International Journal Dental and Medical Sciences Research
Volume 3, Issue 1, Jan-Feb 2021 pp 746-750 www.ijdmsrjournal.com ISSN: 2582-6018

Properties of Pulp Capping Agents for pulp therapy - A Systematic Review Protocol

Dr.Soumyadeep Ghosh[1], Dr. Shruthi Nagaraja[2], Dr.Tejaswini B.D[3].
1-Post Graduate Resident, Department of Conservative Dentistry and Endodontics, Faculty of Dental Sciences, Ramaiah University of Applied Sciences, Bangalore
2-Associate Professor, Department of Conservative Dentistry and Endodontics, Faculty of Dental Sciences, Ramaiah University of Applied Sciences, Bangalore
3- Assistant Professor, Department of Public Health Dentistry, Faculty of Dental Sciences, Ramaiah University of Applied Sciences, Bangalore

Submitted: 20-01-2021 Revised: 31-01-2021 Accepted: 03-02-2021

ABSTRACT: Background: Mostly the biological properties were taken into considerations for pulp capping agents but there are other properties (compressive strength, Ca++/OH- release etc) which plays a pivotal role in success of pulp therapy, and to ensure all the properties are given equal importance so as to select the best pulp capping agent which fulfils all the required properties for the success of the therapy in a given clinical scenario
Methods : We will searchthe following electronic bibliographic databases (MEDLINE (PubMed), Google Scholar and The Cochrane Library. The literature search will be carried out by two independent reviewers until August 2019. Studies included Literature Review from 2008 – 2018.
Discussion :Strength of evidence will be interpreted as high,moderate, low or very low using GRADE framework of in vitro studies. This systematic review will potentially improve research practice, by identifying risk of bias and design features which compromise transability and contribute to evidence based clinical trial design.
Systematic Review Registration : PROSPEROCRD 42020160461
Keywords : Direct pulp capping, pulp capping agents, properties

I. BACKGROUND :-

Vital pulp therapy is performed to maintain the vitality of pulp [1]. In deep carious lesions, the inflammation is confined to superficial coronal pulp, whereas tissue deep inside the radicular pulp remains normal [2].

An important function of vital pulp therapy is to stimulate the pulp odontoblasts to lay down reparative dentin and promote remineralization of existing dentin; thus encouraging the dentin–pulp complex and eventually, the carious lesion, to heal [3].

Clinicians have used many materials and techniques for pulp capping like calcium hydroxide, hydrophilic resins, resin modified glass ionomer cement, tricalcium phosphate and more recently Calcium silicate-based cements eg. Mineral Trioxide Aggregate (MTA), Biodentine, Calcium enriched mixture, Bioaggregate and Theracal LC.

Calcium hydroxide ,gold standard for Direct Pulp Capping (DPC) has been successfulfor many years because of its excellent antimicrobial property, induction of mineralization [4] and low cytotoxicity [5]. But studies revealed it has several disadvantages high solubility, lacking adhesion [6] obliteration of pulp chamber and tunnel defects and this all had led to the advent of newer material with improved properties.

MTAemerged as a good DPC agent after several researches which exhibits less pulpal inflammation, good cytocompatibility [7] and better antibacterial properties but are highly soluble [8], longer setting time and have poor handling characteristics .

Later, in 2011, a new material appeared in the market: Biodentine™ (Septodont, Saint Maur des Fosses, France), which is indicated as a replacement for both coronal and root dentin. The quick hardening of this cement, in comparison with previous calcium silicates, and its improved mechanical properties made it suitable for definitive restorations in replacing dentin and as a temporary cement to restore enamel [9]. Other materials, such as TheraCal LC (Bisco Inc., Schamburg, IL, USA), have been developed more recently suggesting the use of calcium silicates mixed with composite resins, which can control hardening times since they are light-curing materials. One of the greatest advantages of calcium silicates is their so-called bioactivity property.

International Journal Dental and Medical Sciences Research
Volume 3, Issue 1, Jan-Feb 2021 pp 746-750 www.ijdmsrjournal.com ISSN: 2582-6018

Bioactive materials are defined as those that "trigger a biological response in the tissue-material interface, resulting in the formation of bonding between material and tissue"[10]. This is evident in the favourable responses observed when the material is in contact with soft tissues such as pulp and periodontal tissues, or with hard tissues such as dentin.

Research shows that these cements can produce strong bonding with dentin through an area of mineral infiltration, with formation of mineral tags and diffusion of calcium and silicon to dentin [11].In addition, in contact with pulp tissue, the material can stimulate dentin bridge formation [12].

