ORIGINAL PAPER

The use of triple antibiotic paste and blood clot for revascularization and regeneration of the pulp in endodontics.

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Abstract

Objective: The main reason of the present study is to analyse the methods and protocols that have been discovered and used until now in endodontic therapy for a necrotic tooth with or without immature root.

Methods: An electronic search was done in ResearchGate and PubMed using terms about revascularization and regeneration in endodontics between 2004 and 2018. Every clinical trial was read and selected based on the most interesting cases no regardless of the results.

Results: Thirty publications are noted in this research that used triple antibiotic paste consisting of metronidazole, ciprofloxacin, and minocycline as an intracanal medicament. All canals were irrigated with sodium hypochlorite 2.25% or higher and in no case were they mechanically instrumented. In 93% of the relevant studies, mineral trioxide aggregate was used as an intracanal coronal barrier.

Conclusions: Modern endodontic therapy on immature teeth with immature apex and necrotic pulp has achieved excellent results using antibiotic paste and blood clotting without any mechanical instrumentation.

Keywords: regenerative endodontics, triple antibiotic paste, irrigation system, non-invasive treatment, blood clot.

Introduction

The ultimate goal of endodontic treatment is to save the tooth from extraction and long-term arcade maintenance of the tooth whose pulp is irreversibly compromised [1]. The pulp, the living tissue inside the tooth, is protected against the harmful factors in the external environment by the harsh tissues that surround it outside [1, 2]. Various aggressions, the most common carious processes but also traumas and dental treatments, lead to the destruction and reduction of the quantity of harsh tissues. If irritation factors whether physical, chemical or biological act brutally, physiological pulp defences will be overwhelmed, resulting in irreversible inflammation or necrosis of the pulp tissue [2, 3]. When pulp necrosis occurs, the pulpal blood supply is non-existent, and the pulpal nerves are not functional. This dead space, privately vascularized and safe from the immune system, offers the right conditions for life and represents the ideal shelter for bacteria [4].

Compared to a normal pulp which is symptom-free and responds normally to the pulp tests, pulp necrosis is usually nonresponsive to the pulp testing. The tooth remains in this condition until such time when the bacteria affects the periradicular tissues and become symptomatic to percussion. Losing an immature permanent tooth can lead to malocclusion and loss of function. An incompletely formed root in need of endodontic treatment is a real challenge for the clinicians, having an immature apex that cannot be cleaned and shaped properly [5]. The most common procedure in those cases is apexification which has the potential disadvantage to reduce root strength [6].

Nowadays, non-surgical root canals have become a routine procedure. That being said, regenerative endodontic procedures are aiming to replace the damaged structures keeping the normal function of the pulp-dentin complex with the continuing development of the root [8]. The effectiveness of combination of ciprofloxacin, metronidazole, and minocycline has been demonstrated, as seen in the publications listed below [Table 1], in the destruction of the bacteria from the root canals. Compared to the apexification using calcium hydroxide, the triple antibiotic paste does not reduce the root strength. It would be expected that the lack of mechanical

instrumentation would result in the persistence of the bacteria in the canal roots but the irrigation with sodium hypochlorite whether in combination with other solutions such as chlorhexidine or ethylenediaminetetraacetic or without aims to disinfect the canal space [7, 8, 9].

That being said, the purpose of the present review is to evaluate the results obtained in endodontic regeneration treatments of the last period and to identify variations in clinical procedures.

Materials and methods

An electronic search was executed in Research Gate and PubMed database between January 2004 and October 2018. The publications have been selected according to the search terms: dental pulp, revascularization, regenerative, revitalization, endodontic, endodontic therapy, triple antibiotic paste. The search was conducted for human clinical studies or case reports in vitro or ex vivo. All articles containing one or more of the above-listed terms have been evaluated and selected if they met the requirements of this study. All publications using, sodium hypochlorite, blood clot, mineral aggregate trioxide, a triple antibiotic paste consisting of metronidazole, ciprofloxacin and minocycline but not using mechanical treatment were included.

Results

Out of four hundred seventy-two articles found on the electronic search, four hundred forty-seven were removed, and thirty were finally included in this review. All of the selected studies involved human participants.

