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· 综述 ·

## 防根面龋牙科材料的研究进展

熊净迪, 程兴群, 吴红崑

口腔疾病防治国家重点实验室 国家口腔医学中心 国家口腔疾病临床医学研究中心 四川大学华西口腔医院老年口腔科, 四川 成都(610041)

**【摘要】** 根面龋是老年人口腔常见病和多发病, 发病率和未治疗率高, 治疗难度大, 可迅速发展引起牙髓根尖周病或残冠根, 是老年人失牙的重要原因, 已成为严重影响老年人生活质量的常见口腔慢性病之一。因此, 根面龋早期干预和防治非常重要。传统防根面龋牙科材料如氟化物、氯己定等在临床中广泛应用, 但是其具有牙齿着色、再矿化及杀菌效率低下等缺点。近年来, 一系列新兴防根面龋牙科材料如无机纳米材料、胶原交联剂等逐步成为研究热点, 新材料具有促进深部牙体组织再矿化、作用时间延长、黏附力增强等优点。未来防龋材料应根据根面龋的特点及应用人群进行设计, 朝着简便化、高效化、低毒性方面发展。本文对目前防根面龋牙科材料的研究及应用进行综述, 以期能够为防根面龋牙科材料的研究提供理论基础, 对促进根面龋的有效预防, 改善老年人的口腔健康状况和生活质量具有重要意义。

**【关键词】** 根面龋; 防龋材料; 再矿化; 口腔保健; 人口老龄化; 龋病预防; 抗菌材料; 氟化物

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**Research progress on dental materials for preventing root caries** XIONG Jingdi, CHEN Xingqun, WU Hongkun. State Key Laboratory of Oral Diseases & National Center for Stomatology & National Clinical Research Center for Oral Diseases & Department of Geriatric Dentistry, West China Hospital of Stomatology, Sichuan University, Chengdu 610041, China

Corresponding author: WU Hongkun, Email: 8111120691@qq.com, Tel: 86-28-85503561

**【Abstract】** The high incidence and untreated rate of root caries, a common and frequently occurring oral disease with challenging treatment in elderly individuals, is the main cause of tooth loss among elderly people, as rapid development results in pulpitis and periapical periodontitis or residual crown and root, which has been regarded as one of the common chronic oral diseases seriously affecting the quality of life of elderly people. Thus, early intervention and prevention are important. Traditional dental materials for preventing root caries have been widely used in clinical practice; however, they have the disadvantages of tooth coloring, remineralization and low sterilization efficiency. A series of new dental materials for preventing root caries have gradually become a research hotspot recently, which have the advantages of promoting the mineralization of deep dental tissue, prolonging the action time and enhancing adhesion. Future caries prevention materials should be designed according to the characteristics of root surface caries and the application population and should be developed toward simplicity, high efficiency and low toxicity. This review describes current research regarding anti-caries prevention material application, serving as a theoretical underpinning for the research of root caries prevention materials, which is important for both promotion in the effective prevention of root caries and improvement in the status of oral health and the quality of life among old people.

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**【作者简介】** 熊净迪, 硕士, Email: 1154896221@qq.com

**【通信作者】** 吴红崑, 教授, 博士, Email: 8111120691@qq.com, Tel: 86-28-85503561

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根面龋是老年人口腔常见病,是指发生于釉质牙骨质界下方的牙根部龋损,常累及牙骨质和牙本质。根据第四次全国口腔健康流行病学调查结果,我国55~64岁年龄组根面龋患病率为51.0%,而65~74岁年龄组根面龋患病率达61.9%,根面龋患病率随着年龄增长而增高<sup>[1]</sup>。随年龄增长,老年人牙周病发病率增加,牙龈退缩、牙根暴露等原因导致老年人易罹患根面龋。根面龋早期干预和防治非常重要。本文对目前防根面龋牙科材料的研究及应用进行综述,以期对根面龋防治牙科材料的研究提供理论基础,促进根面龋的有效预防,改善老年人的口腔健康状况和生活质量。

## 1 常规防根面龋材料

### 1.1 氟化物的应用

氟化物是预防根面龋的最常用的方法,氟化物在牙齿表面形成的氟化物储存层,不仅可改变致龋菌群微生态的平衡,抑制糖酵解和细胞氧化等相关酶活性终止龋病进展;也可以置换牙体组织中的羟基磷灰石晶体中的羟基,形成更耐酸的氟磷灰石,抑制脱矿,促进再矿化,可在一定程度上逆转和修复早期根面龋<sup>[2]</sup>。近来研究发现高氟牙膏(5 000  $\mu\text{g/g}$ )能够增加唾液和牙菌斑生物膜中的氟浓度,减少菌斑积聚,在恢复牙根中牙本质丢失的矿物质方面具有优势<sup>[3]</sup>。

