CASE REPORT

# Radiographic Evaluation of Reparative Dentin Formation after Direct Pulp Capping Using Rosuvastatin vs Mineral Trioxide Aggregate on Young Mature Permanent Molar—90 Days of Follow-up: A Split-mouth Study

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## Abstract

Direct pulp capping (DPC) includes covering the exposed pulp with a medication, dressing, or dental material to preserve its vitality. The idea behind this method of therapy is to induce the pulp to start a dentin bridge, "walling" the exposed site in the process. The most effective dental material to heal exposed pulp is calcium hydroxide. Mineral trioxide aggregate (MTA) causes the formation by causing cytologic and functional alterations in pulpal cells. Rosuvastatin shows pleiotropic effects like increased odontoblastic differentiation, increased mineralization, proliferation of odontoblasts, and induction of angiogenesis. Thus, the aim of the present study is to investigate pulp-dentin complex reactions following DPC with rosuvastatin vs MTA as pulp-capping materials in permanent human molars.

**Keywords:** Case report, Dentinal bridge, Mineral trioxide aggregate, Pulp-dentin complex, Rosuvastatin.

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## Introduction

While dentin and cementum have a limited capacity for regeneration, tooth enamel is incapable of doing so.[1] Vital pulp therapy is essentially referred to as a course of action started to keep and maintain healthy pulp tissue that has been harmed by caries, trauma, or restorative operations. After direct pulp capping (DPC), the exposed pulp surfaces must produce dentin bridges as part of the restoration procedure.[2] Calcium hydroxide has historically been utilized for pulp therapy, but it has certain drawbacks, such as generating persistent dental pulp irritation, having no natural adhesive properties, and offering a poor seal. Another disadvantage of calcium hydroxide is that it causes "tunnel defects" in the reparative dentin that forms under the capping made of calcium hydroxide pulp.[3,4] Recently, it was shown that mineral trioxide aggregate (MTA) stimulates the production of bone morphogenetic protein-2 (BMP-2) to induce the creation of hard tissues and is biocompatible.[3,4] Being the industry's gold standard for critical pulp treatments, MTA (Angelus, Brazil) is predominantly used as an endodontic root filling material. It can cause the creation of hard tissue and has an improved nonresorbable seal over the essential pulp thanks to the release of cytokines from bone cells. Mineral trioxide aggregate has a few shortcomings, including handling traits, cost, composition, and setting time, which has prompted researchers to look for novel materials.[5,6]

Statin ingredients are widely known for their ability to promote regeneration. It has been demonstrated that statins, such as simvastatin, rosuvastatin, atorvastatin, and cerivastatin, are highly successful at lowering cholesterol in people and are frequently used to treat hypercholesterolemia.[6,7] Statins have been found to have other pleiotropic effects, though, anti-inflammatory effects, enhanced bone production, and increased angiogenesis due to pro-angiogenic activity. Statins have also been shown to increase osteoblast development and mineralization in MC3T3-E1 cells and to boost the expression of bone anabolic factors, including vascular endothelial growth factor and BMP-2.[7]

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Okamoto et al. recently demonstrated that simvastatin-treated dental pulp stem cells exhibit improved odontogenic differentiation and quicker mineralized tissue formation.[8] Simvastatin is a potential additional pulp-capping drug. According to Min et al.,[9] it encourages odontogenesis in human dental pulp cells (hDPCs). Rosuvastatin's regenerative potential is primarily caused by elevated BMP-2 expression and elevated alkaline phosphatase activity.[9] As compared to simvastatin and atorvastatin, rosuvastatin is more effective, has stronger anti-inflammatory effects, and has a longer half-life of elimination. Similar to this, *in vivo* research by Gautam et al.[10] showed the synergistic benefits of adding 1.2 mg of rosuvastatin gel, platelet-rich fibrin, and autologous bone graft, characterizing their usage as a regenerative material in the treatment of intrabony defects. According to Kalani et al.,[11] osteogenic differentiation and cell proliferation were both improved in stem cells cultivated on rosuvastatin-loaded nanofibers.

## Case Description

A 10-year-old boy presented at the department of pediatric and preventive dentistry with the chief complaint of food impaction in the upper back region of his teeth for the last 5 months. After a clinical examination, occlusal caries was found on both upper 1st permanent molars (Fig. 1). Radiographically evaluated a deep dentinal carious lesion in relation to teeth 16 and 26 (Fig. 2). The study only included teeth that did not have radiographic signs of pulp degeneration, such as pulpal necrosis, internal and external root resorption, furcal radiolucency, interradicular bone loss, and/or periapical bone loss, which are some symptoms of periodontal ligament widening (PDL widening).

