Biomedical communication

Historical evolution of treatment in necrotic immature permanent teeth

Evolución histórica del tratamiento en dientes permanentes inmaduros necróticos

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ABSTRACT

The treatment of necrotic immature permanent teeth constitutes a challenge in the pediatric dentistry, and there are multiple therapeutic options to solve this problem. To such effects the present investigation was carried out with the objective of exposing the historical evolution of this treatment, reason why an exhaustive literature review was carried out. The dialectical-materialistic method was assumed as the general one of the investigation and in a particular way, the historical-logical, analysis-synthesis and inductive-deductive methods of documental review. Three stages were established based on certain historical landmarks, each one with its contributions and limitations; also, regularities and tendencies were identified, as well as the foundations that sustain the necessity to continue investigating on new therapeutic approaches.

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Keywords: permanent teething; non vital tooth; apexification; regenerative endodontics.

RESUMEN

El tratamiento de dientes permanentes inmaduros necróticos constituye un desafío en la odontopediatría, y son múltiples las opciones terapéuticas propuestas para solucionar esta problemática. A tales efectos se realizó el presente estudio con el objetivo de exponer la evolución histórica de dicho tratamiento, para lo cual se efectuó una exhaustiva búsqueda bibliográfica. Se consideró como método general de la investigación el dialéctico-materialista y, de manera particular, los métodos de revisión documental histórico-lógico, de análisis-síntesis e inductivo-deductivo. A partir de determinados hitos históricos se establecieron 3 etapas, cada una de ellas con sus aportes y limitaciones; asimismo, se identificaron las regularidades y tendencias, así como los fundamentos que sustentan la necesidad de continuar investigando sobre nuevos enfoques terapéuticos.

Palabras clave: dentición permanente; diente no vital; apexificación; endodoncia regenerativa.

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Introduction

One of the challenges in paediatric dentistry is the treatment of immature permanent teeth, which Canalda Sahli⁽¹⁾ defines as those erupted teeth that have not completed their development and therefore present characteristics that make endodontic procedures difficult, such as short roots, wide apical foramen and thin dentine walls.⁽²⁾ In this regard, González, quoted by Moyetones and Zavarce,⁽³⁾ states that irreversible pulp damage in permanent teeth in formation results in the loss of pulp vitality and,

therefore, the sudden halt of root development, which gives rise to the so-called immature necrotic permanent teeth, which become weak and unable to resist the physiological forces of mastication; hence, they cause a high rate of root fractures, with unfavourable prognosis in the medium and long term.⁽⁴⁾ According to Diogenes *et al*,⁽⁵⁾ it has been shown that, despite endodontic treatment, more than 50 % of teeth will be lost within the first 10 years following trauma.

In young patients with mixed dentition, these sequelae can lead to alterations in maxillary and mandibular bone development, interference with phonetics, breathing and chewing, as well as severe psychosocial impairment, which is so detrimental in this population group.⁽⁶⁾

Multiple therapeutic options have been proposed to solve this problem,⁽⁷⁾ which are the result of scientific and technical advances; however, in the medical bibliography consulted, there are no studies that address the historical evolution of this treatment.

Taking into consideration the above arguments, the authors felt motivated to carry out the present article with the aim of presenting the historical evolution of treatment in patients with immature necrotic permanent teeth, for this reason an exploratory literature review study⁽⁸⁾ was carried out at the Faculty of Dentistry of the University of Medical Sciences of Santiago de Cuba, between September 2022 and March 2023. For this purpose, the dialectical-materialist method was used as the general research method and, in particular, the historical-logical documentary review, analysis-synthesis and inductive-deductive methods.

Stages of treatment in immature necrotic permanent teeth

As a result of the historical-logical analysis, the following milestones were identified: the introduction of biomaterials into clinical dental practice and the emergence of regenerative endodontics. These events made it possible to establish 3 stages in the treatment of immature necrotic permanent teeth, each with its contributions and limitations.

Stage 1 (from antiquity to 1963). Extraction of the dental organ

Before the 1960s the usual treatment for immature necrotic teeth was extraction.⁽⁹⁾ As a result of the few advances of the time and the existence of theories such as Hunter's focal infection theory, quoted by Canalda and Brau,⁽¹⁰⁾ Dentistry was blamed for creating and maintaining foci of infection in the mouth. Hunter considered that depulped teeth were infectious foci and could cause systemic diseases; similarly, Rivas Muñoz⁽¹¹⁾ points out that Rosenow proposed that the bacteria present in these foci were capable of reaching the bloodstream, disseminating to a distant organ and causing alterations.