Mostly the biological properties were taken into considerations for pulp capping agents but there are other properties (compressive strength, Ca++/OH- release etc) which plays a pivotal role in success of pulp therapy, and to ensure all the properties are given equal importance so as to select the best pulp capping agent which fulfils all the required properties for the success of the therapy in a given clinical scenario.

Numerous pulp capping agents are available today, and studies have revealed that many properties like (Ca++/OH- ion release, Compressive strength, solubility, water absorption, depth of cure, pH etc) are involved in the success of pulp therapy besides the biological properties, but no conclusive evidence are available as to which pulp capping agent is most suitable.

However, to the best of our knowledge, there are no/few reviews done to determine which pulp capping agent is the best amongst various properties, so as to ensure easy selection of best pulp capping agents in a given clinical scenario. The purposewas toreview various properties of pulp capping agents and to determine the suitable pulp capping agents that fulfil the requirements for pulp therapy. Therefore, the research question for this review is " which pulp capping material satisfies all the requirements of physical, chemical and biological properties beneficial for pulp therapy?"

II. METHODS

The systematic review protocol had been developed by the review authors in accordance with the Preferred Reporting Items for Systematic Review and MetaanalysisProtocol Guidelines (PRISMA-P) [13]. The authors will make use ofthe PRISMA checklist so as to ensure completeness of reporting items and enhance the quality of the protocol. The systematic review results will be reported by the authors as per the PRISMA guidelines, thePRISMA abstract checklist, and guidelines for reportingsystematic review and meta-analysis of animal studies [14,15]. Our protocol registration number is PROSPERO CRD42020160461. Any amendment and reasonsfor such change to the current protocol will be made public through the PROSPERO database.

Eligibility Criteria

Inclusion Criteria

- In Vitro studies that evaluated physico-chemical properties of pulp capping agents
- In Vitro studies that evaluated biological properties of pulp capping agents

Exclusion Criteria

- Studies that evaluate techniques and not materials
- Studies on patent related dental materials

Intervention

Intervention will include new and improved biocompatible and bioactive agents , with remarkable physicochemical properties, that have been recently tested for the purposes of pulp repair and regeneration

Comparision

The comparision group will include different materials (calcium silicate based) that are currently available as alternatives to traditional DPC dressers, such as calcium hydroxide, considered the "gold standard" in this type of pulp treatment

Information Sources and Literature Search

We will search the following electronic bibliographic databases (MEDLINE (PubMed), Google Scholar and The Cochrane Library. The literature search will be carried out by two independent reviewers that will include studies from 2008 – 2018.

After the screening and eligibility criteria, if a consensus was reached by the two reviewers, the article will be included, if not, a third author will be invited to discuss the study. Only papers that fulfilled all the eligibility criteria will be admitted.

Search Strategy

The search strategy will use a combination of MeSH terms and keywords. The search terms are divided into three components, i.e., " Properties" with the words "Cytototoxicity,""Calcium Ion release ," "Hydroxyl ion release,"" Antimicrobial activity ". Pulp Capping materials which include the words "Tricalcium Silicate," "Theracal," "Biodentine,"

International Journal Dental and Medical Sciences Research
Volume 3, Issue 1, Jan-Feb 2021 pp 746-750 www.ijdmsrjournal.com ISSN: 2582-6018

"MTA," "Calcium Hydroxide," .Thematerial component which include the words ". Pulp Capping materials" "Tricalcium Silicate," "Theracal," "Biodentine ," "MTA," "Calcium Hydroxide," .Finally, the end component " Direct Pulp Capping". The three search components will be combined with the Boolean logic term "OR" while the keywords within each component will be combined with "AND." The Hooijmans (2010) and de Vries (2011) search filters for the identification of preclinical studies in PubMed and Embase respectively will be applied to enhance search efficiency [16,17]. The language would not be restricted during the search and identification of studies. In order to get hold of the most recent studies suitable for inclusion, the searches will again be made just before the final analyses.

Study Records

Data Management : Identified articles will be pooled into Mendeley software ver. 2.1(Elsevier). Passwords will be shared between authors and whenever new articles are added they will recieve an update.

Study Selection : Titles and abstract of studies obtained by using the search strategy along with additional sources will be screened by two review authors to identify studies that meet the predetermined inclusion criteria.

In Vitro studies that evaluated physicochemical properties of pulp capping agents, In Vitrostudies that evaluated the biological properties of pulp capping agents. Each relevant article was independently and critically evaluated by two authors (S.G. and S.N.) for itsmethodological research quality (potential risk of bias); these reviewers were previously calibrated forinterexaminer agreement (Cohen's kappa = 0.93). Any discrepancy was resolved by discussion andconsensus with a third author (T.B.D.).