As first irrigation, sodium hypochlorite in concentration smaller than 5% was used in 36.7 % of the clinical studies. Sodium hypochlorite in concentration bigger than 5% was used in 60% while in 3.3% of the clinical studies no sodium hypochlorite was used. In 30% of the clinical studies, chlorhexidine was used as primary irrigation among the use of sodium hypochlorite. As final irrigation, sodium hypochlorite was used in 66.6%; chlorhexidine was used in 3.3%, sterile saline in 53.3% and ethylenediaminetetraacetic in 13.3%. [Table 1] [Chart 1]

In 93.3% of the clinical studies, mineral trioxide aggregate was used as an intracanal coronal barrier. The blood clot was created in 83.3% of the cases, while the rest of the authors used platelet-rich fibrin or platelet-rich plasma. [Table 1] [Chart 1]

In the end, 66% out of thirty clinical cases have resulted in an asymptomatic tooth with or without root formation while 27% declared positive responses to the cold and electric pulp tests and 7% resulted in pain or new periapical lesion. [Table 1] [Chart 1]

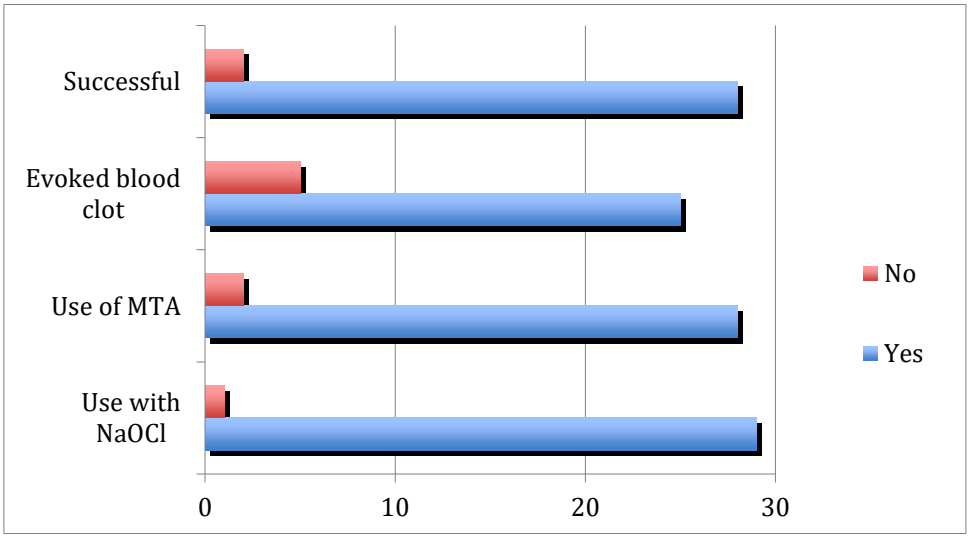

Chart 1. Summary of Succes, Agents, Methods, and Medicaments used in the clinical cases

Table 1. Presentation of the Clinical Cases and the Protocols used for Regenerative Endodontic Procedures

Study	Dental History	Initial Irrigation	Duration of medicament	Final irrigation	Evoked blood clot	Latest follow-up	Results	Intracanal coronal barrier
Banchs & Trope, 2004 [1]	Pulp necrosis Immature Apex	5.25% NaOCl + 0.12% CHX	26 days	5.25% NaOCl	Yes	2 years	Asymptomatic Closed Apex	MTA
Ding et al, 2009 [2]	Acute or chronic apical periodontits Immature apex	5.25% NaOCl	7 days	5.25% NaOCl	Yes	1 year	Complete revasculari-zation + pulp sensibility	MTA
Jung et al, 2008 [3]	Open Apex Large radiolucency	2.5% NaOCl	7 days	2.5% NaOCl	Yes	2 years	Aymptomatic Closed Apex	MTA
Reynolds et al, 2009 [4]	Pulp Necrosis Immature Apex	6% NaOCl + 2.0% CHX	30	6% NaOCl	Yes	18 months	Bone healing Root development	MTA
Kim et al, 2010 [5]	Pulp necrosis	3% NaOCl	42	3% NaOCl	Yes	8 months	Apical closure	MTA
Petrino et al, 2010 [6]	Pulp necrosis Chronic apical abcess	5.25% NaOCl + 0.12% CHX	21	5.25% NaOCl	Yes	1 year	Thickness of apical area	MTA
Jung et al, 2011 [7]	Pulp necrosis Symptomatic apical periodontitis Open Apex	2.5% NaOCl	14	2.5% NaOCl+ sterile saline	Yes	31 months	Asymptomatic	MTA
Torabine jad & Turman, 2011 [8]	Pulp necrosis Symptomatic apical periodontitis Open Apex	5.25% NaOCl	22 days	Sterile saline	No	5 months	Positive response cold and EPT test Apical closure	MTA
Jeeruph an et al, 2012 [9]	Pain Percussion sensitivity	2.5% NaOCl	29 days	2.5% NaOCl	Yes	24 months	Revascularize-tion	MTA

