APICAL EXTRUSION OF CALCIUM HYDROXIDE: A SYSTEMATIC REVIEW

Thamyres Magalhães Monteiro[1], Kaline Romeiro[2], Luciana Ferraz Gominho[3], Flávio Rodrigues Ferreira Alves[1], Isabela das Neves Rôças Siqueira[1], José Freitas Siqueira Jr[1].

1- Programa de Pós-Graduação em Odontologia Afya UNIGRANRIO, Rio de Janeiro.

2- Departamento de Endodontia do Centro Universitário UNIFACOL, Vitória de Santo Antão.

3- Departamento de Odontologia Restauradora da Universidade Federal da Paraíba, João Pessoa.

ABSTRACT

Introduction: Accidental apical extrusion of calcium hydroxide is a rare but potentially severe iatrogenic complication of endodontic treatment that may result in neurological, vascular, sinus, and soft tissue injuries. This systematic review aimed to synthesize the available evidence on calcium hydroxide extrusion, identify patterns of clinical presentation, management, and outcomes. **Methods:** Searches were performed in PubMed, Web of Science, Embase, and ProQuest up to July 2026. Observational studies reporting complications associated with calcium hydroxide extrusion during endodontic treatment were included. Risk of bias was assessed using the Joanna Briggs Institute checklist. **Results:** Of 3,446 articles initially retrieved, 42 were selected for full-text reading, and 35 met the inclusion criteria and were included. Most studies were case reports or case series and showed moderate to high methodological quality. Mandibular molars (40%) and maxillary incisors (26.7%) were the most frequently affected teeth, with injectable application representing the main delivery technique (52.5%). Foreign body reaction (42.4%), paresthesia (39.0%), Nicolau syndrome (13.6%), and sinusitis (5.1%) were the most common complications. Conventional radiography was the primary imaging modality, whereas cone-beam computed tomography and angiography were essential for assessing severe anatomical and vascular involvement. Management ranged from conservative treatment to surgical intervention, with nearly half of the patients recovering without permanent sequelae. **Conclusions:** Calcium hydroxide extrusion represents a potentially serious complication requiring prompt recognition and individualized management.

Keywords: *calcium hydroxide; Nicolau syndrome; paresthesia; foreign body; sinusitis.*

INTRODUCTION

Calcium hydroxide [$Ca(OH)_2$] has been the intracanal medicament of choice in endodontics for decades because of its antimicrobial activity, ability to neutralize bacterial endotoxins, and favorable biological properties[1-5]. Owing to its high alkalinity (pH ≈ 12.5)[6], it creates an unfavorable environment for most endodontic pathogens and remains widely indicated for the management of persistent apical periodontitis, inflammatory root resorption, traumatic injuries, apexification, and regenerative endodontic procedures[7]. Although considered safe when confined to the root canal system, accidental extrusion beyond the apical foramen or through root perforations may result in severe tissue injury[8].

Accidental calcium hydroxide extrusion is an uncommon but potentially devastating iatrogenic complication of endodontic treatment[9]. Because of its highly alkaline nature, contact with soft tissues, neurovascular structures, or adjacent anatomical spaces may cause chemical burns, coagulation necrosis, vascular compromise, inflammatory reactions, and irreversible neurological injury[10]. The severity of these injuries depends on the volume of extruded material, injection pressure, delivery technique, anatomical location, and proximity to critical structures, including the inferior alveolar, mental, and infraorbital nerves, blood vessels, and the maxillary sinus.

Current evidence is limited to isolated observational studies describing severe pain, soft-tissue necrosis, persistent paresthesia, vascular ischemia, and maxillary sinus involvement following accidental extrusion[11,12]. Reported management ranges from conservative treatment to surgical intervention, with outcomes varying from complete recovery to permanent sequelae. Despite the increasing number of reports, the available evidence remains fragmented, and no systematic review has comprehensively synthesized these complications. Therefore, this systematic review aimed to synthesize the available evidence on the clinical presentation, management, and outcomes of accidental calcium hydroxide extrusion during endodontic treatment.

METHODS

This study followed the PRISMA guidelines and is registered in PROSPERO (registration number 420251186007). Eligibility criteria included observational studies (case reports, case series, cohort studies, and retrospective studies) describing apical extrusion of calcium hydroxide during endodontic treatment, with clinical, radiographic, or surgical documentation of the complication, with no restrictions regarding patient age, sex, tooth type, follow-up duration, or language. Exclusion criteria comprised laboratory studies, reviews, letters to the editor, book chapters, conference abstracts, animal studies, and incomplete articles.

Two reviewers conducted independent searches in four databases (PubMed, Web of Science, Embase, and ProQuest) for studies published until July 2026. Records were imported into Covidence for duplicate removal and screening of titles and abstracts, followed by full-text assessment; disagreements were resolved by a third author. Extracted data included patient characteristics, tooth type, extruded material, delivery technique, symptoms, imaging findings, treatment, follow-up, and sequelae.

Risk of bias in each included study was independently assessed by two authors using the Joanna Briggs Institute (JBI) critical appraisal tools for case reports and case series[13].