Prior to the experimental technique, teeth underwent electrical pulp testing and the removal of calculus and debris from the tooth surface. The armamentarium used for this procedure is depicted in Figure 3. After administering local anesthesia with 2% lidocaine and 1:1,00,000 epinephrine (Fig. 4), isolation was

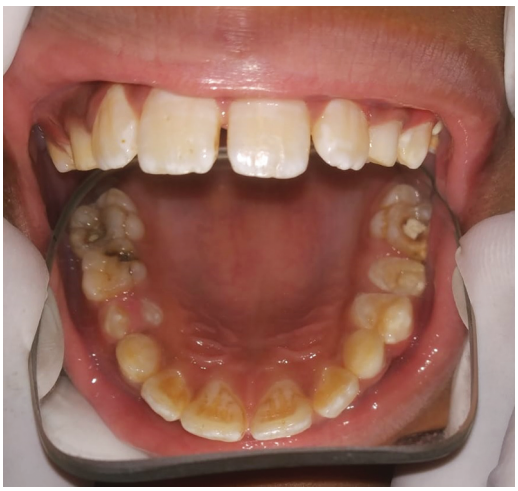
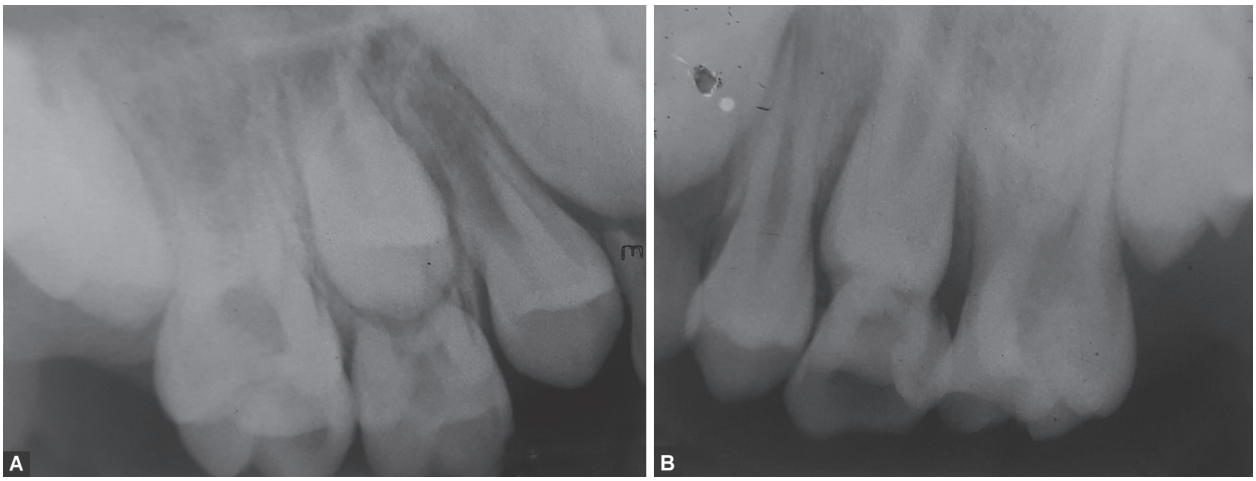


**Fig. 1:** Preoperative intraoral photographs




**Figs 2A and B:** Preoperative intraoral periapical radiograph

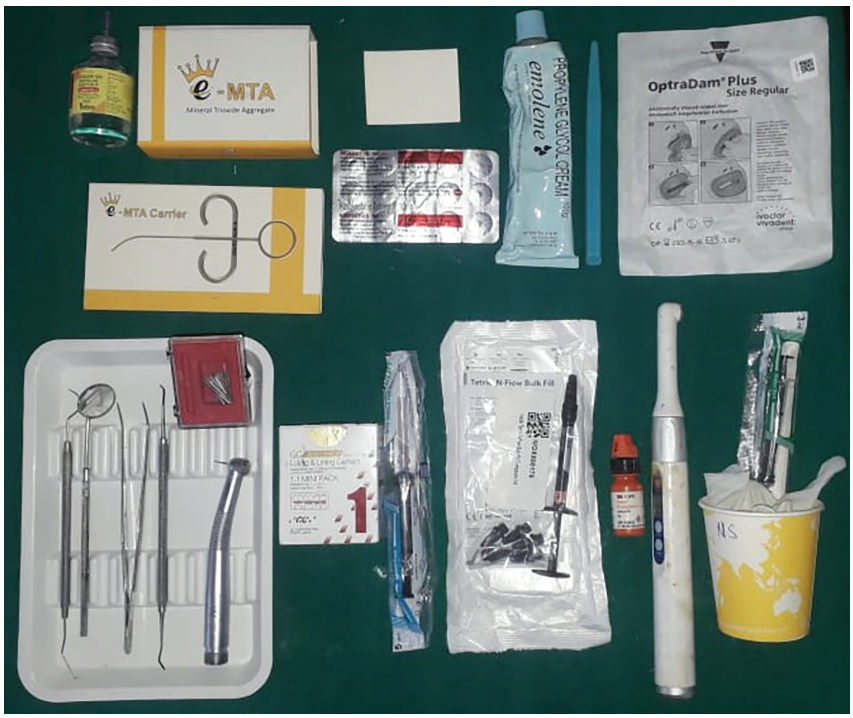



**Fig. 3:** Armamentarium

achieved using a liquid dam due to the patient's strong gag reflex. All the teeth were cleaned using prophylactic paste using rubber cup and prophylactic paste at a low pace. The next step was to wash this area with 2% chlorhexidine. With a clean, sharp spoon excavator, the whole cavity was dug up (Fig. 4). Using a sterile round diamond bur (BR-45, Mani Corp., Japan) at high speed under water spray cooling, occlusal cavities with dimensions of approximately 1.5 mm wide, 2 mm long mesiodistally, and about 2.5 mm deep were created. Normal saline was used to clean the cavity walls. Fresh, sterilized burs were utilized for each surgery to ensure sterility.