All these postulates constituted limitations for the development of endodontics, as well as for the teaching and practice of endodontic care; however, an important group of dentists maintained their efforts to prove that devitalised teeth could remain in the mouth without causing disease. It was not until the 1940s and 1950s that it was demonstrated that these teeth did not play a direct role in the development of systemic diseases.⁽¹¹⁾

In the opinion of the authors of this article, the contribution of this stage was that the infection was eliminated, while the limitation consisted in the mutilation of the dental organ.

Stage 2 (1964 to 2000). Apexification with biomaterials

Due to this, with the intention of favouring the preservation of these teeth, a great interest in the subject arose, so that in 1964 the introduction of biomaterials into clinical dental practice began.

In the same year, Kaiser described a technique based on the use of calcium hydroxide with camphorated paramonochlorophenol, given its osteogenic properties, which was popularised by Frank in 1966.⁽¹⁾ The procedure consisted of filling the root canal with calcium hydroxide and replacing it every 3 months until an apical barrier was formed — over a period of one year or more— and then performing an additional filling with gutta-percha, which became known as the "Frank technique" or apexification with calcium hydroxide.

The described technique has many advantages, as it stimulates the formation of a mechanical apical healing barrier through osteoblastic activation; likewise, the calcium hydroxide used has an antibacterial effect, as its hydrogenion potential (pH) is ideal for fighting infections in the root canal and periapical tissues. Furthermore, the material used is easily accessible and easy to handle.^(12,13)

Nevertheless, some limitations of the above-mentioned technique are described; on the one hand, the treatment involves numerous consultations over a long period of time, which requires a high level of commitment on the part of the patient, which in its absence could lead to possible therapeutic neglect and consequent failure; on the other hand, calcium hydroxide reduces the resistance of the root due to its proteolytic effect, weakens the dentine and increases the risk of fracture.⁽¹³⁾

During this stage, despite the drawbacks regarding the prolonged use of calcium hydroxide, this technique became the standard therapeutic protocol in patients with necrotic immature teeth.

In Cuba, the proposed treatment for these teeth is apexification with calcium hydroxide. Limitations include tooth loss, corono-radicular fractures, fractures of the cervical third and dyschromia.⁽¹⁴⁾

On the other hand, in the United States, in 1998, Staffoli *et al*⁽¹⁵⁾ comment on Torabinejab, who described another type of apexification, where the addition of mineral trioxide (a biocompatible powder, with fine hydrophilic particles, which hardens with humidity) was used. This material, composed of tricalcium oxide powder, silicate oxide and tricalcium silicate, has a high pH and antibacterial qualities similar to those of calcium hydroxide; it is also biocompatible and induces hard tissue formation. However, this technique does not achieve root thickness and length development, while the material has disadvantages such as tooth discolouration, difficulties in retreatment and over-obturation.^(16,17)

Contributions

 Preservation of the affected teeth, with modification of the pre-existing treatment of mutilation of the dental organ.

- Biomechanical preparation of the root canal and use of calcium hydroxide in infection control, given its antibacterial effect.
- Replacement of pulp tissue with artificial materials, which prevents the penetration of pathogens (gutta-percha and mineral trioxide aggregate).
- Appearance of therapeutic options that constituted an important starting point for contemporary Dentistry: Kaiser and Frank's apexification, as well as the application of mineral trioxide aggregate as an apical seal.

Limitations

- Failure to increase dentine wall thickness.
- Increased risk of fracture in these teeth.

Stage 3 (from 2001 to 2023). Apexification with regenerative therapies

In this period, dental therapies are increasingly oriented towards conservative procedures that make use of the restorative and regenerative potential of the human body, rather than treatments that replace lost vital tissue with biomaterials.⁽¹⁸⁾

Consequently, apexification with regenerative therapies is developed as a biologically based procedure performed on the necrotic immature permanent tooth, with the aim of replacing the damaged dentin-pulp complex with the formation of a loose connective tissue, consisting of cellular, vascular and nervous elements, surrounded by a neoformed mineralised tissue. These tissues are the result of the interaction of dental stem cells from the apical papilla, growth factors and biomaterials, with the microenvironment where this process takes place.⁽¹⁹⁾

Torabinejad and Abu-Tahun, quoted by Canalda Sahli,⁽¹⁾ defined regenerative endodontics as biological procedures performed on permanent teeth, with unformed apex and pulp necrosis, aimed at replacing damaged tissues, including dentine and root structure, as well as the cells of the dentin-pulp complex.

