Review Article

Outcomes of vital pulp therapy in permanent teeth with different medicaments based on review of the literature

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ABSTRACT

Vital pulp therapy (VPT) is a biologic and conservative treatment modality to preserve the vitality and function of the coronal or remaining radicular pulp tissue in vital permanent teeth. A search was conducted via the Cochrane database, PubMed, MEDLINE, and Ovid for any articles with the criteria for "pulp-capping," or "pulp-capping materials" and "VPT outcomes" from 1978 to mid 2014. All articles were evaluated and the valid papers were selected. The outcomes of various VPT techniques, including indirect pulp treatment, direct pulp treatment, partial pulpotomy, and complete pulpotomy in vital permanent teeth were extracted. Although various studies have different research approach, most studies noted a favorable treatment outcome. Mineral trioxide aggregate (MTA) appears to be more effective than calcium hydroxide $(Ca(OH)_2)$ for maintaining long-term pulp vitality after indirect and direct pulp-capping. However, it seems that the success rate for partial pulpotomy and pulpotomy with $Ca(OH)_2$ is similar to MTA.

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Key Words: Dental cements, calcium hydroxide, permanent dentition, mineral trioxide aggregate, root canal therapies

INTRODUCTION

The aim of treatment after pulp exposure is to promote the pulp tissue healing and facilitate the formation of reparative dentin in order to preserve the pulp vitality and health.^[1] Vital pulp therapy (VPT) procedures involve removal of local irritants and placement of a protective material directly or indirectly over the pulp.^[2] These treatments must be followed by an overlying tight-sealed restoration to decrease bacterial leakage from the restorationdentin interface. VPT is performed to treat reversible pulpal injury in order to promote root development,

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Website: www.drj.ir www.drjjournal.net www.ncbi.nlm.nih.gov/pmc/journals/1480 apical closure and accomplish complete root canal therapy.^[1,3-5]

There are controversies within the studies on VPT regarding judgment criteria and pulpal status at the time of treatment, optimal technique and treatment outcomes.^[1,3,5] There is no consensus as to the best therapeutic technique and comprehensible diagnostic indications for the management of caries-exposed permanent teeth.^[1,3,5] No long-term data regarding the outcome and the survival rate of VPT is available, either.^[2] The purpose of this paper was to review

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the outcomes of various VPT techniques, including indirect pulp treatment (IPT), direct pulp treatment (DPT), partial pulpotomy, and full pulpotomy in vital permanent teeth.

A search was conducted via the Cochrane database, PubMed, MEDLINE and Ovid for any articles with the criteria for "pulp-capping," or "pulp-capping materials" and "VPT outcomes" from 1978-2014. No specific inclusion or exclusion criteria were applied as to what articles would be included in this review. It was hoped that the extent of the literature reviewed would be as comprehensive as possible.

FEATURES OF SUCCESSFUL VITAL PULP THERAPY

In accordance with several authors,^[1-3,5,6] the two major clinical and radiographic criteria below are the indicators for successful treatment: Maintenance of pulp vitality, minimum pulp inflammatory responses, formation of a continuous layer of reparative dentin, absence of postoperative clinical signs or symptoms of thermal or periapical and/or both sensitivity, as pain, or swelling, absence of radiographic evidence of internal or external root resorption, periapical and/or inter-radicular radiolucency. irregular calcification, or other pathologic changes, continuous root development and apexogenesis of teeth with incompletely formed roots.^[2,4]

Various publications demonstrated that success rates decrease with time.^[2,4,6,7] However, there is no clear

explanation for this fact, and further investigations are needed. Unfavorable outcomes are caused by infection due to either remaining bacteria, or new bacteria from penetrating restoration margins. Thus, beside the immediate placement of a bacteria-tight restoration, the use of rubber dam and aseptical treatment conditions are strongly recommended.^[6]

Although clinical studies point out that the VPT success rates of caries-exposed immature permanent teeth might be comparable with the success rate of root canal treatment,^[8] the clinicians are less confident about the success of VPT.^[5] Some complications may develop after VPT, so patients should be regularly followed up. It has been shown that a tooth with a favorable treatment outcome 5 years after VPT, the likelihood that it will stay vital in the following years is more than 95%. Consequently, the time for an adequate postoperative 1-2 years follow-up examination, as often recommended, may well be too short.^[6]

FACTORS INFLUENCING TREATMENT OUTCOMES OF VITAL PULP THERAPY TECHNIQUES

The VPT success rate in caries-exposed permanent teeth is the subject of many debate fluctuating between $13\%^{[9]}$ and 100% after^[10] [Tables 1-4]. The 10-year success rate was 13% in Barthel *et al.* study in which pulp-capping treatments were performed by students. After rubber dam placement and cleansing with 3% H₂O₂, a setting calcium hydroxide (Ca(OH)₂) paste