Nosrat et al, 2012 [10]	Immature Apex Pulp necrosis	5.25% NaOCl	28 days	5.25% NaOCl	Yes	Yearly	Formed apices	MTA
Lenzi & Trope, 2012 [11]	Pulp Necrosis	2.5% NaOCl	35 days	Sterile Saline	Yes	21 months	Succesful revitalization	MTA
Shivashankar et al, 2012 [12]	Pulp necrosis Coronal Fracture	5.25% NaOCl + 0.2% CHX	21days	Sterile Saline	No	1 year	Positive response to cold and EPT test	MTA
Miller et al, 2012 [13]	Pulp necrosis	2.0% CHX + 17% EDTA	42 days	2.0% CHX + 17% EDTA	Yes	18 months	Pulp vitality	MTA
Gelman & Park, 2012 [14]	Pulp necrosis Immature apex	6% NaOCl	35 days	6% NaOCl	Yes		Periapical area healed	MTA
Narayana et al, 2012 [15]	Pulp necrosis Dens in dente	5.25% NaOCl	14 days	5.25% NaOCl	Yes	1 year	Asymptomatic No increase in the root canal wall	MTA
Keswani & Pandey, 2013 [16]	Pulp Necrosis Immature Apex	5.25% NaOCl	21 days	Sterile Saline	Yes	15 months	Positive response to cold and EPT test	MTA
Forghani et al, 2013 [17]	Pulp Necrosis Crown Fracture	5.25% NaOCl	21 days	5.25% NaOCl + Sterile saline	Yes	18 months	Increased root lenghts Apical closure	MTA
Sonmez et al, 2013 [18]	Pulp necrosis Immature Apex	5.25% NaOCl	14 days	5.25% NaOCl	Yes	24 moths	Root development	MTA
Yang et al, 2013 [19]	Pulp necrosis Dens invaginatus	5.25% NaOCl	28 days	2.5% NaOCl + Sterile saline	No	24 months	Asymptomatic Normal periodontal codition	Glass ionomer cement
Noy et al, 2013 [20]	Coronal hypoplasia Immature root	2.25% NaOCl + 2.0% CHX	21 days	2.5% NaOCl + Sterile saline	Yes	4 years	Healing of the periapical radiolucency	MTA

	Periapical radiolucency							
Chen et al, 2013 [21]	Pulp necrosis Chronic apical abcess	3% NaOCl + 2.0% CHX	28 days	3% NaOCl + Sterile saline	Yes	1 year	Increased thickening of the root canal wall and lengthening of the root	MTA
Becerra et al, 2014 [22]	Pulp necrosis Chronic apical abcess	5.25% NaOCl + 2.0% CHX	26 days	5.25% NaOCl + Sterile saline	Yes	2 years	Normal periapical condition Apex closure	MTA
Lin et al, 2014 [23]	Pulp necrosis Immature apex	5.25% NaOCl	28 days	5.25% NaOCl	Yes	16 months	Pain Local sweling	MTA
Nagata et al, 2014 [24]	Pulp necrosis Immature apex	6% NaOCl + 2.0% CHX	21 days	17% EDTA + Sterile saline	Yes	19 months	Crown coloration Repair of periapical lesion	MTA
Sachdeva et al, 2014 [25]	Pulp necrosis Immature apex	5.25% NaOCl	28 days	sterile saline	No	36 months	Resolution of periapical lesion Closed apex	MTA
Santiago et al, 2015 [26]	Pulp necrosis chronic apical abcess	2.5% NaOCl	30 days	5.25% NaOCl + Sterile saline	Yes	30 months	New periapical radiolucency	MTA
Vasundara et al, 2017 [27]	Pulp necrosis Immature apex	5.25% NaOCl	21 days	sterile saline	Yes	12 months	Vitality response	MTA
Wang et al, 2015 [28]	Pulp Necrosis Apical periodontitis	2.5% NaOCl + sterile saline	14 days	sterile saline	No	30 months	Bone healing	MTA
Bekhtiar et al, 2017 [29]	Pulp necrosis	1.5% NaOCl + normal saline	3 weeks	17% EDTA	Yes	6 months	Apical closure	Biodentine

Nagas et al, 2018 [30]	Pulp necrosis	5.25% NaOCl + normal saline	28 days	5.25% NaOCl + Normal saline + 17% EDTA	Yes	60 months	Resolution of radiolucency regeneration of periradicular tissues	MTA

Discussion

Regenerative endodontics is the replacement of diseased, absent or traumatized pulp tissue. In recent years, obturations have been developed to induce the three-dimensional closure of the root canal [10, 11, 12]. In the first half of the last century, calcium hydroxide was used as a permanent rooting material [10, 11, 12]. However, it has been shown that calcium hydroxide dissolves quite rapidly in tissue fluids, so the obturation of the canal root has been improved. It is currently used in modern endodontic treatment like pulp capping and pulpotomies [12]. Nowadays, one of the most interesting experiments is the attempt to induce new connective tissues in the root canal creating a blood clot [13].