有学者指出在根面龋风险患者中,每天使用0.2%氟化钠漱口水可作为含氟牙膏刷牙的辅助手段阻止病变进展。老年患者行动受限,局部应用含氟漱口水和含氟凝胶或泡沫更为简便。目前研究表明使用浓度为12 000 mg/L的氟化钠凝胶涂布龋损处,每4个月1次,1年内能使活动性根面龋转化为非活动性龋<sup>[4]</sup>。研究证实了 $\text{TiF}_4$ 清漆可在牙面上形成一个富含氟化钙、氧化钛和水合磷酸钛的玻璃层作为机械屏障,增加牙体组织的耐酸性,促进了氟化钙的沉积,在减少矿物质流失和损伤

深度方面的效果优于氟化钠,对牙本质龋有良好的预防效果<sup>[5]</sup>。

### 1.2 氯己定/氯己定

氯己定/氯己定(chlorhexidine, CHX)在高浓度时具有杀菌作用,低浓度时具有抑菌作用。CHX可在病变顶部形成扩散屏障,使表层氟穿透量增加,从而阻碍牙本质细菌的营养供应,提示氯己定与含氟清漆可联合应用效果显著<sup>[6]</sup>。在高风险根面龋人群中进行的随机研究发现,使用氯己定清漆使得根面龋发生率显著降低<sup>[7]</sup>。CHX的有效性与浓度和使用频率有关,浓度越高,效果越好,但是高浓度和长时间使用CHX,可能会发生广泛的牙齿染色。

### 1.3 氟化氨银

氟化氨银(silver diamine fluoride, SDF)中的银离子具有较强的抗菌作用,当羟基磷灰石与SDF反应时,会产生氟化钙、磷酸银和氢氧化铵,促进再矿化,可预防和阻止老年人根面龋损的发生发展<sup>[8]</sup>。Chan等<sup>[9]</sup>文献回顾结果表明,每年将38%的SDF用于老年人暴露的牙根表面是一种简单、经济且有效的预防龋齿发生和发展的方法,可使暴露的牙根表面龋病的发生率降低。虽然SDF非常适用于老年人的口腔保健,但会引起牙齿颜色变黑。Shimizu等<sup>[10]</sup>通过应用碘化钾试图解决与SDF相关的颜色变化问题,结果表明碘化钾虽然解决了牙齿变色问题,但降低了脱矿预防效果。

### 1.4 玻璃离子水门汀

玻璃离子水门汀(glass ionomer cement, GIC)不仅仅可以用于根面龋的充填治疗,一些流动性好的GIC也可以用于预防根面龋,低黏度的GIC覆盖在暴露的牙根表面可作为物理屏障防止细菌侵入牙骨质和牙本质小管,同时避免菌斑在牙根表面附着,预防根面龋的发生;含有高浓度氟离子的GIC材料覆盖在皮革化牙本质的初期根面龋的病变表面,能够促进病变区域再矿化,从而避免更复杂的

修复治疗<sup>[11]</sup>。临床上,使用释放氟化物的修复材料有利于抑制根面龋病变脱矿和促进再矿化<sup>[12]</sup>。

## 2 新型防根面龋材料

### 2.1 无机纳米材料

目前研究较多的无机纳米材料主要有生物活性玻璃(bioactive glasses, BAG)、酪蛋白磷酸肽-无定形磷酸钙(casein phosphopeptide-amorphous calcium phosphate, CPP-ACP)和季铵化合物等。BAG通过磷灰石形成再矿化修复底层脱矿牙本质,封堵暴露的牙本质小管,从而改善牙本质界面的粘接。但是BAG处理后的牙本质的力学性能远低于天然牙本质<sup>[13]</sup>。研究发现在无氟牙膏中添加含锶生物活性玻璃陶瓷可以抑制微生物产酸,对致龋菌的生长有潜在的抑制作用<sup>[14]</sup>。

CPP-ACP是一种唾液仿生物物质,通过酪蛋白稳定牙齿表面的磷酸钙,维持钙和磷酸盐离子的高浓度梯度,防止氟离子在表层快速沉淀,在脱矿牙釉质及其下方深层病变的再矿化作用中具有显著优势,能够改善釉质的纳米力学性能<sup>[15]</sup>。显微放射学图像证实在含氟清漆中加入CPP-ACP能促进白垩斑病变深层的再矿化<sup>[16]</sup>。含CPP-ACP和氟化物的清漆,在口腔干燥症患者中应用1年以上可以阻止根面龋的发生发展<sup>[17]</sup>。

