Zinc oxide-eugenol based	Lentulo spiral	N/A	Yes	No	Pain, paresthesia	Medication	1 week, 2 months, 30 months	Yes	N/A
Buyukkurt et al., 2011	F/23	Clean	#46 N/A	Zinc oxide-eugenol based	Lentulo spiral	N/A	Yes	No	Numbness, burning sensation increasing at night and when touched, pain	Surgical removal of material	1 week, 2 weeks, 4 month, 16 months	Yes	Yes
Poveda et al., 2006	F/40	Clean	#44/ N/A	Zinc oxide-eugenol based	Lentulo spiral	N/A	Yes	Yes	Numbness	Follow-up	7 months	Yes	N/A
Tamse et al., 1982 (First patient)	F/28	N/A	#35/ N/A	Epoxy resin-based	N/A	N/A	Yes	No	Paresthesia, itching sensation	Follow-up	12 months	Yes	N/A
Tamse et al., 1982 (Second patient)	F/45	N/A	#36/ N/A	Epoxy-resin based	N/A	N/A	Yes	No	Numbness	Follow-up	1 year, 2 years	No	N/A

Table 5: Summary of quality appraisal of included studies

Study	Selection bias	Age/ gender	Medical history	Tooth involved	Endodontic diagnosis	Endodontic procedure details	Endodontic sealer material	Diagnostic process details	Symptoms	Management	Follow-up
González–Martín et al.		Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Alves et al.		Yes		Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
López et al.		Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Ezpeleta et al.		Yes		Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Escoda–Francoli et al.		Yes	Yes	Yes				Yes	Yes	Yes	Yes
Frohes et al.		Yes	Yes	Yes			Yes	Yes	Yes	Yes	Yes
Buyukkurt et al.		Yes	Yes	Yes			Yes	Yes	Yes	Yes	Yes
Poveda et al.		Yes	Yes	Yes			Yes	Yes	Yes	Yes	Yes
Tamse et al.		Yes		Yes			Yes	Yes	Yes	Yes	Yes

follow-up visits. These included a 3-year follow-up (n = 1), one year follow-up (n = 2), and 7 months follow-up (n = 1). One study reported the absorption of the epoxy-based sealer in 12 months, and another study reported the partial absorption of the zinc oxide-eugenol based sealer in 30 months follow-up visit. In both of these cases, the symptoms reported were resolved. The follow-up visit timelines showed a variability among the reported studies.

Discussion

The aim of this review was to systematically accumulate and analyze the available evidence on potential factors resulting in the development of paresthesia as a result of endodontic sealer extrusion, as well as on its management approaches. The literature search revealed no available prospective studies. Ultimately, only nine case reports were included in the review. This can be considered a limitation, because case reports are low quality of evidence.[29] In addition, the number of studies that matched our inclusion criteria is low to deduct results. In absence of standardized criteria to methodologically assess the quality of included case reports, a custom set was formed. The need for a universal critical appraisal tool for case reports in Endodontology is highlighted. A meta-analysis was not performed due to the low quality of evidence available.

All patients were females, and the most frequently involved tooth was the second mandibular molar. This can be explained because studies have shown that women are more likely to visit the dentist.[30–32] Furthermore, females exhibit a shorter vertical distance between the inferior alveolar nerve and root apexes of molars compared to males.[33,34]

Patient medical history, which can be considered an essential requirement, was only reported only in six studies. The endodontic procedure was not reported adequately either. For the purpose of this review, to assess the factors on the development of paresthesia as a result of sealer material extruded, a detailed description of the obturation stage was vital. However, only six studies reported any information for this specific stage. The only relevant data was on how the sealer material was introduced in the root canal. More detailed information on the procedure such as how the working length was established, instruments used, irrigation and filling materials used, as well as the techniques utilized ought to be reported in every case report. Conclusions on the factors affecting the development cannot be drawn.

Currently, no standardized treatment protocols for nerve injuries related to endodontic treatment exist. Only six patients of the included case reports fully recovered. Of those, two were treated with a combination of prednisone and pregabalin, two were treated with surgical removal of the material, one was treated with the prescription of naproxen NSAID along with follow-up visits, and one was managed through monitoring *via* follow-up visits. Pregabalin has been shown to effectively reduce neurological pain and aid with paresthesia.[35] Surgical decompression of the nerve has also exhibited positive results in the management of paresthesia. However, management remains empirical and a need for prospective studies to investigate it is highlighted. Many patients were hesitant to receive surgical treatment. Therefore, future prospective studies ought to be focused on non-surgical treatment options. In addition, the variability of follow-up times signposts the need for a standardized follow-up protocol.

Prevention of the complications is the cornerstone of every dental procedure. Preoperative radiographic evaluation is important to identify the proximity of teeth to anatomical structures. Use of proper techniques to avoid the extrusion of sealer material is pivotal.[36]

Some authors mention a close relationship between the time elapsed until the treatment of nerve damage and prognosis of the paresthesia.[37] Therefore, early diagnosis and management are of paramount importance. Indicators of sealer extrusion may include pain in treated tooth during filling of the root canal and local inflammatory symptoms such as the tooth being painful to percussion.[25] Early diagnosis of the nerve injury can be achieved through anamnesis, clinical and radiographic evaluation. Clinical sensory testing has been shown to aid in the diagnostic process of paresthesia.[38] However, this may be beyond the practitioner's abilities. Therefore, it is better for patients suspected of experiencing

paresthesia because of the extrusion of sealer material, to be referred to a specialist. A uniform diagnostic process should be developed to identify paresthesia and nerve injury in general as a result of endodontic therapy.

Conclusion

Paresthesia constitutes an infrequent but alarming complication that can occur during endodontic treatment, as a result of the extrusion of sealer material. Studies included in this review, show a variability of data reported and conclusions about the factors affecting its development cannot be deduced. Early diagnosis and management are of the utmost importance for the prognosis of paresthesia. Management approaches remain empirical, and future prospective studies are needed for a more holistic investigation of the topic.

Extrapolation of the results should be treated with caution due to the small amount and low quality of evidence available.

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