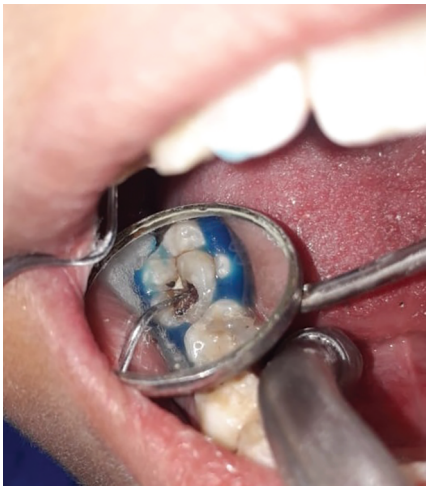
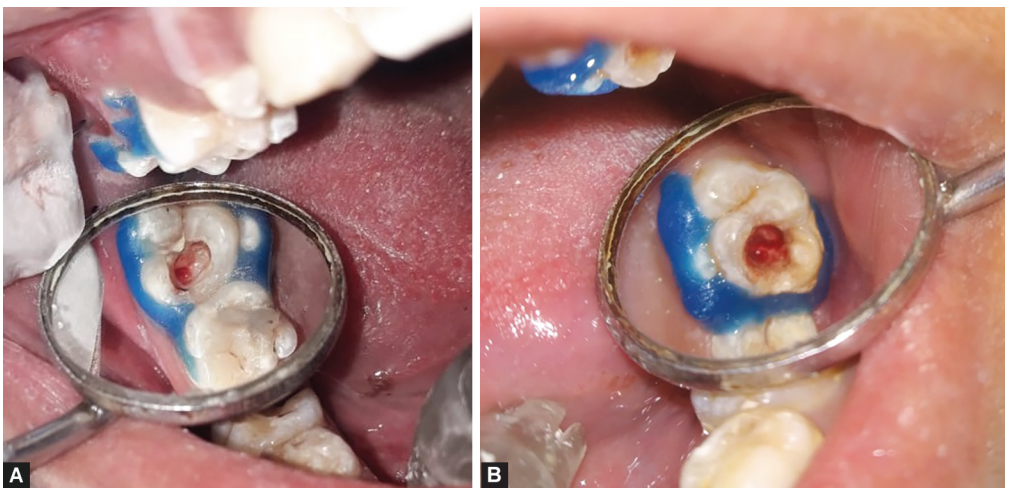
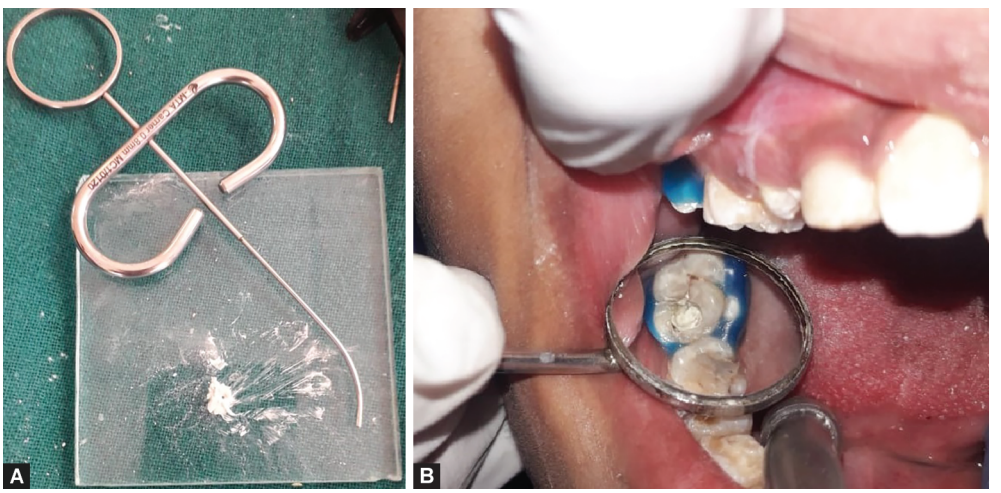


**Fig. 4:** Isolation and excavation

To promote hemostasis, sterile cotton pellets wet with saline were lightly pressed on the severed pulpal stumps for 2–3 minutes (Fig. 5). Following the removal of the cotton pellet, hemostasis was apparent. After mixing the e-MTA® (Kids-e-dental) tricalcium silicate-based material as directed by the manufacturer to achieve the desired putty-like consistency, it was applied using an MTA applicator to the exposed pulp and the cavity floor of tooth 16 and slightly compressed with a dampened sterile cotton pellet to ensure a thickness of 2–3 mm was obtained (Fig. 6). When the coating materials covering the medicinal items were removed, they were ground into fine powders using porcelain mortars and pestles and kept in airtight containers to prevent contamination in Roseday® (Manufacturer: USV Pharmaceuticals). The Rosuvastatin-containing powder form was mixed with propylene glycol on a glass slab and