Authors	Year	Observation period	Sample size	Success rate (%)	Type of material
Nirschl and Avery[11]	1983	6 months	38	94.1	Ca(OH) ₂
Bjørndal and Thylstrup ^[12]	1998	6 months	94	94.6	Ca(OH)
Orhan et al.[13]	2008	3 months	52	97.8	Ca(OH)
Orhan <i>et al.</i> ^[14]	2010	Over 1-year	154	92-94	Ca(OH)
Gruythuysen et al.[15]	2010	3 years	66	93	Ca(OH)
Bjørndal <i>et al.</i> ^[16]	2010	1-year	Stepwise excavation (<i>n</i> =143) Direct complete excavation (<i>n</i> =149)	74.1 62.4	Ca(OH) ₂
Maltz <i>et al.</i> ^[17]	2011	1.5 year 3 years 5-year 10-year	32	97 90 82 63	Ca(OH) ₂
Leye Benoist <i>et al.</i> ^[18]	2012	3 months MTA 6 months MTA 3 months Ca(OH) ₂ 6 months Ca(OH) ₂	60	93 89.6 73 73	MTA Ca(OH) ₂ (Dycal(®))
Petrou et al.[19]	2014	6 months	31	86.9	Ca(OH) ₂
			29	90.5	Portland cement
			26	94.5	MIA

Table 1: Treatment outcome of indirect pulp-capping in permanent teeth

MTA: Mineral trioxide aggregate.

