



## “THE EFFECTIVENESS OF CALCIUM HYDROXIDE INTRACANAL MEDICAMENT IN REGENERATIVE ENDODONTIC PROCEDURES: AN IN-DEPTH ANALYSIS”

### Dentistry

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### ABSTRACT

Regenerative endodontics is a growing field that enables the completion of root development in necrosed immature tooth. The procedure involves disinfection of the root canal with copious irrigation and an efficient intracanal medicament followed by induced bleeding in the canal to attract the stem cells as well as growth factors and formation of scaffold to support the formation of pulp-dentine complex. In regenerative endodontic procedure, disinfection phase of the root canal seems to be very crucial for the success of the treatment. The most commonly used intracanal medicament were antibiotic pastes and calcium hydroxide. Studies suggest that calcium hydroxide intracanal medicament gave acceptable clinical outcomes but still some factors needs to be assessed before considering calcium hydroxide as intracanal medicament. The present review aims to address the effects of calcium hydroxide(CH) on various factors affecting the success of regenerative endodontic treatment.

### KEYWORDS

calcium hydroxide, disinfection, intracanal medicament, regenerative endodontics.

#### INTRODUCTION:

Treatment of immature teeth with open apices and blunderbuss canals present a myriad of challenges to clinicians. The intricate process of canal cleaning and shaping is compounded by the delicate nature of the thin walls, which are prone to fracturing during filing. Regenerative endodontics(RE) is currently considered the preferred treatment for incompletely developed teeth due to the benefits it offers in terms of root development. This includes root lengthening and increased root dentin wall thickening, resulting in enhanced tooth resistance compared to conventional apexification techniques using calcium hydroxide or MTA which fail to achieve increased dentin wall thickness or root lengthening.<sup>1</sup> The proper disinfection of the root canals is paramount in the field of regenerative endodontics. During the disinfection phase of the root canal system, antibiotic pastes and calcium hydroxide have been utilized. Triple antibiotic paste(TAP), comprising metronidazole, ciprofloxacin, and minocycline, induces coronal discoloration due to minocycline. Consequently, the traditional triple antibiotic paste has been refined into a double antibiotic paste or by substituting minocycline with alternative antibiotics like amoxicillin, clindamycin, doxycycline, or cephalosporins. Additionally, calcium hydroxide has been integrated to supplant antibiotic pastes during the disinfection phase of the regenerative technique.<sup>2</sup>

However, there is a paucity of published studies comparing the efficacy of antibiotic pastes or calcium hydroxide as intracanal medicaments in the disinfection of the root canals in regenerative endodontic procedures. An efficient infection control, ensuring the uninterrupted cellular functions crucial for regeneration, stands as a pivotal factor in achieving treatment success concerning root development. The present article aims to explore the effects of using calcium hydroxide(CH) as intracanal medicament on various factors affecting the success of regenerative endodontic treatment.

#### Antimicrobial Aspect Of Calcium Hydroxide:

Calcium hydroxide is a potent alkaline substance with a pH range of 12.5–12.8. The elevated pH level, coupled with the disassociation of calcium hydroxide into Ca<sup>+</sup> and OH<sup>-</sup> ions, confers upon it antibacterial properties.<sup>3</sup> These hydroxide ions (OH<sup>-</sup>) disrupt the integrity of the cytoplasmic membrane, inhibit bacterial enzyme activity, induce protein denaturation, cause DNA damage leading to replication inhibition, and deactivate endotoxins. Calcium dihydroxide exhibits a low dissociation coefficient (0.17), a favorable characteristic enabling sustained release of Ca<sup>2+</sup> and OH<sup>-</sup> over an extended period. A duration of seven days appears adequate for achieving a significant reduction in bacterial colonization within the root canal, ultimately resulting in negative culture status.<sup>4</sup>

However, the antibacterial efficacy of CH further diminished by remnants of pulp necrosis, acidic bacterial byproducts and phosphates derived from the hydroxyapatite of the dentin and inflammatory exudates impede the diffusion of H<sup>+</sup> and OH<sup>-</sup> ions, swiftly normalizing its pH levels. Furthermore, calcium hydroxide lacks efficacy in combating *Enterococcus faecalis*.<sup>5</sup>