**Figs 5A and B:** Hemostasis using cotton pellets



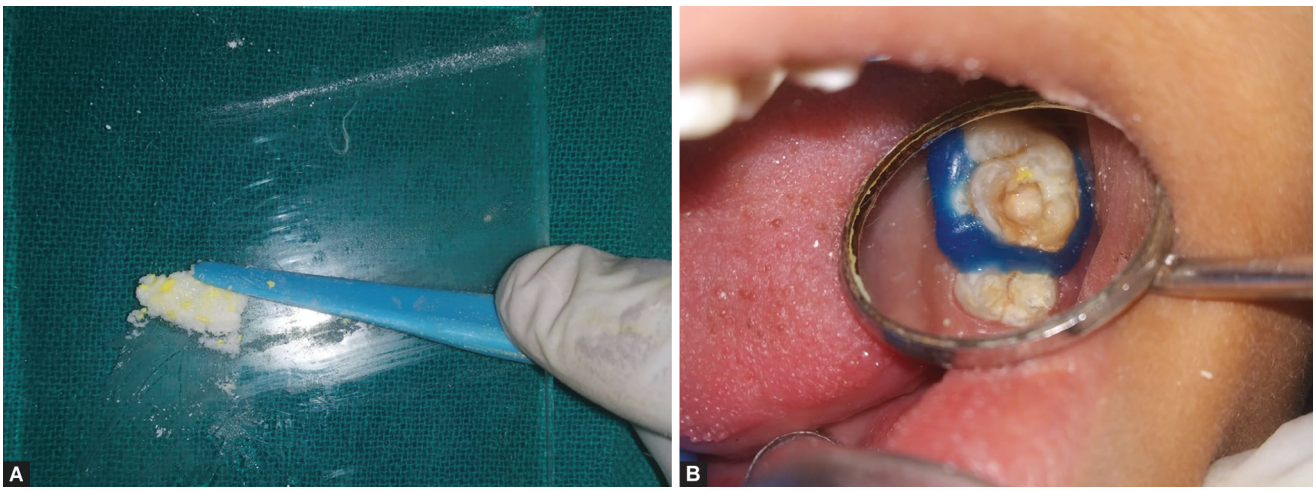

**Figs 6A and B:** Mineral trioxide aggregate mixing and placement

placed in the prepared cavities with a stainless-steel carrier, then lightly pressed onto tooth 26 (Fig. 7).

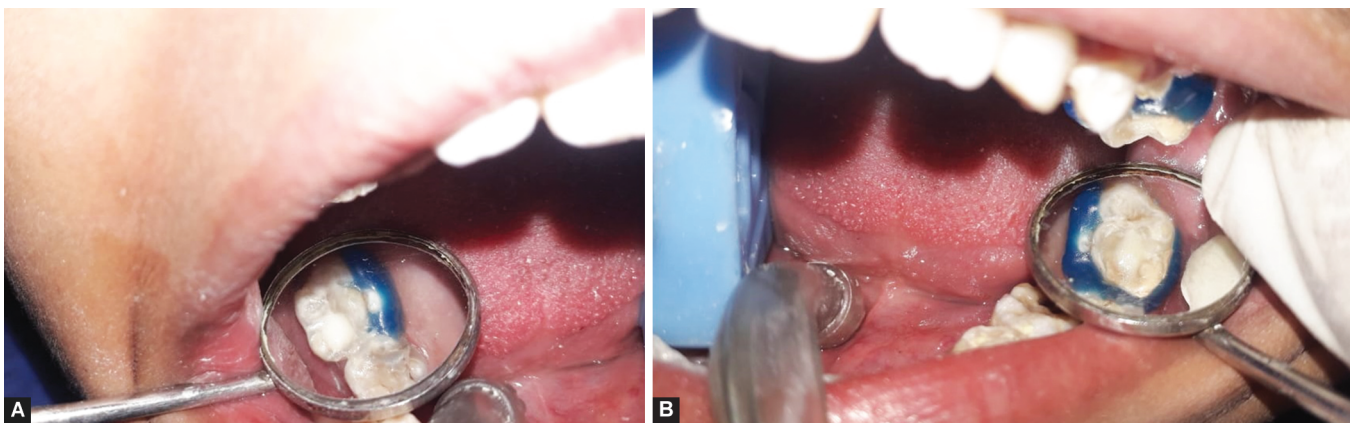
Glass ionomer cement (GC Fuji IX GP) was used to fill the voids once the appropriate test materials had been used (Fig. 8). To ensure proper placement of the test material and restorative material, a postoperative intraoral radiograph was obtained (Fig. 9). Radiographs collected at intervals of 1, 3, and 6 months were used for follow-up radiographic examination, comparing them to the preoperative radiograph (Figs 10 to 12).