RESULTS

The electronic search identified 3,446 articles. After duplicate removal and screening, 42 articles were assessed in full text, and 35 were included in the final analysis (27 case reports, 5 case series, and 3 retrospective studies), comprising 59 patients and 60 teeth, published between 1993 and 2026, with a geographic distribution spanning 20 countries (South Korea contributed the highest number of reports, 14.29%).

Mandibular molars were the most frequently affected teeth (40%), followed by maxillary incisors (26.67%), reflecting their close anatomical relationship with the inferior alveolar neurovascular bundle and the maxillary sinus, respectively [14-16]. Injectable application was the most commonly reported delivery technique associated with extrusion (52.54%), followed by the use of a Lentulo spiral (16.95%).

The most frequently reported complications were foreign body reaction (42.37%), paresthesia (38.98%), Nicolau syndrome (13.56%), and sinusitis (5.08%). Regarding clinical presentation, the most common signs and symptoms were paresthesia (38.98%) and pain (37.29%); swelling (15.25%) and tissue necrosis (13.56%) were also frequent. Among cases diagnosed with Nicolau syndrome, abnormal bleeding during the procedure was reported in 5 cases.

Conventional radiography was the primary imaging modality (88.14%), followed by computed tomography (33.90%); angiography was essential for assessing vascular compromise, while magnetic resonance imaging was used in one case to evaluate soft-tissue involvement.

Management ranged from non-surgical endodontic treatment to surgical intervention, each performed in 44.07% of cases, tooth extraction (11.86%), and pharmacological management (35.59%). The mean follow-up duration was 25.0 ± 23.0 months (range 1-96 months). Nearly half of the patients (49.15%) experienced no reported sequelae; among the reported sequelae, residual material remnants (18.64%) and persistent paresthesia (16.95%) were the most frequent, followed by scar formation, tooth loss, depression, gingival recession, chronic pain, and bone defects.

Among the 35 included studies, 29 were rated as having low risk of bias and 6 as having moderate risk of bias according to the JBI tool [13].

DISCUSSION

Although calcium hydroxide has long been considered a safe and effective intracanal medicament [4,5], this systematic review demonstrates that inadvertent extrusion beyond the apical foramen may result in a diverse spectrum of clinically significant complications involving neurological, vascular, and adjacent anatomical structures. Despite being uncommon, these events may lead to permanent functional impairment such as persistent paresthesia, material remnants, scars, tooth loss, or

depression, representing a challenging clinical scenario given that the available evidence remains fragmented and consists almost exclusively of observational studies.

Rather than representing a single pathological entity, calcium hydroxide extrusion appears to encompass multiple biological mechanisms of tissue injury. The predominance of foreign body reactions, neurological complications, and vascular injuries suggests that the clinical consequences are largely determined by the anatomical structures affected. Neurological injuries were typically characterized by immediate pain and sensory disturbances, whereas Nicolau syndrome consistently presented with severe pain, atypical bleeding during treatment, and subsequent ischemic tissue damage, supporting a predominantly vascular mechanism.

The anatomical distribution of the reported cases further emphasizes the importance of patient-specific risk assessment before calcium hydroxide placement, given the close relationship of mandibular molars and maxillary incisors with the inferior alveolar neurovascular bundle and the maxillary sinus, respectively[14-16]. Injectable delivery was the placement technique most frequently associated with extrusion, supporting the importance of careful working length determination, preservation of the apical constriction, detailed preoperative imaging assessment, and controlled intracanal delivery without excessive hydraulic pressure — with particular caution warranted in teeth presenting open apices, apical resorption, perforations, or a compromised apical constriction.

An additional relevant aspect concerns the influence of contrast agents, such as barium sulfate, incorporated into commercial calcium hydroxide formulations to improve radiographic visualization, which may alter the biological behavior of the extruded material. Orucoglu and Cobankara[17] described persistent periapical radiopacity after extrusion of a barium sulfate-containing paste, suggesting delayed resorption of the radiopaque component despite clinical resolution.

Considerable variability was observed in therapeutic management, reflecting both the heterogeneity of clinical presentation and the absence of standardized treatment recommendations — ranging from conservative and pharmacological therapy, surgical removal of extruded material, and nerve decompression to extraction and extensive resective surgery. Nevertheless, early recognition and prompt intervention appeared to improve clinical outcomes. The development of depression in three patients underscores the importance of integrating psychological support into the management of these complications.

Limitations of this review include publication bias, since severe or unusual complications are more likely to be reported; selective and incomplete data reporting; the descriptive nature of the evidence, which precludes estimation of incidence or comparative treatment effectiveness; and substantial heterogeneity across studies, which prevented quantitative synthesis. Nevertheless, systematic

reviews of case reports remain the most appropriate methodology for investigating rare adverse events that cannot realistically be studied through prospective comparative designs.

CONCLUSIONS

Calcium hydroxide extrusion is a rare but potentially devastating iatrogenic complication requiring prompt recognition and individualized management. Prognosis depends on the affected anatomical structures, severity of tissue injury, and timely intervention. Accurate clinical evaluation combined with appropriate imaging — particularly cone-beam computed tomography and angiography when vascular involvement is suspected — is essential for diagnosis and treatment planning.

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