Presented at the International Association for Dental Research Pan European meeting, 2014

Chlorhexidine hexametaphosphate nanoparticles for controlled chlorhexidine delivery in oral disease

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Objectives

Chlorhexidine is a broad-spectrum biocide used in aqueous solution as both an oral rinse and a topical antimicrobial for treatment of periodontal disease and in endodontic treatment and oral surgery. In this study, novel chlorhexidine-based nanoparticles are investigated as an alternative delivery vector to aqueous solutions.

Methods

Chlorhexidine hexametaphosphate nanoparticles were synthesised by mixing equimolar solutions of chlorhexidine digluconate and sodium hexametaphosphate to effect total, bound and unbound, chlorhexidine and hexametaphosphate concentrations of 1, 2.2 and 5mM. Aqueous 1, 2.2 and 5mM chlorhexidine digluconate solutions were used for comparison. Hydroxyapatite discs were etched in 0.3% citric acid for 30 min, rinsed with deionised water and dried. Discs (n=6) were immersed in the solution/nanoparticle suspension for 15s, rinsed in deionised water for 30s and allowed to dry. Discs were placed in UV-transparent cuvettes containing 2mL deionised water, sealed and sampled at intervals for soluble chlorhexidine. Data were analysed using repeated-measures ANOVA with LSD post-hoc test.

Results

All of the discs exhibited a gradual release of soluble chlorhexidine. The initial (<1h) release owing to aqueous solutions and nanoparticle suspensions was comparable, but after this time chlorhexidine release from solution-treated hydroxyapatite proceeded at a lower rate, reaching a plateau at ~3.6h (1, 2.2mM) and ~29h (5mM). When exposed to chlorhexidine nanoparticles, chlorhexidine release proceeded for longer, reaching a plateau at ~70h (1, 2.2mM) and >170h (5mM). The LSD test indicated that significantly more CHX release was observed from NP suspensions than aqueous solutions at 2mM ($p=0.020$) and 5mM ($p=0.013$) but not 1mM ($p=0.172$).

Conclusions

Applying chlorhexidine in the form of chlorhexidine hexametaphosphate nanoparticles, rather than as an aqueous solution, resulted in a more prolonged, and greater, release of soluble chlorhexidine. This may find application in the development of oral rinses and topical antimicrobials in the fields of oral medicine and oral care.