季铵化合物能够抑制与活动性根面龋病变相关微生物群的生长潜力。Balhaddad等<sup>[18]</sup>发现5%甲基丙烯酸二甲氨基十六烷基酯(DMAHDM)和20%无定形磷酸钙纳米粒子分别通过减少细菌生长和释放高浓度的钙离子和磷酸根离子来发挥抗龋功能,二者结合能够抑制牙菌斑积聚,而且在配制过程中可以灵活定制,不会对机械功能产生不利影响,可作为一种前瞻性的治疗策略预防高危老年患者根面龋病变周围的继发龋。Zhou等<sup>[19]</sup>在根龋模型中进行测试时发现NACP+DMAHDM纳米复合材料具有抗菌、促进钙离子释放的功效,不仅显著降低了根牙本质脱矿程度,而且可以保护生物膜下修复体周围的牙本质硬度。

### 2.2 胶原交联剂

胶原交联剂包括合成交联剂、天然交联剂和物理交联剂三种类型。戊二醛(glutardialdehyde, GA)是一种合成交联剂,GA预处理可以为胶原的成核提供亲和位点,从而诱导胶原的矿化,成为促进牙本质矿化的潜在策略。但是GA具有细胞毒性,因此使用含戊二醛的粘接剂作为封闭剂预防

根面龋的临床效果有待进一步研究<sup>[20]</sup>。

天然交联剂包括原花青素、黄酮类等,黄酮类交联剂包括鞣酸、橙皮苷、甘草等。天然交联剂的作用机制是和胶原蛋白的羟基、酰胺基等基团形成氢键,抑制胶原降解、保护牙本质的胶原蛋白,防止酸进入以及钙和磷酸根离子的流失,增强树脂-牙本质结合强度,提高力学性能<sup>[21-22]</sup>。此外, Kim等<sup>[23]</sup>临床随机试验结果证实含甘草提取物的漱口水对变异链球菌具有抗菌和抗黏附作用,对人体副作用小,可作为一种有效的防龋剂。

核黄素是光氧化中使用的一种物理交联剂,通过吸收紫外光产生活性氧自由基发挥杀菌功效,促进胶原蛋白网络的有效物理交联,提高脱矿和非脱矿牙本质的力学性能,其缺点为导致牙齿颜色变黄,而且其临床实用性以及细胞毒性问题仍存在争议<sup>[24]</sup>。

### 2.3 抗菌肽

抗菌肽是由12~50个氨基酸的短链组成的寡肽,具有抗菌、抗病毒或抗真菌活性。抗菌肽可以破坏细胞质膜,并穿透细胞并结合细胞内分子,干扰蛋白质的合成,阻止细胞壁的合成。天然抗菌肽,如人源性抗菌肽、防御素等对口腔致病菌具有抗菌特性,但是它们半衰期短,稳定性低;合成抗菌肽具有杀菌作用,少数对羟基磷灰石具有再矿化特性,可以更加安全、有效地促进口腔生态平衡和整体健康,是传统抗菌治疗的潜在替代方案<sup>[25]</sup>。

### 2.4 新型脱敏剂

纳米密封剂Nanoseal通过不溶性纳米颗粒聚集在牙齿表面来减少矿物丧失,新型含锌脱敏剂CAREDYNE Shield通过诱导牙本质小管的化学闭塞,释放锌离子来减少牙釉质和牙本质的脱矿,抑制生物膜的形成和牙本质-胶原蛋白的降解,故二者不仅可以作为脱敏剂封闭牙本质小管,还可作为根龋抑制剂避免牙根表面脱矿<sup>[26-27]</sup>。Yamamoto等<sup>[28]</sup>发现脱敏涂层材料表面预反应玻璃离子聚合物(S-Prg),能够抑制生物膜的形成,减少致龋菌对牙本质表面的黏附,可用于根面龋的防治。

### 2.5 其他

臭氧(ozone)是一种强氧化剂,通过破坏微生物的细胞壁导致微生物死亡,从而阻止牙菌斑生物膜的形成。研究表明定期施用臭氧40s和再矿化产品,可以使老年人早期根面龋发生逆转,但是臭氧治疗很难作为日常保健措施,需要在特定场所和专业技术人员的看护下进行<sup>[29]</sup>。

光动力疗法(photoactivated disinfection)是一种无创性、利用特定波长的光激活光敏剂产生光化学效应的一种新疗法,通过光敏剂可特异性滞留于致病微生物体内,实现选择性杀伤病原微生物而不伤及周围正常组织。CO<sub>2</sub>激光照射牙本质会引起矿物部分和有机基质的变化,可以防止牙根和牙釉质表面的脱矿,而且不伤害牙髓<sup>[30]</sup>。Mocuta等<sup>[31]</sup>体外研究发现 Nd:YAG 激光对于脱矿部位的形态以及矿物含量具有一定的改善作用,阻止脱