This was further ascertained in a study done by Zancan et al., where they compared the pH, solubility, and antimicrobial efficacy of Calcium Hydroxide Paste (CH), Double Antibiotic Paste (a combination of metronidazole and ciprofloxacin - DAP), Calcium Hydroxide combined with DAP (CH/DAP), and Triple Antibiotic Paste (a mixture of metronidazole, ciprofloxacin, and minocycline - TAP). Both CH and CH/DAP exhibited no significant deviation in antimicrobial activity against *E. faecalis* biofilm when compared to the Control group. DAP is recommended for eradicating *E. faecalis* within biofilms due to its antimicrobial potency similar to TAP. The addition of Calcium Hydroxide to DAP notably diminished its antimicrobial effectiveness. Despite its low solubility and elevated pH levels, the CH paste demonstrated modest antimicrobial activity against *E. faecalis* within biofilms.<sup>6</sup>

In contrast, a study conducted by Pereira et al., compared the *in vitro* intradental antimicrobial efficacy of the calcium hydroxide and tri-antibiotic pastes. The results revealed no statistically significant difference between the two groups. Consequently, they deduced that both the tri-antibiotic paste and the calcium hydroxide paste exhibit equivalent effects on intra-tubular decontamination against *E. faecalis*. Nonetheless, they favored the calcium hydroxide paste for dental decontamination in regenerative procedures due to its numerous advantages.<sup>7</sup> Apart from this, the *in-vivo* application of calcium hydroxide for disinfecting the root canal in regenerative endodontics has been extensively researched in the literature and yielded favorable outcomes.<sup>8,9,10,11</sup> We suggest that calcium hydroxide can be used as intracanal medicament for disinfecting root canals in RE. Nevertheless, the clinician must consider the use of more potent antibiotic paste in teeth having long standing infection.

#### Effect Of Calcium Hydroxide On Dental Stem Cells:

The intracanal medicaments utilized in Regenerative Endodontic Procedures (REPs) must be chosen not solely for their antimicrobial properties, but also for their capacity to facilitate or even stimulate the survival, proliferation, and differentiation of the dental stem cells. Presently, the most frequently used intracanal medicaments employed in REPs include antibiotic combination paste (TAP) and calcium hydroxide.<sup>12</sup>

Earlier, the use of calcium hydroxide as an intra-canal medicament was

discouraged due to concerns regarding its potential deleterious effects on remaining viable pulp cells, including essential stem and progenitor cells in the dental pulp tissue and/or apical papilla crucial for subsequent root maturation.<sup>13,14,15</sup> According to a study conducted by Nosrat et al., it appears that the alkaline nature of calcium hydroxide leads to the denaturation of proteins and has the potential to induce necrosis of apical tissue.<sup>16</sup>

However, in a recent study conducted by Ruparel NB et al., the impact of various intracanal medicaments on the viability of human Stem Cells from Apical Papilla was examined. The research revealed that elevated concentrations of antibiotics in triple antibiotic paste had an adverse effect on the survival of Human Stem Cells from Apical Papilla (SCAP). Conversely, lower concentrations of triple antibiotic paste and CH, across all tested levels, were found to support the survival and proliferation of SCAP.<sup>17</sup> This observation was corroborated by Althumary RI et al.,<sup>18</sup> who noted that triple antibiotic paste or double antibiotic paste typically contained a concentration of 1000mg/ml when utilized in a clinical paste form. This heightened concentration exhibited a lethal impact, impeding the survival of SCAP and Dental pulp stem cells (DPSCs).<sup>19</sup> However, this detrimental effect of triple antibiotic paste or double antibiotic paste could be mitigated by reducing the concentration of these medicaments by 1 mg/ml. Achieving such a lower concentration of triple antibiotic paste in a clinical setting is only feasible when it is administered in a solution form rather than a paste form. Additionally, it was suggested that CH fosters the survival and proliferation of SCAP.<sup>18</sup>

The complete eradication of intracanal medicaments from the root canal system has been deemed unattainable,<sup>20</sup> and the influence of the remnants of these medicaments on stem cells appears to be pivotal. The study conducted by Gougousis et al. examined the impact of residual amounts of intracanal medicament on the viability of cells on root canal dentin. Their findings indicated that stem cells cultivated on root canal surfaces treated with calcium hydroxide exhibited superior quality compared to those grown on surfaces treated with the triple antibiotic paste. Cells cultured in a substrate containing remnants of calcium hydroxide displayed enhanced morphology with widened structures and more pronounced cores, characteristics that enhance their survival, proliferation, and potential for differentiation.<sup>21</sup> The growth of cells could be because of the release of growth factors from the dentin by alkaline hydrolysis. Also, studies suggested that CH improved cellular attachment to dentine and release of Tissue growth factor-beta (TGF- $\beta$ 1) and thus helps in dentine regeneration.<sup>21</sup> It can be deduced that CH and lower concentration of antibiotic paste both has a proliferative effect on dental stem cells.

