Clinical and Molecular Perspectives of Reparative Dentin Formation

Lessons Learned from Pulp-Capping Materials and the Emerging Roles of Calcium

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KEYWORDS

• Reparative dentin • Calcium hydroxide • Hydraulic calcium-silicate cements • Calcium • Odontoinductive • Odontoconductive • ORAI1

KEY POINTS

- Direct pulp capping is often performed on the exposed pulp after deep caries removal to induce reparative dentin, a physical barrier that functions as a "biological seal" to protect the underlying pulp tissues and maintain pup vitality.
- Although calcium hydroxide (CH) has been used as the "gold standard" pulp-capping material for many decades, recently introduced hydraulic calcium-silicate cements (HCSCs), such as mineral trioxide aggregate (MTA), have increasingly gained popularity due to their superior material properties that are biocompatible, odontoconductive, and to a certain degree, odontoinductive.
- These pulp-capping materials confer capacity to induce reparative dentin by providing an alkaline environment and antibacterial activity; however, increasing lines of evidence support a notion that the release of calcium ions (Ca^{2+}) actively induces in reparative dentin formation by eliciting intracellular Ca^{2+} signaling pathways.

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- Among the intracellular Ca^{2+} regulators, ORAI1 protein was recently shown to have an indispensable role in odontogenic differentiation and mineralization in dental pulp stem cells by regulating Ca^{2+} influx.
- Successful clinical outcomes of direct pulp capping depend on the operator technique, the material properties, and the host pulpal responses. Therefore, it is important to develop strategies that maximize the efficacy of each component for regenerating reparative dentin in a predictable and reproducible manner.

INTRODUCTION

Dental caries is the most prevalent infectious oral disease experienced by more than 90% of adults in the United States.[1,2] A quarter of US populations do not have dental insurance,[3] and more than 60% of underserved areas are still in need of dentists.[4] Considering these potentially unidentified individuals, it is expected that almost all individuals may have experienced dental caries at least once in their lifetime.

Due to its high prevalence, removing dental caries is one of the most common procedures performed in routine dental practices. During caries removal, deep caries penetrating through the enamel and dentin frequently leads to either indirect or direct pulp-capping procedures to induce tertiary (reactionary or reparative, respectively) dentin formation.[5] Several pulp-capping materials, including calcium hydroxide ($Ca[OH]_2$ or CH) and hydraulic calcium-silicate cements (HCSCs), such as mineral trioxide aggregate (MTA), are used for this purpose. For indirect pulp capping, these materials are placed on the "unexposed" pulp to enhance reactionary dentin formation from the existing odontoblasts at the dentino-pulpal complex. In contrast, direct pulp capping refers to placing the pulp-capping materials on the "exposed" pulp, where odontoblast layers are breached, to enhance reparative dentin formation mediated by odontoblast-like cells differentiated from dental pulp stem cells (DPSCs) at the materio-pulpal complex (MPC).

Unlike indirect pulp capping, which usually has predictable clinical outcomes, direct pulp capping has outcomes that are often variable depending on the operator technique, the material properties, and the host pulpal responses. In direct pulp capping, the ultimate goal is to preserve the underlying pulp and maintain pulp vitality by regenerating reparative dentin at the MPC, which functions as a "biological seal" to protect the underlying pulp tissues, to increase the life expectancy of the tooth, and to improve the overall oral health. A successful pulp-capping procedure can avoid more invasive and expensive dental treatment, such as root canal therapy. Therefore, it is important to optimize direct pulp-capping techniques, improve biocompatibility of the materials, and enhance biological responses of the pulp tissues to maximize regeneration of reparative dentin.

Here, we discuss the current status of different types of direct pulp-capping materials with specific focuses on CH and HCSCs due to their extensive clinical utilization and substantial amounts of available studies. We then attempt to delineate molecular mechanisms by which reparative dentin forms based on the common properties of these pulp-capping materials, as well as known bone-grafting materials. Finally, we suggest possible roles of calcium ions (Ca^{2+}) in the formation of mineralized tissues, including reparative dentin and bone.