REVIEW ANALYSIS & EVALUATION // DIAGNOSIS/TREATMENT/PROGNOSIS

CPP-ACP MAY BE EFFECTIVE, BUT NOT SIGNIFICANTLY GREATER THAN USING FLUORIDES ALONE, IN PREVENTING AND TREATING WHITE SPOT LESIONS AROUND ORTHODONTIC BRACKETS

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Do products containing casein phosphopeptide–amorphous calcium phosphate (CPP-ACP) have preventive and therapeutic effects on white spot lesions occurring during fixed orthodontic treatment ?

REVIEWERS
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ARTICLE TITLE AND BIBLIOGRAPHIC INFORMATION
Effectiveness of casein phosphopeptide–amorphous calcium phosphate–containing products in the prevention and treatment of white spot lesions in orthodontic patients: A systematic review. ***Pithon MM, Baião FS, Sant'Anna LID, Tanaka OM, Cople-Maia L.*** *J Invest Clin Dent 2019;e12391.*

SUMMARY

Selection Criteria

The authors conducted an electronic search of 7 databases (PubMed, Scopus, Web of Science, Cochrane, Virtual Health Library, ClinicalTrials, and OpenGrey) in May 2017, with no restrictions on language and year of publication. Also, the reference lists of the selected articles were manually searched.

A total of 599 records were initially identified through electronic searches. No additional item was found through the hand search. Two independent researchers screened the titles and abstracts of all identified records, after which 11 studies met the eligibility criteria and were included in the review.

Key Study Factors

Among the 11 included studies, 9 were randomized controlled trials (RCTs) and the other 2 were nonrandomized controlled trials (NRCTs). All 11 trials compared the effects of products containing casein phosphopeptide–amorphous calcium phosphate (CPP-ACP) including topical cream GC tooth mousse (6 trials), fluorine-associated CPP-ACP (4 trials), and fluorine-free CPP-ACP toothpaste (1 trial), with other oral agents or placebos in the prevention and treatment of white spot lesions (WSLs) around orthodontic brackets.

SORT SCORE			
A	**B**	C	N/A

SORT, Strength of Recommendation Taxonomy.

LEVEL OF EVIDENCE		
1	**2**	3

See article 101433 for complete details regarding SORT and LEVEL OF EVIDENCE grading system.

SOURCE OF FUNDING
No financial support was reported.

TYPE OF STUDY/DESIGN
Systematic review.

KEYWORDS
Casein phosphopeptide–amorphous calcium phosphate, Orthodontics, Tooth remineralization, White spot lesions

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A total of 556 orthodontic patients with labial fixed appliance were involved in these trials. The length of follow-up varied from 4 weeks to 6 months. In addition, the updated version of Cochrane Risk of Bias tool (RoB 2.0) and Risk of Bias In Non-randomized Studies (ROBINS-I) were used to assess the risk of bias (ROB) of included RCTs and NRCTs, respectively.

Main Outcome Measures

The predetermined primary and secondary outcome measures were not specifically reported in either the registered protocol or review article. Among the included trials, a variety of outcome measures were used, including area (measured with visual inspection, digital photos, and quantitative light-induced fluorescence [QLF]), depth (measured with QLF), integrated loss of fluorescence (measured with QLF), salivary and plaque pH, enamel microhardness, and the degree of demineralization and remineralization (measured with Enamel Demineralization Index, the International Caries Detection and Assessment System, and DIAGNOdent).

Main Results

Because of substantial heterogeneity among the included trials in their study design (eg, randomized vs nonrandomized, different products and protocols, and different outcome measures), the authors decided to present the findings of included trials in a descriptive manner and not to perform meta-analyses.

Three trials investigated the effects of CPP-ACP–containing products in prevention. Of these, two trials compared CPP-ACP plus fluoride (CPP-ACPF) with placebo, suggesting CPP-ACPF can significantly prevent the appearance of new WSLs during orthodontic therapy. The other trial made a comparison among CPP-ACP, NaF topical gel, and fluoridated toothpaste and found that both CPP-ACP and fluoridated gel were effective in preventing the WSL formation, but with no significant differences between these two interventions.