Back in 1961, Nygaard Ostby [14] insisted that a blood clot might be beneficial in healing a dental pulp, similar to the clot formed after the dental extraction, coming in 1971 with another research proving that creation of a blood clot can form a new conjunctive tissue in the root canal space. Since then, many regenerative protocols have covered the step of induced bleeding [8]. There have been reports where bleeding cannot be induced so no blood clot could be created, but the studies were declared successful. One of the biggest challenges is the suitable placement of the mineral trioxide aggregate over the blood clot in the coronal part of the root canal [8, 9].

The first selection principle of the clinical cases listed below [Table 1] is that root canal walls have not been mechanical prepared. This way, the stem cells would be protected, and the regeneration would be improved. The only needle used was in most cases #10 k-file to establish the length of the canals. In the first appointment, every tooth was isolated with a rubber dam, and access cavity was created until the exposure of the pulp. As mentioned before, the root canal length was determined, followed by copious irrigation using sodium hypochlorite, chlorhexidine, sterile saline solution or ethylene-di-amine-tetra-acetic.

An outstanding outcome was shown by Ding et al., in 2009 on a tooth with necrotic pulp and immature formed apex and chronic apical periodontitis which, after it was irrigated with 20 mL of 5.25% sodium hypochlorite solution, the tooth was sealed for only seven days with the triple antibiotic paste. In the second appointment, the antibiotic was flushed away with the same solution, and the blood cloth was created by irritating the vital tissue [15]. After the cloth was created, a grey mineral trioxide aggregate was placed over it, and the tooth was restored with resin composite [15]. After one year, the teeth regained sensibility to the tests and normal colour [15].

Like it can be seen [Table 1] sodium hypochlorite is the most used irrigation solution and can dissolve the necrotic pulp with more effect on the biofilm. Eight of the authors used chlorhexidine combined with sodium hypochlorite and one of them declared positive responses to the cold and electric tests as a result [16]. The disadvantages of sodium hypochlorite are the odor, the toxicity and the impossibility of removing anorganic components from hardly accessible anatomical areas that need to be mechanically cleaned by endodontic instruments [17]. Compared to the efficiency, sodium hypochlorite is better than chlorhexidine solution [18] but as a final irrigate compared to the saline, chlorhexidine solution has shown a greater reduction of positive cultures [19]. A study from 1998 [20, 21] showed that sodium hypochlorite used combined with chlorhexidine on single rooted nonvital teeth had better results than using them separately. It is important to say that when those two solutions are in contact, they produce a change of color and create a red precipitate [22]. Also, as a primary irrigate, ethylenediaminetetraacetic is used in only one

publication because it cannot remove the smear layer properly [23].

The mixture composed of metronidazole, ciprofloxacin, and minocycline was first tested against bacteria from carious dentin and infected pulp in 1996 [7, 24]. It is considered the most popular intracanal medicament [25]. However, two worrying reasons were that the use of minocycline, a broad-spectrum tetracycline, would cause tooth discoloration and the possibility of creating bacterial resistance [26]. It has been shown that the antibiotic paste can destroy the bacteria from dentinal tubules [7] due to its wide spectrum of action.

When it comes to the intracanal barrier, the mineral trioxide aggregate has been proven to offer a better sealing ability, biocompatibility and less cytotoxicity [27, 28]. Notably, the presence of the blood does not alter the properties of this material [28]. In 1995, Torabinejad et al. reported that the mineral trioxide aggregate, after hydration, is composed of 33% calcium, 49% phosphate, 2% carbon, 3% chloride and 6% silica so that it would prove the biocompatibility with cells and tissues [29]. Twenty-eight studies out of thirty listed below used this material as a coronal barrier.

Conclusion

The use of sodium hypochlorite and/or chlorhexidine as irrigates, a triple antibiotic paste consisting of metronidazole, ciprofloxacin, and minocycline, induced blood clot and intracanal corona barrier have shown great results over the years.

Conflict of interest: None to declare.

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