## Discussion

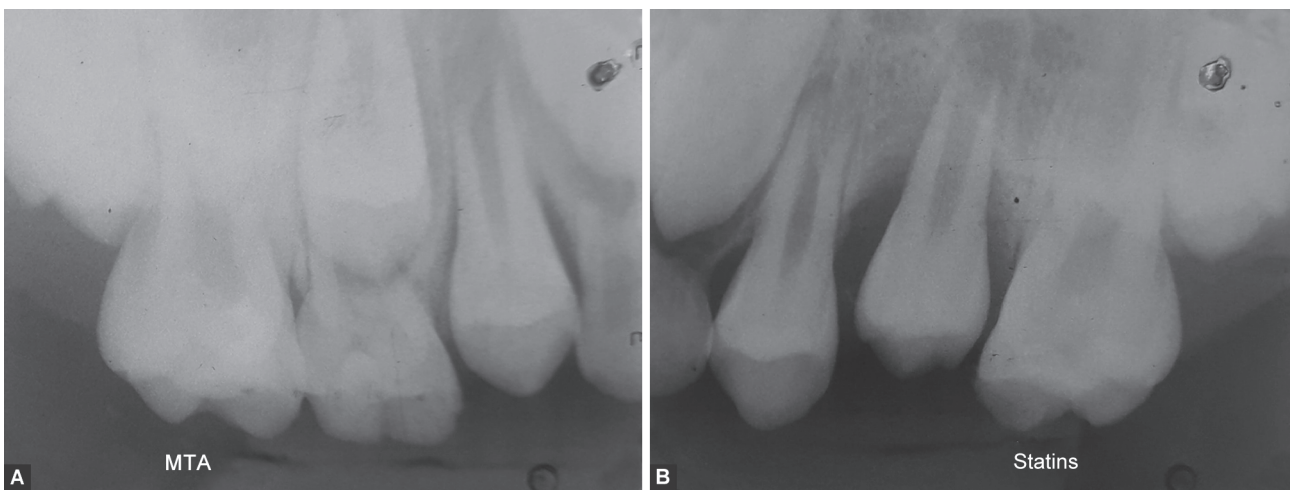
In primary dentition, dental caries progresses rapidly into pulpal tissue, causing pulpal inflammation near the caries lesion. With