Akhlaghi and Khademi: Outcomes of vital pulp therapy

	Authors	Year	Observation period	Sample size	Success rate (%)	Type of material	Type of exposure
	Beetke et al [20]	1990	1-vear	106	93.4	Ca(OH)	Artificial exposure
Matsuo et al. 1996 >6 months to 1-year 25 80 Ca(OH) ₂ Caries exposure Santucci ^[63] 1999 6 months 18 76 Ca(OH) ₂ Caries exposure Barthel et al. ^[61] 2000 >5-year 123 37.0 Ca(OH) ₂ Caries exposure Al-Hiyasat et al. ^[64] 2006 3-5 years 204 59.3 Ca(OH) ₂ Caries exposure Farsi et al. ^[66] 2006 3-5 years 204 59.3 Ca(OH) ₂ Caries exposure Farsi et al. ^[66] 2006 3-5 years 204 59.3 Ca(OH) ₂ Caries exposure Farsi et al. ^[66] 2006 3-5 years 204 59.3 Ca(OH) ₂ Caries exposure Parsi et al. ^[66] 2006 >6 months to 1-year 30 93.3 MTA Caries exposure Bogen et al. ^[101] 2008 >6 months to 1-year 49 100 MTA Caries exposure Orhan et al. ^[101] 2010 0.4-16.6 years 248 76.3 after 13.3 years Ca(OH) ₂ Caries exposure Dammaschke et al. ^[101] 2010	Fitzgerald and Hevs ^[21]	1991	>6 months to 1-vear	18	75	Ca(OH)	Caries exposure
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Matsuo <i>et al.</i> ^[22]	1996	>6 months to 1-year >1-2 years	25 10	80 100	Ca(OH) ₂	Caries exposure
Barthel et al. ^[9] 2000 >5-year 10-year 123 37.0 13.0 Ca(OH) ₂ Ca(OH) ₂ Caries exposure Al-Hiyasat et al. ^[24] 2006 >5 wears 204 59.3 Ca(OH) ₂ Caries exposure Farsi et al. ^[26] 2006 >6 months to 1-year 30 93.3 MTA Caries exposure Farsi et al. ^[26] 2008 >6 months to 1-year 30 93.3 MTA Caries exposure Bogen et al. ^[16] 2008 >6 months to 1-year 49 100 MTA Caries exposure Sigman et al. ^[16] 2008 >6 months to 1-year 49 100 MTA Caries exposure Dammaschke et al. ^[16] 2010 0.4-16.6 years 248 76.3 after 13.3 years Ca(OH) ₂ Caries exposure Dammaschke et al. ^[16] 2010 1-year 22 31.8 Ca(OH) ₂ Caries exposure Mente et al. ^[26] 2010 1-year 12 78 MTA Caries exposure Naito ^[26] 2010 1-year 51 67.7	Santucci ^[23]	1999	6 months 4.5 years	18	76 43.6	Ca(OH) ₂	Caries exposure
$\begin{array}{c c c c c c } Al-Hiyasat et al. $ \eqref{Al-Hiyasat et al.} $ Al-Hiyasat et$	Barthel <i>et al.</i> ^[9]	2000	>5-year 10-year	123	37.0 13.0	Ca(OH) ₂	Caries exposure
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Al-Hiyasat et al.[24]	2006	3-5 years	204	59.3	Ca(OH) ₂	Caries exposure
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Farsi <i>et al.</i> ^[25]	2006	>6 months to 1-year >1-2 years	30 28	93.3 100	MTA	Caries exposure
Orhan et al. 2008 3 months 52 74.4 Ca(OH) ₂ Caries exposure Dammaschke et al. ^[6] 2010 0.4-16.6 years 248 76.3 after 13.3 years Ca(OH) ₂ Caries exposure Bjørndal et al. ^[14] 2010 1-year 22 31.8 Ca(OH) ₂ Caries exposure Orhan et al. ^[14] 2010 Over 1-year 154 78 Ca(OH) ₂ Caries exposure Mente et al. ^[26] 2010 6.5 year 122 78 MTA Ca(OH) ₂ Caries exposure Miles et al. ^[27] 2010 1-year 2-year 51 67.7 MTA Caries exposure Caries exposure Naito ^[28] 2010 1-year 2-year 51 67.7 MTA Caries exposure Caries exposure Willershausen et al. ^[29] 2010 1-year 5-year 9 years 1075 80.1 68.0 Ca(OH) ₂ Caries exposure Nowicka et al. ^[81] 2013 2 years 195 80.3 68.5 MTA Ca(OH) ₂ Caries exposure Nowicka et al. ^[81] 2013	Bogen <i>et al</i> . ^[10]	2008	>6 months to 1-year >1-2 years >2-3 years >3 years	49 49 12 17	100 100 100 98	МТА	Caries exposure
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Orhan et al.[13]	2008	3 months	52	74.4	Ca(OH) ₂	Caries exposure
Bjørndal et al. ^[14] 2010 1-year 22 31.8 Ca(OH) ₂ Caries exposure Orhan et al. ^[14] 2010 Over 1-year 154 78 Ca(OH) ₂ Caries exposure Mente et al. ^[26] 2010 6.5 year 122 78 MTA Caries exposure Miles et al. ^[27] 2010 1-year 51 67.7 MTA Caries exposure Naito ^[28] 2010 5-year 69 78.17 MTA Caries exposure Naito ^[28] 2010 5-year 69 78.17 MTA Caries exposure 9 78.17 MTA Caries exposure 53 69.5 Ca(OH) ₂ Caries exposure Willershausen et al. ^[29] 2011 1-year 1075 80.1 Ca(OH) ₂ Caries exposure 9 years 5 80.3 Ca(OH) ₂ Caries exposure 53 69.5 Ca(OH) ₂ Caries exposure Nowicka et al. ^[30] 2013 2 years 195 80.3 Ca(OH) ₂ Caries exposure 20(OH) ₂ Caries exposure 59 Ca(OH) ₂ Caries	Dammaschke et al.[6]	2010	0.4-16.6 years	248	76.3 after 13.3 years	Ca(OH) ₂	Caries exposure
Orhan et al. 2010 Over 1-year 154 78 Ca(OH) ₂ Caries exposure Mente et al. 2010 6.5 year 122 78 MTA Caries exposure Miles et al. 2010 1-year 51 67.7 MTA Caries exposure Miles et al. 2010 1-year 51 67.7 MTA Caries exposure Naito ^[28] 2010 5-year 69 78.17 MTA Caries exposure Willershausen et al. 2011 1-year 1075 80.1 Ca(OH) ₂ Caries exposure 9 years 5-year 1075 80.1 Ca(OH) ₂ Caries exposure Nowicka et al. 2013 2 years 195 80.3 MTA Caries exposure Nowicka et al. 2013 6 weeks 11 100 MTA Mechanically exposed Mente et al. 2014 Over 10-year 229 80.5 MTA Caries exposure 630 2014 13.4 months 28	Bjørndal <i>et al.</i> ^[16]	2010	1-year	22	31.8	Ca(OH)	Caries exposure
Mente et al.20106.5 year12278 60MTA Ca(OH)2Caries exposure Ca(OH)2Miles et al.20101-year 2-year5167.7 5.2MTACaries exposure Caries exposureNaito20105-year69 5-year78.17 69.5MTACaries exposure Ca(OH)2Willershausen et al.20111-year 5-year 9 years107580.1 68.0 5-year 9 yearsCa(OH)2 68.0 58.7Ca(OH)2 Ca(OH)2Caries exposure Ca(OH)2Hilton et al.20132 years195 18180.3 68.5MTA Ca(OH)2Caries exposure ca(OH)2Nowicka et al.20136 weeks11 11100 11MTA BiodentineMechanically exposedMente et al.2014Over 10-year229 22980.5 59 29MTA Caries exposure Ca(OH)2Caries exposure exposureAsgary et al.201413.4 months2896.4CEM cementCaries exposure	Orhan <i>et al.</i> ^[14]	2010	Over 1-year	154	78	Ca(OH) ₂	Caries exposure
Miles et al. 2010 1-year 2-year 51 67.7 56.2 MTA Caries exposure Naito ^[28] 2010 5-year 69 78.17 MTA Caries exposure Willershausen et al. ^[29] 2011 1-year 5-year 1075 80.1 69.5 Ca(OH) ₂ Caries exposure Willershausen et al. ^[29] 2013 2 years 1075 80.1 5-year Ca(OH) ₂ Caries exposure Hilton et al. ^[30] 2013 2 years 195 80.3 181 MTA Caries exposure Nowicka et al. ^[31] 2013 6 weeks 11 11 100 MTA Mechanically exposed Mente et al. ^[32] 2014 Over 10-year 229 80.5 59 MTA Caries exposure Ca(OH) ₂ Asgary et al. ^[33] 2014 13.4 months 28 96.4 CEM cement Caries exposure caries exposure	Mente et al.[26]	2010	6.5 year	122	78 60	MTA Ca(OH)	Caries exposure
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Miles <i>et al.</i> ^[27]	2010	1-year 2-year	51	67.7 56.2	MTA	Caries exposure
Willershausen et al.20111-year 5-year 9 years107580.1 68.0 58.7Ca(OH)_2Caries exposureHilton et al.20132 years195 18180.3MTA 68.5Caries exposureNowicka et al.20136 weeks11 11100 11MTA BiodentineMechanically exposedMente et al.2014Over 10-year229 201480.5 13.4 monthsMTA 28Caries exposure 68.0 2014	Naito ^[28]	2010	5-year	69 53	78.17 69.5	MTA Ca(OH) ₂	Caries exposure
Hilton et al.20132 years195 18180.3 68.5MTA Ca(OH)_2Caries exposure Ca(OH)_2Nowicka et al.20136 weeks11 11100MTA BiodentineMechanically exposedMente et al.2014Over 10-year22980.5 59MTA Caries exposure 	Willershausen et al. ^[29]	2011	1-year 5-year 9 years	1075	80.1 68.0 58.7	Ca(OH) ₂	Caries exposure
Nowicka et al.20136 weeks11100MTAMechanically exposedMente et al.2014Over 10-year22980.5MTACaries exposure 59Asgary et al.201413.4 months2896.4CEM cementCaries exposure	Hilton <i>et al.</i> ^[30]	2013	2 years	195 181	80.3 68.5	MTA Ca(OH) ₂	Caries exposure
Mente et al.2014Over 10-year22980.5MTACaries exposure 59 $Ca(OH)_2$ Asgary et al.201413.4 months2896.4CEM cementCaries exposure	Nowicka <i>et al.</i> ^[31]	2013	6 weeks	11 11	100 100	MTA Biodentine	Mechanically exposed
Asgary <i>et al.</i> ^[33] 2014 13.4 months 28 96.4 CEM cement Caries exposure	Mente <i>et al.</i> ^[32]	2014	Over 10-year	229	80.5 59	MTA Ca(OH) ₂	Caries exposure
	Asgary et al.[33]	2014	13.4 months	28	96.4	CEM cement	Caries exposure