Data Collection Process

The necessary available information will be extracted from each initially included article, through a standardized and pre-piloted form. This information will include name of theauthors , year of publication, sample size, materials and methodologies, results, conclusion and the statistical significance of properties . Evidence tables will then be constructed.

Data Items

Table Data Collection Items

Domain	Data Collection Items
Study Characteristics	Authors, Year of Publication, Research Focus, Materiala and Methodologies, Research Findings
Study Population	Extracted tooth, Sample disc
Intervention	New and improved Biocompatible and Bioactive agents with remarkable physicochemical properties
Comparision	Traditional Direct capping dresser , Calcium hydroxide
Outcome measures	Ca++, OH- ion release, solubility ,water absorption, pH, compressive strength, setting time, agar overlay cytotoxicity test, gene expression, antimicrobial activity and cytocompatibility(MDPC -2)
Risk of bias assessment and quality of reporting of preclinical studies	Using GRADE assessment

Outcome Measures

Primary Endpoint :

To know exactly which material exhibits the best properties in terms of Ca++, OH- ion release, solubility ,water absorption, pH, compressive strength, setting time, agar overlay cytotoxicity test, gene expression,antimicrobial activity and cytocompatibility(MDPC -2).To review various properties of pulp capping agentsand to determine the suitable pulp capping agents that fulfil the requirements for pulp therapy

Risk of Bias Assessment :-

Risk of bias for each in vitro studies will be determined by GRADE assessment [18].

Each relevant article was independently and critically evaluated by two authors (S.G. and S.N.) for itsmethodological research quality (potential risk of bias); these reviewers were previously calibrated forinterexaminer agreement (Cohen's kappa = 0.93). Any discrepancy was resolved by discussion andconsensus with a third author (T.B.D.).

Even though in most of studies an independent examiner was selected to avoid risk of bias, the difference between partial and inadequate information about the properties of pulp capping materials is very subjective.

Taxanomical assessment of included Studies :
Review authors will give
Grade A with full information about the pulp capping material and its result of properties
Grade B with partial information about the pulp capping material and its result of properties
Grade C with inadequate information about the pulp capping material and its result of properties

Strategy for data Synthesis

Quantitative assessment : - Quantitative data assessment will be assimilated in statistical meta analysis using Review Manager Software (RevMan) 5.3 .The outcomes includes best properties in terms of Ca++, OH- ion release, solubility ,water absorption, pH, compressive strength, setting time, agar overlay cytotoxicity test, gene expression, antimicrobial activity and cytocompatibility(MDPC -2).

Heterogeneity Assessment

Cochran's Q will be applied to assess heterogeneity. Cochran's Q can be tested using a chi-squared($\chi 2$) test and its P value to evaluate heterogeneity between primary studies intervention effects. A lowP value (or a large $\chi 2$ statistic relative to its degree of freedom) is suggestive of the fact that the observed variation in estimates of effect is not due to chance alone. However, a non-significant P value does not necessarily indicate absence of heterogeneity since few comparisonsand small sample size as always is the case in in vitro studies usually lead to falsified results. We will, therefore, use additional measure; I^2 statistic for assessing heterogeneity severity as this statistic is independent of the number of comparisons in meta-analysis [19].

Publication Bias

Publication bias for each outcome will be evaluated by testing the asymmetry of the funnel plot using Egger's test [20,21]. The test for funnel plot asymmetry will not be used when there are fewer than ten primary studies in the meta-analysis. The reason behind this is that test power often happens to be too low in general to differentiate chance from real asymmetry[22]. If publication bias proves to be significant, trim and fill method willbe used to correct the probable publication bias. In addition, the significant asymmetry of the funnel plot will also beanalysed in the context of susceptibility to other biases that might explain it.

Knowledge Translation

This review will be beneficial to the undergraduates, postgraduates Dental students, Research Scholars in the field of dentistry to obtain a thorough knowledge about which pulp capping will be best suited in a particular clinical scenario along with academicians and practitioners.

III. DISCUSSION

This work provides a protocol for systematic review of in vitro studies which investigated various properties of pulp capping agents. The overall aim of this review was to provide an updated summary of the existing literature. Results of this study will be helpful for clinical researchers, practitioners and dental students while performing pulp capping. Factors such as internal validity, differences in experimental design may influence the result.

This systematic review is the need of the hour as it compares all the properties required for an ideal pulp capping agent. Over the last decade new pulp capping materials have been introduced and no single study exists which compares all the properties to the best of our knowledge. If sufficient preclinical evidences are available then authors may recommend no further animal model studies thereby reducing the number of animals sacrificed.