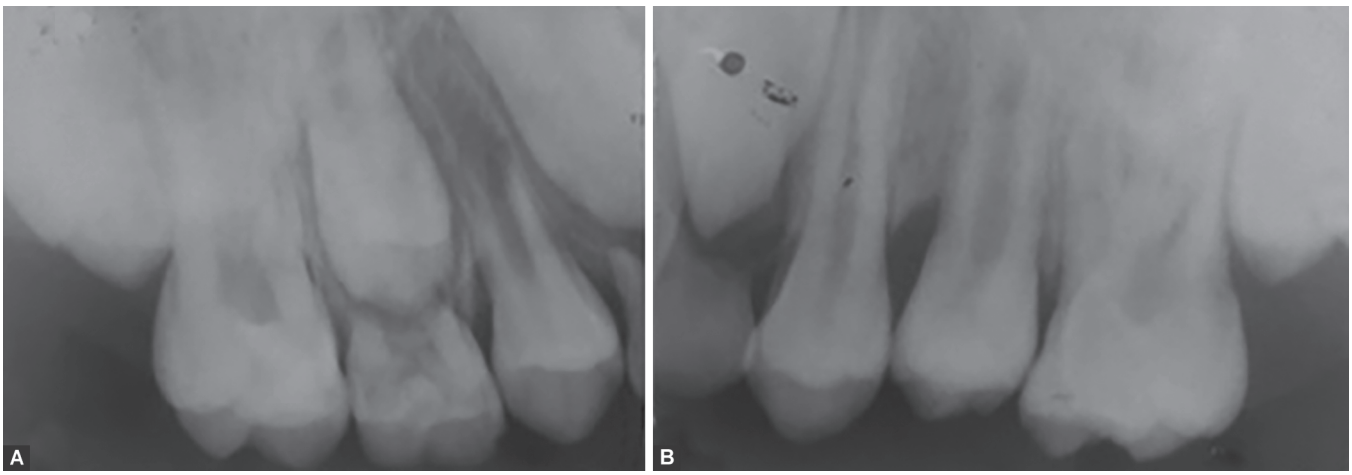

**Figs 7A and B:** Rosuvastatin mixing and placement



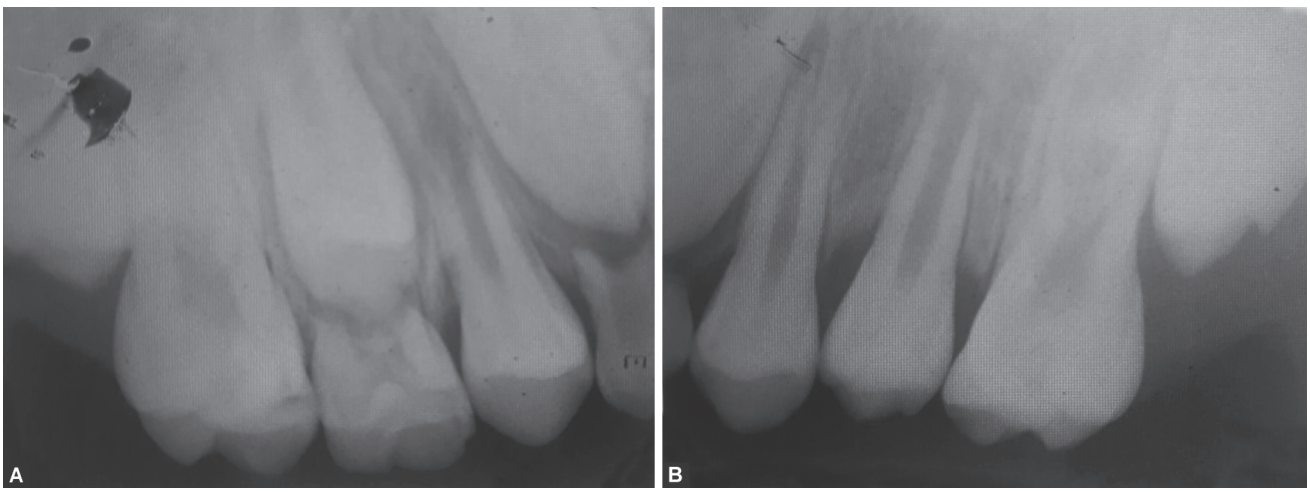

**Figs 8A and B:** Glass ionomer cement filling



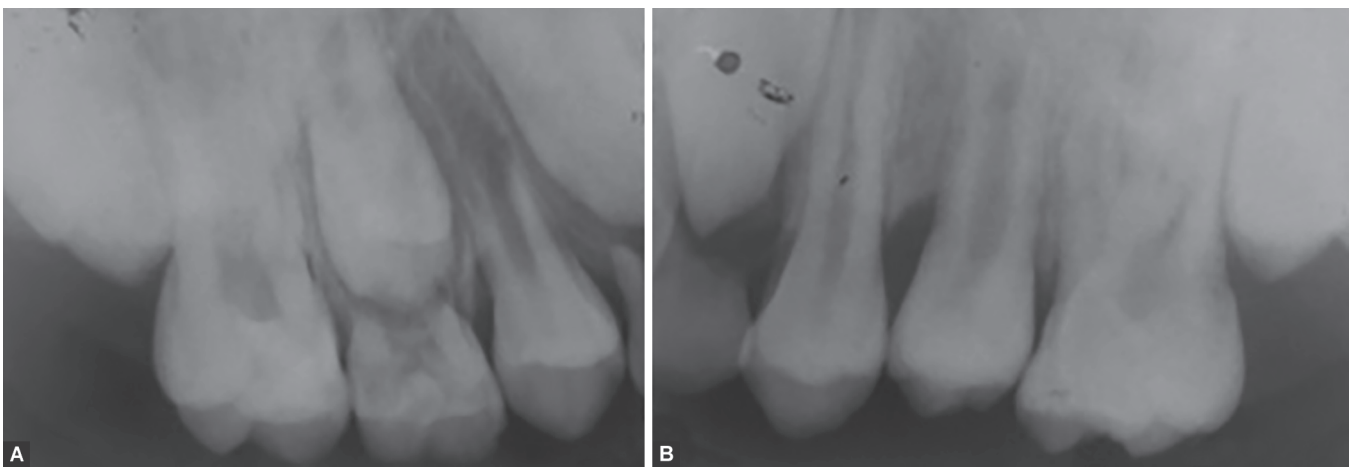

**Figs 9A and B:** Postoperative intraoral periapical radiograph




**Figs 10A and B:** Follow-up of 1 month




**Figs 11A and B:** Follow-up of 3 months




**Figs 12A and B:** Follow-up of 6 months

further development of the carious process, the inflammatory process can spread throughout the coronal pulp. If the pulp in the root canals remains unaffected and symptom-free in permanent teeth, preserving radicular pulp vitality, DPC can be the management procedure. The preservation of a living and healthy pulp is the primary objective of any restoration, whether it be a direct placement composite resin, a full-coverage crown, or an amalgam restoration.[12] According to conventional understanding, pulp capping can be either indirect or direct. DPC is employed when the pulp is exposed due to cavities, mechanically exposed due to trauma, or exposed during dental procedures in areas where the pulp is viable and asymptomatic. Pulp vitality is preserved using

a therapeutic base or liner.[13] Some carious-affected dentin is left near the pulp after indirect pulp capping to maintain a healthy, symptom-free tooth.

A vital tooth with carious exposure should exhibit minimal pulpitis symptoms, no radiological signs of periapical disease, and a history of asymptomatic disease. These are critical considerations when considering pulp capping. An ideal material for DPC should prevent infection, adhere to dentin to prevent microleakage, be easy to use in a clinical setting, and promote the formation of dentin bridges.[14–16] Several research studies in the field of dentistry have been conducted to understand the impact of statins both *in vitro* and *in vivo*. Research indicates that dental pulp stem cells treated with statins exhibit odontogenic development *in vitro*.[17] Simvastatin has been shown to enhance the differentiation and cell proliferation of human dental pulp stem cells.[18]