Table 2: Treatment outcome of direct pulp-capping in permanent teeth in literature

MTA: Mineral trioxide aggregate.

Table 3: Treatment outcome of partial pulpotomy in permanent teeth in literature

Authors	Year	Observation period	Sample size	Success rate (%)	Type of material	Type of exposure
Zilberman <i>et al.</i> [34]	1989	1-8 years	15	93.3	Ca(OH) ₂	Caries exposure
Mejàre and Cvek ^[8]	1993	>1-2 years >2-3 years >3 years	37 33 17	91.9 100 98.8	Ca(OH) ₂	Caries exposure
Mass <i>et al.</i> ^[35]	1995	>6 months to 1-year >1-2 years >2-3 years >3 years	35 32 21 6	97.1 96.9 95.2 100	Ca(OH) ₂	Caries exposure
Nosrat and Nosrat ^[36]	1998	>6 months to 1-year >1-2 years	6	100	Ca(OH) ₂	Caries exposure
Barrieshi-Nusair and Qudeimat ^[37]	2006	>6 months to 1-year >1-2 years	28 21	82.1 95.2	MTA	Caries exposure
Qudeimat et al.[38]	2007	3 years	50	91 93	Ca(OH) ₂ , MTA	Caries exposure
Bjørndal <i>et al.</i> ^[16]	2010	1-year	29	34.5	Ca(OH) ₂	Caries exposure
Caprioglio et al.[39]	2014	3 years	27	85	MTA	Trauma exposure
Chailertvanitkul et al.[40]	2014	2 years	84	99.8 99.8	MTA Ca(OH) ₂ : Dycal	Caries exposure

MTA: Mineral trioxide aggregate.

Authors	Year	Observation period	Sample size	Success rate (%)	Type of material	Type of exposure
Caliskan ^[41]	1995	>6 months to 1-year >1-2 years >2-3 years >3 years	24 8 6 6	91.7 100 100 100	Ca(OH) ₂	Caries exposure
Waly ^[42]	1995	>6 months to 1-year >1-2 years >2-3 years >3 years	20 20 19 18	100 95 94.7 100	Ca(OH) ₂	Caries exposure
Teixeira et al.[43]	2001	>6 months to 1-year	41	82.9	Ca(OH) ₂	Caries exposure
DeRosa ^[44]	2006	>6 months to 1-year >1-2 years >2-3 years >3 years	26 24 21 13	92.3 87.5 90.5 97.8	Ca(OH) ₂	Caries exposure
Witherspoon et al.[45]	2006	>6 months to 1-year >1-2 years	13 10	100 90	MTA	Caries or complicated enamel dentin fractures
El-Meligy and Avery ^[46]	2006	>6 months to 1-year	30	93.3 86.6	Ca(OH) ₂ , MTA	Caries exposure
Nosrat <i>et al.</i> ^[47]	2013	12 months	49	76.8 73.8	CEM cement MTA	Caries exposure
Barngkgei <i>et al.</i> ^[48]	2013	24-42 months	11	100	MTA	Caries exposure
MTA Mine and this side a serve						

Table 4: Treatment outcome of pulpotomy in permanent teeth in litera
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MTA: Mineral trioxide aggregate.