#### Effect Of Calcium Hydroxide On Root Development:

In the history of regenerative endodontics, disinfection using calcium hydroxide gave successful results in root development.<sup>1,8,9,10,11</sup> The use of calcium hydroxide as intracanal medicament in regenerative endodontics gave comparable results in respect to the apical closure, dental wall thickening, lengthening of the root and periapical repair when compared to other medicaments like triple antibiotic paste or double antibiotic paste.<sup>1,9</sup> However, a meta-analysis, suggests that calcium hydroxide tends to stimulate a greater percentage of apical closure and a lower percentage of dentin wall thickening as compared to antibiotic pastes in which greater dentin wall thickening and lower apical closure were found. This finding is helpful in selecting the intracanal medicament according to the stage of root development. Also, both calcium hydroxide and antibiotic pastes gave desirable results in respect to the apical repair and root lengthening.<sup>1</sup> In a study, thickening of the dentinal wall occurred apical to the level of calcium hydroxide placement.<sup>22</sup> The placement of calcium hydroxide upto the middle third of the root gave better results than its placement upto apical level.<sup>23</sup> From the present review we suggest that its better to use calcium hydroxide in cases with open apex but have sufficient dentinal wall thickness. The immature tooth having considerable thin walls, its preferable to use antibiotic paste.

#### Effect Of Calcium Hydroxide On Intracanal Calcification:

There was always a concern of intracanal calcification after regenerative endodontic procedure when calcium hydroxide is used as intracanal medicament. The intracanal calcifications would hinder with the continued thickening of the dentinal walls and thus render the root susceptible to fracture.<sup>14,22</sup> The factors responsible for intracanal calcifications are presently not known. However, the prolonged use of calcium hydroxide was considered as one of the factors responsible for

intracanal calcifications. In a retrospective study, it has been found that the cases medicated with calcium hydroxide exhibit high frequency of intracanal calcifications than those TAP/DAP and concluded that the use of calcium hydroxide and induced bleeding are contributory factors for intracanal calcifications. The intracanal calcifications would impair the vitality of revascularized pulp tissues and would gravely compromise future endodontic treatment if required.<sup>24</sup> Studies suggested that intracanal calcifications are not solely the complication of using CH rather is a compound effect from multiple factors. The intracanal calcification is more frequent in tooth in which necrosis occurred because of trauma, in tooth in which bleeding was induced rather than cases without induced bleeding.<sup>24,25</sup> These factors must be considered before selecting the intracanal medicament.

#### Effect Of Calcium Hydroxide On Dentine Structure:

Regenerative endodontics is a procedure that essentially requires either minimal or no instrumentation of the dentinal walls of the root canal, therefore, the proper disinfection needed to eliminate the root canal bacteria solely relies upon gentle and thorough irrigation and placement of effective antibacterial intracanal medicament. The physical and mechanical properties of radicular dentin such as dentin flexure strength, microhardness and root fracture resistance has been found to be significantly reduced by the various irrigants and medicaments used in regenerative endodontics.<sup>26</sup> A study suggested that the microhardness reduction and superficial demineralization of dentin was significantly higher in teeth treated with triple antibiotic paste as compared to calcium hydroxide or lower concentration of triple antibiotic paste used during endodontic regeneration.<sup>26</sup> However, double antibiotic paste showed less destructive effect on the chemical structure of dentin than calcium hydroxide.<sup>27</sup> Further, future studies are suggested to confirm the effects on different irrigants and intracanal medicament used in regenerative endodontic procedure on dentinal structure.

#### CONCLUSION:

From the present review we conclude that calcium hydroxide gave acceptable clinical outcome in regenerative endodontic procedures. Yet, clinicians must consider all the factors before selecting intracanal medicaments such as type and duration of infection, stage of root development, esthetic requirement like antibiotic paste should be avoided in anterior teeth because of risk of tooth discoloration, type and severity of tooth injury like minor luxation injuries, such as concussion and subluxation or severe luxation injuries such as lateral luxation, extrusive luxation, intrusive luxation and avulsion to avoid post-treatment complications as well as duration of intracanal medicament used. We suggest more randomized clinical trials comparing intracanal medicaments which will be helpful for clinicians to select the appropriate disinfection method while planning regenerative endodontic procedures.

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