These studies support the use of statins as materials for bone and dentin repair. However, statins have not yet been documented for use in capping human pulp. Nevertheless, due to its widespread and long-term use, Rosuvastatin has been identified as a safe and affordable medicine in the current investigation. The search for a suitable material for DPC continues. Therefore, statins should possess the following characteristics: they should be bioactive, localized and retained at the application site, nontoxic, biodegradable, and biocompatible. They should also exhibit biomechanical properties, including optimum tensile, compressive, and flexural strength, and act as a matrix and substrate for cell infiltration, growth, and differentiation.[19]

Polypropylene glycol is a class of nonionic, amphiphilic triblock copolymers where each molecule consists of blocks of poly(propylene oxide) at the center and poly(ethylene oxide) chains on both sides facing the aqueous phase. These monomers self-organize to form micelles in aqueous solutions, enhancing the availability of encapsulated medications and serving as carriers for compounds with poor solubility, variable pharmacokinetics, and limited physiological stability. Due to additional properties such as minimal immunogenicity and thermosensitivity, poloxamers are commonly used to create semisolid topically applied drug carriers or in situ gels. Studies have shown that the sol-gel phase transition of formulations containing rosuvastatin mixed with simvastatin was effectively facilitated by polypropylene glycol. According to their findings, this combination initially caused rapid release of rosuvastatin over 24 hours, followed by a slow and steady release over 14 days. It is possible that the physical entrapment of the hydrophobic chemicals within the material's pores contributes to the consistent release mechanism.[20] Cruz et al.[21] showed that polypropylene glycol has effective role in dentin penetration. Its results show that continuous differentiation of the pulp-dentin complex leads to the formation of a dentinal bridge by chelating calcium ions from the pulpal blood vessels. Similarly, 0.5 mg of atorvastatin was mixed with 1 mL of polypropylene glycol in a ratio of 1:1 for use in this study. Here, polypropylene glycol was utilized as the carrier for statins.[22–24]

Due to its biocompatibility and ability to induce odontogenesis, MTA was chosen as the study's positive control since it has been determined to be a promising material.[25,26] Successful DPC depends on controlling bleeding and preventing microbial ingress into the pulp. In the current investigation, a rubber dam was used to ensure strict isolation and prevent microbial leakage. Complete hemostasis was achieved by applying pressure with a cotton pellet saturated with sterile saline.[26,27] Glass ionomer cement (GC Fuji IX GP) is then used as the final repair. When used as an immediate final restoration after pulp capping, glass ionomer cement with a shorter setting time of 6 minutes has shown stronger prognostic value due to its ability to create a microbiologically tight seal. Additionally, it releases fluoride, which helps prevent secondary caries.[8,12,19]

A thin or partial dentin bridge, consisting of scattered dentin particles, formed during the 30-day observation period. Evaluation of hard tissue formation was based on the reparative dentin formed at the pulp exposure site in the tooth treated with rosuvastatin (Fig. 10). After 90 days, evidence showed complete dentin bridge formation, closing the previously exposed area treated with simvastatin (Figs 11 and 12). Strong clinical and radiological evidence is essential for considering pulp capping treatment successful. In our case, a tooth exhibiting normal function and radiographic appearance after 90 days indicates successful treatment. Therefore, rosuvastatin can be considered as a suitable agent for DPC in young permanent teeth.

## Conclusion

There is evidence that rosuvastatin has anti-inflammatory effects, which could facilitate the healing of infected pulp tissue. Therefore, rosuvastatin can be recommended as an ideal substance for pulp capping, potentially as an alternative to calcium hydroxide.

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## References

1. Huang GT. Dental pulp and dentin tissue engineering and regeneration: advancement and challenge. Front Biosci (Elite Ed) 2011;3(2):788–800. DOI: 10.2741/e286
2. Varalakshmi PR, Kavitha M, Govindan R, et al. Effect of statins with α-tricalcium phosphate on proliferation, differentiation, and mineralization of human dental pulp cells. J Endod 2013;39(6):806–812. DOI: 10.1016/j.joen.2012.12.036
3. Cox CF, Sübay RK, Ostro E, et al. Tunnel defects in dentin bridges: their formation following direct pulp capping. Operative Dent 1996;21(1):4–11.
4. Moghaddame-Jafari S, Mantellini MG, Botero TM, et al. Effect of ProRoot MTA on pulp cell apoptosis and proliferation *in vitro*. J Endod 2005;31(5):387–391. DOI: 10.1097/01.don.0000145423.89539.d7
5. Yasuda Y, Ogawa M, Arakawa T, et al. The effect of mineral trioxide aggregates on the mineralization ability of rat dental pulp cells: an *in vitro* study. J Endod 2008;34(9):1057–1060. DOI: 10.1016/j.joen.2008.06.007
6. Fajardo ME, Rocha ML, Sanchez Marin FJ, et al. Effect of atorvastatin on chronic periodontitis: a randomized pilot study. J Clin Periodontol 2010;37:1016–1022. DOI: 10.1111/j.1600-051X.2010.01619.x
7. Du Z, Chen J, Yan F, et al. The effects of Simvastatin on bone healing around titanium implants in osteoporotic rats. Clin Oral Impl Res 2009;20(2):145–150. DOI: 10.1111/j.1600-0501.2008.01630.x
8. Okamoto Y, Sonoyama W, Ono M, et al. Simvastatin induces the odontogenic differentiation of human dental pulp stem cells *in vitro* and *in vivo*. J Endod 2009;35(3):367–372. DOI: 10.1016/j.joen.2008.11.024
9. Min KS, Lee YM, Hong SO, et al. Simvastatin promotes odontoblastic differentiation and expression of angiogenic factors via heme oxygenase-1 in primary cultured human dental pulp cells. J Endod 2010;36(3):447–452. DOI: 10.1016/j.joen.2009.11.021