(Kerr Life, Kerr, Karlsruhe, Germany) was the wound and a base of either zinc phosphate cement or glass ionomer cement was applied. The teeth were then restored with amalgam fillings, composite fillings, gold cast restorations, or with temporary fillings within the first 2 days or more after pulp exposure.^[9]

In Bogen *et al.* study with 97.96% success rate over an observation period of 9 years, one expert operator completed all direct pulp caps. Following placement of a dental dam, using a caries detector dye and caries excavation under magnification, NaOCl for hemostasis within 1 to 10 min, mineral trioxide aggregate (MTA) placed over the exposures and all surrounding dentin. The operator then restored the teeth provisionally with unbonded Clearfil Photocore (Kuraray Medical, Okayama, Japan). During a second visit, within 5 to 10 days the operator restored the teeth with bonded composite after sensibility testing and confirmed MTA curing.^[10]

There is a controversy regarding the VPT procedures outcomes, with many methodological variations between the different studies. Therefore, it may be difficult to compare the various studies because the status of the pulp tissue at the time of treatment, the techniques, observation periods, examination methods, and examination criteria may noticeably differ. Although these studies have different research approach, most studies noted a favorable treatment outcome, which seems to be inconsistent with the clinical standpoint that the VPT outcome is uncertain.^[6] Accurate diagnosis of the pulp status prior to treatment, removal of caries, prevention of leakage, and use of an aseptic technique are the main factors influencing treatment outcomes of VPT. The amount of crown destruction and the ability to restore a tooth are usually associated with the long-term prognosis of VPT.^[1]

The presence of microorganisms with subsequent infection, the inflammatory status of the pulp tissue,^[49] the size of the carious pulpal exposure,^[50] the time of examination,^[9] the final location and the quality of the dentin bridge, the type of pulp therapy material used,^[51] the technique employed were the criteria used to determine success, play a role in determining VPT prognosis as well.^[1] Furthermore, a distinction must be made between failure of the pulp therapy and failure of the overlying restoration.^[52] There are some limitations in determining the long-term success of VPT in permanent teeth such as the difficulty of recalling patients regularly and the impossibility of determining histological success.^[5] The careful decision should be made on the best treatment option of treatment, based on patient history, clinical/ radiographic findings, the long-term prognosis, and the ability to restore a tooth.[52]

THE MATERIALS USED IN VITAL PULP THERAPY PROCEDURES

Materials used in VPT should have several properties, including the ability to eliminate bacteria, to create

an adequate seal and to induce mineralization and normal root development.^[53] At present, Ca(OH)₂ and MTA are the materials of choice according to several studies.^[45,53-55] Bone morphogenetic proteins (BMPs) and transforming growth factor- β (TGF- β), bioceramic, biodentine, enamel matrix derivative (EMD), propolis, calcium-enriched mixture (CEM) cement, tricalcium phosphate cement and some other bioactive materials has been also suggested for VPT.

Calcium hydroxide

Calcium hydroxide is a high-alkaline (pH = 11), white, crystalline, slightly soluble basic salt that dissociates into calcium and hydroxyl ions in solution. It is used in both hard-setting salicylate ester cements and paste (aqueous suspension) forms in VPT.^[6] The advantages of Ca(OH), are its excellent antibacterial properties and the ability to induce reparative bridge formation when applied to pulp tissues.^[54] However, it was unable to kill Enterococcus faecalis in the dentine.^[55] Some disadvantages of Ca(OH), such as producing a dentinal bridge containing multiple defects and porosities, lack of inherent adhesive qualities, dissolution over time, and inability to provide a long-term seal against microleakage may account for its inability to suppress inflammation. However, in more human studies concerning VPT with Ca(OH)₂, the dentinal defects are not a frequent finding^[56,57] and as the bridge gets thicker, the quality of reparative dentin improves.^[51,58]

Zones of obliteration and coagulation necrosis superficial to reparative dentin were detected as well due to very basic pH of some $Ca(OH)_2$ inorganic substances. Stanley suggests that the internal resorption and the dystrophic calcification seen after VPT are less likely to occur with the $Ca(OH)_2$ products at lower-pH such as Dycal (DeTrey Dentsply, Skarpnack, Sweden).^[50] It is known that alkaline pH of $Ca(OH)_2$ irritates the pulp cells and induces the release of bioactive molecules such as BMP and TGF- β 1, which stimulate pulpal repair.^[59,60]

Numerous studies have evaluated the outcomes of CH in vital pulp treatment [Tables 1-4].

Mineral trioxide aggregate

Mineral trioxide aggregate is composed of tricalcium silicate, tricalcium oxide, tricalcium aluminate, silicate oxide, and added bismuth oxides for radiopacity.^[61] After hydration of the powder, colloidal gel forms, which is composed of calcium oxide crystals in an amorphous structure. The biocompatibility of

MTA is due to the formation of $Ca(OH)_2$ in reaction products.^[62] Consequently, many of the advantages of MTA are comparable to those of $Ca(OH)_2$, including high alkaline pH, its antibacterial and biocompatibility properties, radiopacity and its ability to stimulate the release of bioactive dentin matrix proteins.^[61,62] There are some differences between MTA and $Ca(OH)_2$, as well: MTA has demonstrated a superior ability to maintain the integrity of pulp tissue and produces a thicker and less porous dentinal bridge at a faster rate.^[63] In addition, MTA is able to decrease pulp inflammation,^[49] and presents significant less toxicity and pulpal necrosis which is statistically significant compared with Ca(OH)₂ were detected in histological evaluations.^[49,63,64]