REFERENCES

[1]. Parirokh, M., Eskandarizadeh, A., et al. (2011) 'A comparative study on dental pulp response to calcium hydroxide, white and grey mineral trioxide aggregate as pulp capping agents', Journal of Conservative Dentistry, 14(4), p. 351. doi: 10.4103/0972-0707.87196.
[2]. Parirokh, M., Asgary, S., et al. (2011) 'A comparative study of using a combination of calcium chloride and mineral trioxide aggregate as the pulp-capping agent on Dogs' teeth', Journal of Endodontics. Elsevier Ltd, 37(6), pp. 786–788. doi: 10.1016/j.joen.2011.03.010.
[3]. Cohenca, N., Paranjpe, A. and Berg, J. (2013) 'Vital Pulp Therapy', Dental Clinics of North America. Elsevier Inc, 57(1), pp. 59–73. doi: 10.1016/j.cden.2012.09.004.
[4]. Ferracane, J. (2001) Materials in Dentistry, Principles and Applications. 2nd edn. Philadelphia: Lipincot, Williams & Wilkins.
[5]. Kitasako, Y., Ikeda, M. and Tagami, J.

(2008) 'Pulpal responses to bacterial contamination following dentin bridging beneath hard-setting calcium hydroxide and self-etching adhesive resin system', Dental Traumatology, 24(2), pp. 201–206. doi: 10.1111/j.1600-9657.2007.00517.x.

[6]. Cox CF, Sübay RK, Ostro E, Suzuki S, S. S. (1996) 'Tunnel defects in dentin bridges: their formation following direct pulp capping', Operative Dentistry, 21(1), pp. 4–11.

[7]. Camilleri, J. and Pitt Ford, T. R. (2006) 'Mineral trioxide aggregate: A review of the constituents and biological properties of the material', International Endodontic Journal, 39(10), pp. 747–754. doi: 10.1111/j.1365-2591.2006.01135.x.

[8]. Islam, I., Kheng Chng, H. and Jin Yap, A. U. (2006) 'Comparison of the physical and mechanical properties of MTA and portland cement', Journal of Endodontics, 32(3), pp. 193–197. doi: 10.1016/j.joen.2005.10.043.

[9]. Watson, T. F. et al. (2014) 'Present and future of glass-ionomers and calcium-silicate cements as bioactive materials in dentistry: biophotonics-based interfacial analyses in health and disease', Dental Materials. Elsevier, 30(1), pp. 50–61.

[10]. Hench, L. L. (1988) 'Bioactive ceramics', Annals of the New York academy of sciences. Wiley Online Library, 523(1), pp. 54–71.

[11]. Han, L. and Okiji, T. (2013) 'Bioactivity evaluation of three calcium silicate- based endodontic materials', International endodontic journal. Wiley Online Library, 46(9), pp. 808–814.

[12]. Nowicka, A. et al. (2013) 'Response of human dental pulp capped with biodentine and mineral trioxide aggregate', Journal of Endodontics, 39(6), pp. 743–747. doi: 10.1016/j.joen.2013.01.005.

[13]. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al.Preferred reporting items for systematic review and meta-analysis protocols(PRISMA-P) 2015 statement. Syst Rev. 2015;4:1.

[14]. Sena ES, Currie GL, McCann SK, Macleod MR, Howells DW. Systematic reviews and meta-analysis of preclinical studies: why perform them and how to appraise them critically. J Cereb Blood Flow Metab. 2014;34(5):737–42

[15]. Beller EM, Glasziou PP, Altman DG, Hopewell S, Bastian H, Chalmers I, et al. PRISMA for abstracts: reporting systematic reviews in journal and conference abstracts. PLoS Med. 2013;10(4):e1001419.

[16]. Hooijmans CR, Tillema A, Leenaars M, Ritskes-Hoitinga M. Enhancing search efficiency by means of a search filter for finding all studies on animal experimentation in PubMed. Lab Anim. 2010;44(3):170–5.

[17]. de Vries RBM, Hooijmans CR, Tillema A, Leenaars M, Ritskes-Hoitinga M. A search filter for increasing the retrieval of animal studies in Embase. Lab Anim. 2011;45(4):268–70.

[18]. Guyatt GH,Oxman AD,Vist G , et alGRADE guidelines: 4. Ratingthe quality of evidence--study limitations (risk of bias). J Clin Epidemiol 2011;**64**:407–15.doi:10.1016/j.jclinepi.2010.07.017

[19]. Higgins JPT, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med. 2002;21(11):1539–58.

[20]. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysisdetected by a simple, graphical test. BMJ. 1997;315(7109):629–34.

[21]. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. Biometrics. 1994;50(4):1088.

[22]. Sterne JAC, Sutton AJ, Ioannidis JPA, Terrin N, Jones DR, Lau J. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised. BMJ. 2011;342(d4002):1–8.