In that sense, pioneering work supporting the concept of dental tissue regeneration was published more than 60 years ago; However, the non-use of antimicrobials and a

complex protocol led to the decline of this type of treatment. Nygaard Østby evaluated a method to restore the dentin-pulp complex in immature necrotic permanent teeth — based on the importance of the clot for wound healing— by lacerating the periapical tissue with an endodontic file.⁽¹⁾

In 2008, Sonoyama *et al*⁽²⁰⁾ characterised the tissue of the apical papilla of immature teeth through hystolic, immunohistochemical and immunofluorescent analysis, and demonstrated that apical papilla cells proliferated 2-3 times more than pulp cells in cell culture and that these cells co-expressed dentinogenic STRO-1 markers with mineralising capacity; They also demonstrated the existence of a cell-rich zone between the pulp and the papilla, making it likely that stem cells from the apical papilla survive infection, due to their proximity to the periapical tissue.

Subsequently, in 2012, Lovelace *et al*⁽²¹⁾ evaluated the release of mesenchymal stem cells into the root canal after induction of bleeding during regenerative endodontic procedures. In this regard, molecular analyses of blood extracted from the canal system indicated a significant accumulation of stem cell markers CD-73 and CD-105 (up to 600-fold) compared to levels found in systemic blood. The data presented so far demonstrate not only the entry of stem cells into the canal, but also that they originate from local tissues, adjacent to the root apex, and not from the systemic circulation.

Likewise, according to Canalda Sahli,⁽¹⁾ Keswani and Torabinejad introduced a new modification to the regenerative endodontic technique: the use of platelet-rich fibrin, obtained from the patient's own venous blood and processed, in contact with the blood clot provoked after induction, in search of an ideal top that would contribute to the stimulation of stem cells and the formation of hard tissue.

In that sense, other authors⁽²²⁾ determined the presence of mesenchymal stem cells after induction of bleeding in regenerative endodontic procedures. Therefore, the 2-step real-time polymerase chain reaction was shown to be a valid method for this purpose.

According to Santiago *et al*,⁽¹⁹⁾ Hargreaves considered 3 main components of tissue engineering during the development of regenerative endodontics: the first is the existence of a source of stem cells from the apical papilla, mobilised into the root canal through the induction of bleeding; the second, the presence of mediator molecules in cell

stimulation; and the third, the existence of a matrix to promote cell growth and differentiation, as well as signalling molecules.

Regarding the use of irrigants in disinfection and their effect on stem cells, some authors⁽²³⁾ analysed the action of ethylenediamine tetraacetic acid (EDTA) remaining in the formation of the blood clot and found that it inactivates platelets and fibrin formation; therefore, irrigation with EDTA and then with saline is suggested.

In this regard, Hashimoto *et al*⁽²⁴⁾ noted that EDTA exposes collagen fibres and allows better adhesion of stem cells to the dentin matrix. Similarly, they evaluated the effect of irrigation with this acid at different concentrations, which showed that between 3 and 17 % of the stem cells involved survived, although they stated that concentrations of 3 % are sufficient to avoid unnecessary alterations in the dentine.

It is also suggested that sodium hypochlorite at concentrations lower than 2.5 % was used with excellent results, since its potent antibacterial and proteolytic activity dissolves the organic tissue; higher concentrations may damage the involved stem cells.^(24,25)

Recently Widbiller *et al*⁽²⁵⁾ pointed out that chlorhexidine irrigation is detrimental to apical papilla stem cells.</sup>

According to the above reasoning, histological studies have shown encouraging results in treated teeth. In this regard, Digka *et al*⁽²⁶⁾ indicate in their series the formation of fibrous connective tissue, with the presence of fibroblasts, mesenchymal cells and blood vessels, as well as nerve bundles in some cases; they also observed that the neoformed mineralised tissue was similar to cementum and was deposited on the dentine walls and root apex.

Several studies^(15,18,27,28) have shown that in the majority of patients treated with regenerative endodontics, clinical manifestations and periapical lesions disappeared, while apical closure was achieved and root length and dentine root wall thickness increased.

The great advantage of this treatment, apart from being a simple and economical technique, is that it avoids immunological rejection and the transmission of pathogenic germs.

In 2021, the American Association of Endodontics updated a protocol consensus on its website, formed from the considerable number of patients treated with regenerative endodontics;⁽²⁹⁾ similarly, the European Society of Endodontics provided details of similar procedures, but with some differences in terms of medication, blood clot formation, material placement and success criteria.