However, more research studies are required to support this conclusion because optimal randomized clinical studies are lacking, and there are some limitations in the design of these studies. For instance, in one study, the following statement was noted: "In light of the results of the present and other relevant studies, MTA is superior to Ca(OH), for pulp-capping mechanically exposed human teeth."[63] In that study 14 intentionally exposed pulps were divided into two groups. Half of them were covered with MTA and the other half with Ca(OH)₂. Histological evaluation was carried out after 1-4 weeks and 6 months of teeth extraction. By the final assessment (6 months), only one tooth in each group was evaluated. This sample size was too small for statistical analysis. By the way, this study uses a gold standard which is histopathology and for such studies we cannot expect a high sample size due to the difficulties. Therefore, it seems that MTA has a superior property. Other researchers confirmed "the outcomes suggest that MTA is a more predictable pulp-capping material than Ca(OH),."[10] After approximately 4 years of follow-up of 49 teeth treated with MTA (direct pulp-capping [DPC]), a 98% success rate was reported. Although, there was no Ca(OH), control group in that study but in a study using the same procedure with a setting Ca(OH), paste, the 5-year success rate of 123 teeth was 37%.

However, negative aspects of MTA exist, such as its prolonged setting time of approximately 2 h and 45 min and the handling difficulty of the powder-liquid MTA compared to the paste formulations of $Ca(OH)_2$. The presence of iron in the gray MTA formulation may discolor the tooth.^[51] In addition, it has been reported that the discoloration

is seen with white MTA as a result of the chemical interaction of bismuth oxide with dentin collagen.^[65,66] The outcomes of various techniques of VPT using MTA would be discussed later.

Calcium enriched mixture cement

An endodontic cement referred to as CEM cement has been developed, which predominantly consists of different calcium compounds.^[67]

The main components of CEM cement powder are CaO, SO₃, P₂O₅, SiO₂, and minor components are Al₂O₃, Na₂O, MgO, and Cl as necessary ingredients, which provide a bioactive calcium — and phosphate-enriched material when mixed with a water-base solution.^[66,67] Calcium and phosphate ions released from this material form hydroxyapatite not only in simulated body tissue fluid, like MTA, but also in normal saline.^[68]

Some characteristics have been demonstrated for CEM cement, e.g., similar pH, shorter setting time, good handling characteristics, superior film thickness and flow, and a lower estimated price in comparison with MTA.^[69] The antibacterial effect of CEM cement is comparable to that of CH and better than that of MTA or Portland cement.^[69,70]

In addition, CEM cement stimulates hard tissue healing similar to MTA^[71] and provides an effective seal; similar to MTA and superior to IRM.^[67]

Calcium enriched mixture cement has shown favorable results in pulpotomy of permanent molar teeth with irreversible pulpitis, in the management of internal root resorption, in pulp-capping and furcation perforation repair.^[71,72] However, it should be noted that almost all the papers regarding CEM cement are from the same authors who have produced the material and the reports from other researchers are needed.

Adhesive technique

Contemporary researches have stated that healthy pulps without dentine bridges in teeth treated with an etch and composite-resin technique were observed. The theory is that this adhesive system effectively seal the exposed pulp against bacterial microleakage, thus a dentine bridge is not necessary. However, the long-term success of this seal has not been ascertained, and conflicting findings exist. ^[73] Sixty days after direct capping of exposed noninflamed pulp with the bonding technique, a persistent inflammatory reaction without any evidence of pulpal repair was found compared to pulp repair and complete dentine bridging with Ca(OH)₂.^[73] It has been claimed that the moisture and exudation from the exposed pulp may prevent the adhering of resin materials to peripheral dentine, as a result oral bacteria eventually access the pulp through microleakage.^[74] In addition, the potential cytotoxicity of adhesive technique and induction of immune-based hypersensitivity reactions has been reported.^[75] At present, there is little long-term information to support this technique and its use is not recommended.

Resin modified glass ionomers

Although successful results of IPT with resin-modified glass ionomers (RMGIs) have been found, direct contact with the pulp tissue results in inflammation, necrosis and lack of dentin bridge formation. Therefore, it is not recommended to use RMGIs directly on the pulp tissue.^[76,77]

FUTURE ADVANCES IN MATERIALS AND BIOLOGICAL SCIENCES

Recent advances in the field of growth factors offer new therapeutic approaches. BMPs and TGF-B have been reported to induce reparative dentin formation.^[78] At present, commercially available recombinant human BMP-2, -4, and -7 are available for experimentation and clinical trials., bioceramic, biodentine, EMD (STRAUMANN, USA), propolis, tricalcium phosphate cement, and some other bioactive materials has been also suggested for VPT.^[31,79-82] These bioactive molecules have been shown to be inductive by direct or indirect contact with the pulp tissue, and the formed reparative dentin thickness depends on the dose of the biologic agent.^[83] Further evaluation of these factors as new modalities for VPT should be performed. Future development of more efficient wound dressings containing growth factors, proper carrier vehicles with most favorable clinical handling characteristics and delivery, advanced local antimicrobial and anti-inflammatory materials will combine with the improved sealing ability of restorative materials, leading to more definite and predictable results.^[80] At some point, pulpotomies for primary and permanent teeth may be handled with growth factors and predictably induce sound dentin bridges, leaving the remaining radicular tissue entirely surrounded by healthy tissue, eliminating the need for root canal therapy.^[53]

THE TECHNIQUE EMPLOYED

Vital pulp therapy techniques for treatment of exposed immature permanent teeth can be classified into four categories:

- 1. Indirect pulp-capping;
- 2. DPC;
- 3. Partial pulpotomy;
- 4. Indirect pulp treatment.