For the treatment of WSLs, evidence showed that CPP-ACP was able to remineralize demineralized enamel, but its effect was not significantly different from those of fluoride-containing products:

- Three trials showed that in terms of WSL area reduction, the use of CPP-ACP was more effective than fluoride dentifrice or placebos. However, one of these trials and another two suggested that the use of CPP-ACP had no additional benefits than using NaF gel or NaF rinse alone.
- Two trials indicated that CPP-ACPF could achieve a higher level of WSL regression than placebos. However, another two trials showed that the therapeutic effects of CPP-ACPF were not significantly better than fluoride varnish or fluoride toothpaste.

Conclusions

Results of this systematic review (SR) suggest that CPP-ACP–containing products may be effective in the prevention and treatment of WSL. However, it seems that their effects are not significantly greater than using fluorides alone.

COMMENTARY AND ANALYSIS

WSLs are areas of enamel demineralization that appear as white spots on tooth surfaces, which is an undesirable side effect for patients treated with fixed orthodontic appliances.[1] The main cause of WSLs is prolonged plaque accumulation.[2,3] During orthodontic treatment, it is difficult to clean teeth where food accumulates around fixed orthodontic appliances,[2,4] which significantly increases the risk of WSLs. In addition, other factors such as diet, genetic susceptibility, and deficiency in phosphate, calcium, fluoride, and bicarbonate in saliva have also been related to the development and progression of WSLs.[5]

CPP-ACP is a nanocomplex derived from milk, which inhibits demineralization and enhances remineralization by accumulating calcium and phosphate, buffering the activities of calcium and phosphate ions, and thereby helps maintain a supersaturated state.[6-8] For the past few years, studies have shown that CPP-ACP–containing products have positive effects on the enamel remineralization of early caries lesions in vitro,[9,10] but whether they are effective in vivo still remains controversial. Thus, Matheus et al's SR[11] provides a timely summary of evidence for a clinically relevant question.

However, some limitations exist in this review. First, although the authors stated that they followed the PRISMA guidelines, several important aspects of the review (eg, search strategy, source of funding) were not reported. Also, a justification for the inclusion of nonrandomized studies was not provided.

Second, authors used the latest tool (Cochrane RoB 2.0) to assess the ROB among included trials, but the results of bias risk assessment in the SR may be problematic. In this SR, almost all the included studies were deemed as having low ROB. However, we found that the ROB of Andersson et al[12] and Brochner et al[13] were rated as either high or unclear in the SRs by Hochli et al,[14] Tao et al,[15] and Raphael et al[16] but were both considered low ROB in this SR. In addition, authors made modifications to the original RoB 2.0 tool, such as using a new summary category "moderate." However, reasons for these modifications were not provided.

Third, according to a study by Thierens et al,[10] an application period of 12 weeks of CPP-ACP showed superior results compared with a 6-week application. It emphasized the importance of prolonged use of CPP-ACP–containing products to reduce WSLs. However, in this SR, authors could have warned readers that the follow-up length of 4 included RCTs was too short (less than 12 months), which may provide only limited values for clinical practice.

Finally, a study by Miller et al[17] has shown that an immediate application of fluoride to WSLs can restrict remineralization to the surface of enamel, while the deeper layers still remain demineralized. Besides, Willmot[18] suggested that the use of fluoride in high concentration may arrest the remineralization process and lead to unsightly staining. However, adverse effect was not included as an outcome in this SR. Therefore, it is inconclusive whether there are significant differences between CPP-ACP and fluoride products in terms of adverse effects.

In summary, based on existing RCTs and NRCTs, both CPP-ACP and CPP-ACPF may be effective in preventing and treating WSLs around orthodontic brackets, but their effects are not significantly greater than that achieved using fluoride alone. Orthodontists and general dentists can consider using CPP-ACP–containing products as an alternative to fluoride for the prevention and treatment of orthodontically induced WSLs. In addition, further high-quality RCTs that can provide stronger evidence for the effectiveness and safety of CPP-ACP are needed, preferably using long-term follow-up and clinically relevant outcome measures.

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