10. Gautam K, Kapoor A, Mathur S, et al. Comparative evaluation of autogenous bone graft and autologous platelet-rich fibrin with and without 1.2 mg in situ rosuvastatin gel in the surgical treatment of intrabony defect in chronic periodontitis patients. Contemp Clin Dent 2022;13(1):69–77. DOI: 10.4103/ccd.ccd_740_20
11. Kalani MM, Nourmohammadi J, Negahdari B, et al. Electrospun core-sheath poly(vinyl alcohol)/silk fibroin nanofibers with Rosuvastatin release functionality for enhancing osteogenesis of human adipose-derived stem cells. Mater Sci Eng C Mater Biol Appl 2019;99:129–139. DOI: 10.1016/j.msec.2019.01.100
12. Lee Y, Schmid MJ, Marx DB, et al. The effect of local simvastatin delivery strategies on mandibular bone formation *in vivo*. Biomaterials 2008;29:1940–1999. DOI: 10.1016/j.biomaterials.2007.12.045
13. Chak RK, Singh RK, Mutyala J, et al. Clinical radiographic evaluation of 3Mixtatin and MTA in primary teeth pulpotomies: a randomized controlled trial. Int J Clin Pediatr Dent 2022;15(S-1):S80–S86. DOI: 10.5005/jp-journals-10005-2216
14. Ahn KS, Sethi G, Chaturvedi MM, et al. Simvastatin, 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor, suppresses osteoclastogenesis induced by receptor activator of nuclear factor-kappaB ligand through modulation of NF-kappaB pathway. Int J Cancer 2008;123:1733–1740. DOI: 10.1002/ijc.23745
15. Parisay I, Qeidari A, Sabouri E, et al. Cytotoxicity and induced apoptosis of a new bioceramic cement containing simvastatin on stem cells from human exfoliated deciduous teeth. Dent Res J (Isfahan) 2022;19:79.
16. Bellosta S, Ferri N, Bernini F, et al. Non lipid related effects of statins. Ann Med 2000;32:164–176.
17. Kida D, Zakrzewska A, Zborowski J, et al. Polymer-based carriers in dental local healing-review and future challenges. Materials 2021;14:3948. DOI: 10.3390/ma14143948
18. Asl Aminabadi N, Maljaei E, Erfanparast L, et al. Simvastatin versus calcium hydroxide direct pulp capping of human primary molars: a randomized clinical trial. J Dent Res Dent Clin Dent Prospects 2013;7(1):8–14. DOI: 10.5681/joddd.2013.002
19. Accorinte MLR, Loguercio AD, Reis A, et al. Evaluation of two mineral trioxide aggregate compounds as pulp-capping agents in human teeth. Int Endod J 2009;42:122–128. DOI: 10.1111/j.1365-2591.2008.01485.x
20. Gutierrez GE, Lalka D, Garrett IR, et al. Transdermal application of lovastatin to rats causes profound increases in bone formation and plasma concentrations. Osteoporos Int 2006;17:1033–1042. DOI: 10.1007/s00198-006-0079-0
21. Cruz EV, Kota K, Huque J, et al. Penetration of propylene glycol into dentine. Int Endod J 2002;35(4):330–336. DOI: 10.1046/j.1365-2591.2002.00482.x
22. Aripirala M, Bansal K, Mathur VP, et al. Comparative evaluation of diode laser and simvastatin gel in pulpotomy of primary molars: a randomized clinical trial. J Indian Soc Pedod Prev Dent 2021;39(3):303. DOI: 10.4103/jisppd.jisppd_60_21
23. Tziafas D, Pantelidou O, Alvanou A, et al. The dentinogenic effect of mineral trioxide aggregate (MTA) in short-term capping experiments. Int Endod J 2002;35:245–254. DOI: 10.1046/j.1365-2591.2002.00471.x
24. Dammaschke T, Wolff P, Sagheri D, et al. Mineral trioxide aggregate for direct pulp capping: a histologic comparison with calcium hydroxide in rat molars. Quintessence Int 2010;41(2):20–30.
25. Rao M, Narayana V, Prasad BK, et al. Recent advances in biomimetic materials used in restorative dentistry: an updated review. 2022.
26. Ding ZY, Tan Y, Peng Q, et al. Novel applications of platelet concentrates in tissue regeneration. Exp Ther Med 2021;21(3):226. DOI: 10.3892/etm.2021.9657
27. Chang HH, Chang YJ, Yeh CL, et al. Development of calcium phosphate/calcium sulfate biphasic biomedical material with hyaluronic acid containing collagenase and simvastatin for vital pulp therapy. Dental Materials 2020;36(6):755–764. DOI: 10.1016/j.dental.2020.03.018