Indirect pulp treatment is recommended for pulp preservation in asymptomatic teeth with a deep carious lesion adjacent to the pulp, as well as in teeth with a diagnosis of reversible pulpitis. A medicament is then placed over the carious dentin to stimulate and encourage pulp healing.^[4] The placement of a restorative material with adequate seal against the microorganisms is necessary and more important to success than the type of medicament.^[4,6]

Historically several materials have been used for this procedure, including resin-modified glass-ionomer cements, tricalcium phosphates, hydrophilic resins, zinc oxide-eugenol (ZOE), and Ca(OH)₂. The latter two were the most commonly used materials. Within the theory of maintaining pulp vitality, IPT showed no differences in symptoms at 12 months using different formulations of Ca(OH),.^[84]

However, unlike ZOE mineral content of the residual dentin will increase in contact with $Ca(OH)_2$.^[85] A minimum indirect pulp postoperative time period of 6-8 weeks is essential to produce sufficient remineralization of the cavity floor. This favorable outcome is fundamentally dependent on the preservation of a hermetic seal against microleakage by the provisional and final restorations.^[84]

Today treating the dentin with various bioactive molecules, such as enamel matrix protein (emdogain) or TGF- β , is recommended to promote a reactive response in the underlying odontoblasts, stimulate reparative dentin formation and decrease dentin permeability. However, these strategies are being investigated and cannot yet be applied in the clinic.^[86]

One- or two-visit approach IPT in both primary and young permanent teeth can result in a high survival rate and be successful with a one- or two-visit approach. The two-visit treatment method involves the stepwise excavation of deep caries in two steps. The outmost layer of the infected dentin will be removed in the first step, leaving a carious mass above the pulp. The removal of the remaining caries and placement of a final restoration is performed in the second step. Formation of reparative dentin and a definitive pulpal diagnosis will be assessed after 6-8 weeks. An adequately sealed restoration is essential to both steps.^[84]

Partial caries removal significantly diminishes the viable microorganisms, especially during the treatment stages of two-visit IPT, and reduces the risk of pulp exposure during caries excavation by 98%, compared to complete caries excavation in teeth with deep caries.^[84] The IPT success rate with Ca(OH)₂ in permanent teeth is 93%^[15] and 63%^[17] after 3 and 10 years, respectively. Regarding a new study, MTA appears to be more effective than Ca(OH)₂ 6 months after indirect pulp-capping^[18] [Table 1].

Direct pulp treatment

Direct pulp treatment is defined as wound dressing of an exposed healthy pulp tissue with a biocompatible material to promote pulp healing and generate reparative dentin.^[2] The two key points to the success of $Ca(OH)_2$ DPC have been emphasized; pulp-capping should only be performed in asymptomatic teeth and a well-sealed restoration should be placed immediately after DPT.^[39]

A variety of materials have been recommended for use in DPT: Antibiotics, calcitonin, collagen, corticosteroids, cyanoacrylate, resorbable tricalcium phosphate ceramic, resin-based adhesive composite systems, bioceramic, biodentine, CEM cement, tricalcium phosphate cement,^[31,76,87] ZOE, Ca(OH)₂ and MTA. The three last ones have been used more frequently.^[88]

Some disadvantages for ZOE formulations have been known: Eugenol released from ZOE is extremely cytotoxic, and the interfacial microleakage with ZOE increases over time.^[89] In a human clinical study using ZOE as a DPC agent, up to 12 weeks after DPT, chronic inflammation, without any evidence of pulp healing or reparative dentin formation, was observed compared to CH control group in which all the teeth demonstrated healing within 4 weeks.^[90]

Calcium hydroxide has been regarded as the "gold standard" for DPC for several decades. To date, the literature on the treatment outcomes of DPT with $Ca(OH)_2$ after iatrogenic pulp exposure has been inconsistent. The success rates of $Ca(OH)_2$ pulp-capping in a review of 19 clinical studies, including over 2,400 cases, were about 60% to almost 100% if carried out by an experienced clinician [Table 2].