Also, despite the clinical success associated with this therapy, some limitations are noted, such as those of Canalda Sahli,⁽¹⁾ who refers to the dyschromia associated with the bismuth oxide in the mineral trioxide addition, as well as the minocycline in the triple antibiotic paste.

With reference to failure during regenerative endodontic procedures, Almutairi et al⁽³⁰⁾ detail that the main impairment detected in their study was the persistence of infection. Accordingly, it is important to maintain a high degree of disinfection for successful treatment.

Currently, despite the progress achieved, research is being conducted on new therapeutic approaches that allow effective disinfection without altering the stem cells involved or weakening the tooth structure, including laser and ultrasound to enhance the action of the irrigant, as well as chemical and biological compounds such as propolis, nitric oxide and autologous platelet concentrate, among others.⁽¹⁷⁾

Although there is not enough evidence to systematically indicate the use of these compounds in therapy, it is likely that the clinical protocol will be updated in the near future, hence the need for further research on these new approaches to achieve disinfection of treated teeth.⁽¹⁸⁾

Contributions

- The rise of regenerative endodontics with an exponential growth in the number of studies with satisfactory results.
- Analysis of the biological bases that guarantee this procedure.
- Isolation, identification and culture of cells obtained from the bleeding canal, which demonstrated the presence of mesenchymal stem cells with mineralising differentiation.

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- Evaluation of the effect of irrigants and medication used for disinfection on stem cells.
- Demonstration of the results in patients who received regenerative therapy, with the consequent increase of root walls in width and length, as well as the disappearance of clinical and radiographic manifestations.
- Histological studies to determine the characteristics of the neoformed tissues.
- Restoration of lost tissue by regenerated biological tissues.
- Study of the main causes of failure of the regenerative endodontic procedure.

Limitations

- Coronary discolouration associated with the use of minocycline in polyantibiotic paste and bismuth oxide in mineral trioxide aggregate.
- Persistence of infection as the predominant clinical manifestation in failed cases.

On the other hand, when comprehensively analysing the treatment of necrotic immature permanent teeth, some regularities were established, such as the control of infection from the root canal, treatment in favour of the continuity of root development and the existence of limitations in the proposed therapeutic options. Also revealed as a trend is the transition from a mutilating treatment (stage 1) to a conservative treatment that promotes root development in length and width (stages 2 and 3).

In summary, the figure drawn up by the authors of this article shows the historical evolution of the treatment of immature necrotic permanent teeth.

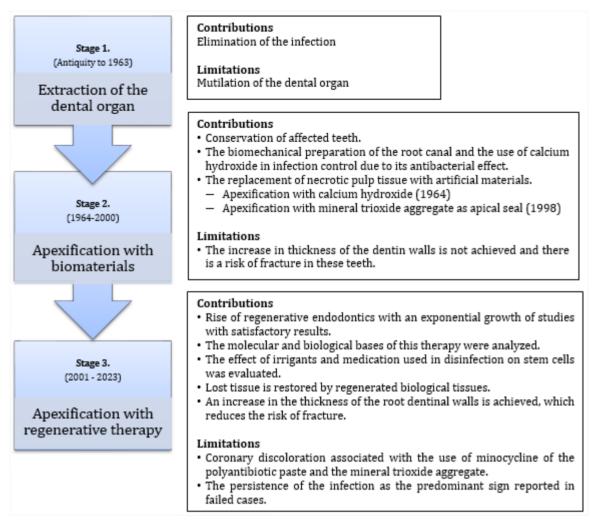


Fig. Historical evolution in the treatment of immature necrotic permanent teeth from antiquity

to 2023

Final considerations

There are still limitations in the treatment of immature necrotic permanent teeth. For this reason, it is considered that therapeutic approaches capable of satisfying the evident problems should continue to be investigated.

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Conflict of interests

The authors of this article declare that they have no conflict of interests.

Authors' contributions

Elizabeth Santiago Dager: conceptualization, data curation, formal analysis, research, methodology, monitoring, writing-final draft, writing-reviewing and editing. Participation: 45 %.

Cecilia Venzant Fontaine: formal analysis, research, writing-final draft, writing-reviewing and editing. Participation: 25 %.

Bárbara Olaydis Hechavarría Martínez: writing-reviewing and editing. Participation: 20 %.

Niurka Odalmis La O Salas: formal analysis, writing-final draft. Participation: 10 %.



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