矿的发展。

pH敏感载药系统的原理是在载体中引入“可离子化”的化学基团,如氨基、羧基等,在体内环境pH值的变化时,这些基团可以接受或者提供质子,通过载体结构改变或者破坏来释放药物发挥杀菌、再矿化等作用,使药物在特定部位能够较长时间维持有效浓度,从而实现药物在疾病治疗中的控制释放和靶向给药<sup>[32-33]</sup>。各种防根面龋牙科材料的防龋机制及优缺点总结见表1。

表1 防根面龋牙科材料的防龋机制及优缺点  
Table 1 Mechanism and key features of dental materials for root caries prevention

Material types	Mechanism	Key features	Reference
Fluoride	Inhibites demineralization and promotes remineralization, affects the metabolism of cariogenic bacteria	Advantages: it has a wide range of clinical application, sterilization and remineralization, and is easy to use Disadvantages: the action time is short, the remineralization is limited to the surface, and the antibacterial effect is limited	[2-4]
Chlorhexidine	Bactericidal at high concentration, bacteriostatic at low concentration	Advantages: the application is simple and convenient, and has bacteriostatic effect Disadvantages: teeth are stained, without re-mineralization	[6-8]
Silver diamine fluoride	Antibacterial, improve local pH value, inhibit demineralization, promote remineralization	Advantages: economical, easy to operate, the effect is obvious Disadvantages: silver ion has toxicity, teeth are stained	[10-11]
Glass ionomer cement	Acts as a physical barrier to prevent bacteria from invading cementum and dentin tubules, and prevents plaque from attaching to the root surface of the tooth	Advantages: it can release fluorine ions and promote remineralization Disadvantages: adhesive force is not strong and easy to fall off	[12-13]
Inorganic nanomaterials	Bacteriostatic, stabilizes the calcium phosphate on the tooth surface and promotes the re-mineralization of the deep lesions below the demineralization site	Advantages: it can promote remineralization in the deep of the lesion Disadvantages: mechanical properties are not as good as the original dental tissue	[14-20]
Collagen crosslinking agent	Cross-linking with collagen groups in dentin inhibits collagen degradation and promotes re-mineralization	Advantages: improve the mechanical properties of demineralized and non-demineralized dentin and promote remineralization Disadvantages: tooth staining, cytotoxicity, etc	[20-25]
Antimicrobial peptide	Disrupts the plasma membrane, interferes with protein synthesis and prevents cell wall synthesis	Advantages: targeted antibacterial effect is significant Disadvantages: the production cost is high and the clinical effect needs further investigation	[25]
Emerging desensitization agent	Formation of physical barriers reduces mineral loss on tooth surface, inhibits biofilm formation and dentin-collagen degradation	Advantages: desensitization and remineralization, and the adhesion is strong Disadvantages: clinical efficacy has not been supported by substantial data	[25-27]
Others (ozone, photodynamic therapy, pH release system, etc.)	Oxidation, photothermal sterilization, drug release based on pH microenvironment change	Advantages: targeted antibacterial, no damage to the surrounding tissue, sustained release effect Disadvantages: it should be carried out in a professional place and under the guidance of professional technical personnel	[29-33]

### 3 总结与展望

根面龋治疗过程中,由于视野容易受限、牙根部有机物含量高、龈沟液干扰等因素,导致充填修复较困难,充填修复材料易脱落,易出现继发龋。对于有患龋高风险、牙根暴露的人群,在做到有效口腔保健的同时,配合使用防根面龋材料,有助于预防根面龋的发生。传统防龋材料氯化物的使用一直被认为是预防和控制龋齿的主要基石,如氟化物、氯己定、氟化氨银等在临床中广泛应用,其防龋疗效已被广泛认可,可作为早期预防根面龋发生的药物,但是其具有牙齿着色、再矿化能力不足、发挥功效时间短暂等缺点,从而促使一系列新研发的防龋材料和技术如无机纳米材料、胶原蛋白交联剂、激光等的发展,它们在抗菌的基础上更有效率地促进病损区域表面及深部的再矿化的效果,黏附性极大增强,并且延长了材料的作用时间。但是,这些新型材料和技术的临床疗效还需进一步研究。深入研究防根面龋材料的临床疗效和作用机制,针对根面龋位置及微环境的特殊性,研究开发新型防龋材料,提升再矿化及杀菌效率,改善黏附性能,延长作用时间,扩大应用范围,对促进根面龋的有效预防,改善老年人的口腔健康状况和生活质量具有重要意义。

**[Author contributions]** Xiong JD wrote the article. Cheng XQ and Wu HK revised the article. All authors read and approved the final manuscript as submitted.

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