Despite this fact, Barthel et al. found only 13% success rate 10-year after capping caries-exposed asymptomatic vital pulps in which dental students were the operators.^[9] However, it should be kept in mind that the short-term success of DPT in immature teeth that leads to the apical closure is valuable. The knowledge of pulpal physiology has progressed so much since then, and better understanding of the pulp healing potential is obtained. In addition, the wide-open apices and high vascularity of immature permanent teeth enhance the successful outcome of direct capping techniques.^[1] Furthermore, even under suboptimal conditions, Ca(OH), has shown a clinical success. Thirty-four traumatically exposed teeth with an approximately 4-h delay before Ca(OH), pulp-capping showed a 97% success rate for periods of up to 17 years.^[91]

Animal DPT studies comparing MTA to Ca(OH), generally exhibit better-quality pulp healing with MTA.^[92] Most human studies illustrated comparable pulp cap outcomes of MTA and Ca(OH),. In a study using 11 pairs of third molars with DPT was possible to observe better pulp healing was demonstrated in MTA groups versus Ca(OH), groups. Pulps of these teeth were mechanically exposed and capped with either MTA or Ca(OH), covered with ZOE, and restored with amalgam. After extraction of teeth histological evaluation at 1-week and 2-, 3-, 4-, and 6-month intervals revealed less pulpal hyperemia, less inflammation and necrosis, and more predictable and consistent dentinal bridge formation in the MTA-treated teeth.[63] Similar results have been reported by other investigators.^[16,18,28,26,31] Long-term studies in large-scale and prospective clinical trials are highly desirable to elucidate the treatment outcome of DPT. The outcomes of studies on DPT with Ca(OH), or MTA in permanent teeth are summarized in Table 2. The 5-year success rate DPT with Ca(OH), in permanent teeth was about 59-69%^[28,24] and for MTA was 78-98%.^[10,28] MTA appears to be more effective than Ca(OH), for maintaining long-term pulp vitality after DPC.^[26,28]

Partial pulpotomy

Partial pulpotomy is indicated in a young permanent tooth for a small (<2 mm) pulp exposure in which the pulpal bleeding is controlled in 1-2 min.^[4] Partial pulpotomy has been shown to be more successful in traumatically exposed rather than caries-exposed young permanent molars.^[8,39,40,93] In immature teeth, this treatment is significantly more successful amongst the VPT techniques as well. Generally, the most common material used in partial pulpotomy of immature permanent teeth is $Ca(OH)_2$.^[83] MTA has been confirmed as a pulp dressing material for partial pulpotomy in caries-exposed permanent molars with the success rate comparable to that of $Ca(OH)_2$.^[5] Fuks *et al.* reported a success rate of 87.5% for partial pulpotomies in complicated crown fractures in permanent incisors for 7.5-11 years. In general, as the duration of the follow-up period increased, the success rate diminished.^[94]

The outcomes of studies on partial pulpotomy with $Ca(OH)_2$ or MTA are summarized in Table 3. The success rate with $Ca(OH)_2$ in permanent teeth was about 91-100%^[8,36] after 2 years and for MTA was 95.2-99.8%.^[40,37] The difference between MTA and Ca(OH)₂ for partial pulpotomy was not significant.

Full pulpotomy

The pulpotomy procedure aims to preserve pulp vitality of young permanent teeth to promote normal root development. The necessity for root canal treatment following pulpotomy is to avoid a possible pulpal necrosis, continuous calcification or internal resorption.^[5] After complete coronal pulpotomy with Ca(OH)₂ dressing, later root canal treatment must be considered because of the dangers of dystrophic calcification of root canals.

Calcium hydroxide is the recommended pulpotomy material due to improved clinical outcomes. Dystrophic calcification in the root canals will be created following Ca(OH), pulpotomy procedure, which may prevent future endodontic treatments.^[83] Besides, this calcification may reduce blood supply, which could lead to pulp necrosis.^[95] The rationale is that a small amount of remaining pulp tissue is confined with a large amount of calcium in full coronal pulpotomy procedures. Therefore, the root canal treatment is performed after complete apical closure.^[83] The success rate of Ca(OH), pulpotomies in cariously exposed teeth ranged from approximately 50-92%[41,43,78] and 72-96% in teeth with traumatic exposures.^[96-99] Similar to DPC, the formation of dentin bridge is not the only indicator of treatment success since this bridge may be incomplete and filled with the tissue remnants. It is also possible that a fibrous tissue without evidence of dentinal bridge covers up the remaining pulp. Studies have shown that MTA may be useful as a substitute for Ca(OH), as the material of choice for pulpotomy procedures.^[45] The calcification of the root canal entrances can occur after long periods of exposure to

 $Ca(OH)_2$ or MTA. The outcomes of studies on pulp therapy with $Ca(OH)_2$ or MTA in permanent teeth are summarized in Table 4.

The success rate with $Ca(OH)_2$ in permanent teeth was about 87.5-100%^[41,44] after 2 years and for MTA was 90-100%.^[45,48] The difference between MTA and $Ca(OH)_2$ for pulpotomy was not significant. MTA has clinical success rate comparable to CH as a pulp dressing material for full pulpotomy in permanent molars with carious exposures.

As a final point, there are still controversies about the treatment outcomes and it is suggested that further randomized controlled clinical trials regarding the VPT long-term outcomes be conducted.

CONCLUSION

There is a controversy regarding the VPT procedures outcomes, with many methodological variations between the different studies. Although various studies have different research approach, most studies noted a favorable treatment outcome. The type of coronal restoration and clinical status of the pulp tissue have a significant influence on the results.

Mineral trioxide aggregate appears to be more effective than $Ca(OH)_2$ for maintaining long-term pulp vitality after indirect and DPC. However, it seems that the success rate for partial pulpotomy and pulpotomy with Ca(OH), is similar to MTA.

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Conflicts of interest

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