Silver-Containing Solutions for Deep Caries Management

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Silver is a broad-spectrum antimicrobial agent that can be used for caries management. Dentists used silver-containing solutions for deep cavity disinfection before restoration. Silver fluoride, silver nitrate, silver diamine nitrate, silver diamine fluoride, and nano-silver fluoride were used in deep cavities for antimicrobial purposes. Indirect silver fluoride application induced pulp inflammation and reparative dentine in most cases, and pulp necrosis in some cases. Direct silver nitrate application caused blood clots and a wide inflammatory band in the pulp, whilst indirect silver nitrate application caused hypoplasia in shallow cavities and partial pulp necrosis in deep cavities. Direct silver diamine fluoride application induced pulp necrosis, while indirect silver diamine fluoride application induced a mild inflammatory response and reparative dentine formation.

Keywords: Silver Fluoride ; Silver Nitrate ; Silver Diamine Nitrate ; Silver Diamine Fluoride ; Nano Silver Fluoride

1. Introduction

The main properties of various silver-containing solutions are summarized in **Table 1**.

Table 1. Properties of silver-containing solutions for deep caries management.

Solution [Ref.]	Wt.% (Concentration According to Manufacturer(s))	Anticaries Properties
Silver fluoride [1][2]	**40% (Ag: 340,000 ppm; F: 60,000 ppm)**	- Inhibits growth of cariogenic bacteria - Prevents demineralization - Promotes remineralization
Silver nitrate [3]	**25% (Ag: 151,130 ppm)**	- Inhibits growth of cariogenic bacteria
Silver diamine nitrate [4]	**48% (Ag: 319,914 ppm *)**	- Inhibits growth of cariogenic bacteria
Silver diamine fluoride [5]	**12% (Ag: 80,170 ppm; F: 14,150 ppm)** **30% (Ag: 200,400 ppm; F: 35,400 ppm)** **38% (Ag: 253,900 ppm; F: 44,800 ppm)**	- Inhibits growth of cariogenic bacteria - Prevents demineralization - Promotes remineralization
Nano-silver fluoride [6]	**1.05% * (Ag: 399.33 ppm; F: 10,147 ppm)**	- Inhibits growth of cariogenic bacteria - Prevents demineralization - Promotes remineralization

* By calculation.

2. Silver Fluoride

The 40% silver fluoride solution was used for deep caries management. The 40% silver fluoride solution contained 34% silver and 6% fluoride. According to this percentage, the fluoride content was supposed to be 59,900 ppm [1]. The chemical analysis of the components of two silver fluoride products found that the fluoride content was higher than expected, ranging from 78,000 to 120,000 ppm [1][7]. As a result of these findings, Gotjamanos & Afonso [7] recommended that the use of silver fluoride in paediatric dentistry be discontinued because these unacceptably high fluoride levels pose a potential risk of toxicity to children and, if it enters the bloodstream, it might result in fluorosis, especially in the case of an undetected pulp exposure [2]. Silver fluoride has antibacterial and remineralising properties. The silver ions present in the silver fluoride act in two different ways: (1) their bactericidal/bacteriostatic effect on the microorganisms present in the carious lesion; (2) mechanical sealing of the carious and sound dentinal tubules [8]. Silver fluoride is used as a cavity conditioner in conjunction with glass ionomer cement as an atraumatic restorative method. After partial caries excavation, silver fluoride is applied, and then the cavity is sealed with a glass ionomer cement restoration. Silver fluoride showed a 100% success rate in 400,000 cases treated at the Dentistry School of Western Australia University [8]. The treatment success was based solely on the absence of symptoms.

3. Silver Nitrate

The first use of silver nitrate was reported around 1846 [7]. The results, reported by Stebbins in 1891, shed light on the clinical significance of silver nitrate [9]. It was mainly used to arrest dental caries and sterilize cavities because of its escharotic, dehydrating, and sclerosing properties [10]. Silver nitrate is acidic in nature, and it causes protein coagulation [11]. In 1917, Howe introduced ammoniacal silver nitrate by adding ammonium hydroxide to silver nitrate [12]. The addition of the ammonium hydroxide converted the acidic silver nitrate into a solution with an alkaline nature, limiting its irritating action [7]. The new compound, which contained 25% silver nitrate, was later known as Howe's solution and was widely used by practitioners.

The nature of dental caries as a noncommunicable disease rather than an infectious disease made the idea of the sole application of silver nitrate debatable. The results of various studies regarding the efficacy of silver nitrate in the prevention of dental caries have not revealed any significant reduction in caries incidence compared to no treatment [13][14] [15]. Other studies examined the efficacy of silver nitrate in arresting carious lesions and reported that it can arrest caries on both permeant and primary dentition [15][16]. The use of silver nitrate in preventing/arresting dental caries decreased significantly after fluoride was introduced [10]. In 2015, silver nitrate was used in conjugation with sodium fluoride, and the reported results exhibited effectiveness in arresting dental caries [17].

4. Silver Diamine Nitrate

Silver diamine nitrate was developed from silver nitrate. The 48% silver diamine nitrate solution was proposed to act as a less expensive alternative to silver diamine fluoride in regions with lower and middle-income economies as it lacks the fluoride component. There is a delay in the mineral induction time of silver nitrate, which affects its remineralization potential [18]. The addition of the diamine group to silver nitrate stabilizes the silver ions, and it is expected to enhance its mineralization potential [4]. When the silver diamine nitrate is applied to a dentine surface, it reacts with the ions present in the environment and produces silver phosphate and silver oxide. The silver compounds may readily react with the chloride in the environment, resulting in the formation of less soluble silver chloride [19][20]. In the presence of silver salts, demineralized dentine becomes harder and dentinal tubules become blocked, preventing any further progress of the acidic by-products responsible for demineralization [19]. The efficacy of silver diamine nitrate in caries control has not yet been reported.

5. Silver Diamine Fluoride

Introduced by Dr Nishino and Dr Yamaga in the 1950s, silver diamine fluoride (SDF) has been used for arresting caries, preventing secondary caries, and decreasing hypersensitivity [21]. Commercial SDF products are available in various concentrations (3.8%, 10%, 12%, 30%, and 38%). Solutions in all of these concentrations are suitable for use as anticaries solutions, with the exception of the 3.8% solution, which is intended for root canal therapy. Silver diamine fluoride is an alkaline solution with a high concentration of fluoride and silver ions [22]. Fluoride changes the hydroxyapatite into fluorapatite, which is more resistant to acid dissolution, so it can remineralise the caries-affected dental hard tissues [23]. In addition, it has an antimicrobial effect on the plaque biofilm [24]. Silver, the other main component of silver diamine fluoride, is well known for its strong antimicrobial effect which helps in sterilizing the infected tissues, and it blocks the dentinal tubules to seal them from microorganisms and their by-products [25]. Combing both silver and fluoride in one

solution so they can perform their actions synergistically resulted in the superior results achieved by the silver diamine fluoride. Despite its effectiveness, silver diamine fluoride usage for arresting caries is still an off-label usage in many countries, where it is used only as a desensitizing agent. Silver diamine fluoride requires only topical application to achieve its effect. This ease of use has led to its widespread use among practitioners recently, especially during the COVID-19 pandemic [26]. The World Health Organization's Center for Quality Improvement and Evidence-Based Dentistry introduced safer aerosol-free emergent dentistry as a protocol for caries management [27]. Silver diamine fluoride was the first choice in this protocol for the treatment of caries and toothache related to caries, as its use can prevent cross-infection. The effectiveness of silver diamine fluoride in caries control has been proved in many previous studies [28][29][30].

6. Nano Silver Fluoride

Silver nanoparticles have been introduced in dentistry for multiple applications, including caries management [31]. The antibacterial effect of silver nanoparticles relies on their large contact area with the microorganisms due to their nanometric particle size [32]. Silver ions can be continuously released by the silver nanoparticles [33]. This disrupts the permeability and respiration of the bacteria by binding to the sulphur proteins in the cytoplasmic membrane and cell wall [34][35][36]. A further instance of this is the detection of reactive oxygen species inside bacterial cells. Reactive oxygen species elevate the oxidative stresses and damage the deoxyribonucleic acid (DNA) [36][37]. In addition, the interaction of the DNA's sulphur and phosphorus, with silver ions, can create issues with DNA replication and cell reproduction, and can even cause microorganism death [38]. The denaturation of the cytoplasmic proteins is another effect of silver ions [39]. Moreover, silver nanoparticles can kill bacteria themselves by accumulating in the pits that form the cell wall after attaching to the cell surface [40]. Furthermore, silver nanoparticles can disrupt bacterial signal transduction, resulting in a decrease in proliferation and cell apoptosis [41]. Fluoride solutions, combined with silver nanoparticles, proved the capability to remineralise carious lesions [42]. Therefore, silver nanoparticles, in the form of nano-silver fluoride, have been developed for caries management [43]. The effectiveness of nano-silver fluoride as a cariostatic agent was investigated by dos Santos et al. [44]. They found that active caries decreased by 50% at 12 months after a single application of nano-silver fluoride [44]. Nagireddy et al. conducted another study in which nano-silver fluoride was applied to dentinal caries, and 65.21% of the carious lesions were arrested after a 1-year follow-up [45].

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