

Guest Editorial

New treatments for old diseases: a proposal for international collaboration and funding of oral health clinical trials

Focused Perspective on Corrocher et al., J Clin Periodontol 2008; 35: 244–248

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Oral lichen planus (OLP) is a relatively rare, chronic oral disease of unknown etiology that affects the oral mucous membranes and gingiva. Its erosive form can have a major impact on quality of life due to the severe pain and burning sensation that often accompanies this disease. Because the cause of this disease is obscure, treatment is varied and symptomatic including topical and systemic corticosteroids, immunosuppressive drugs, antimycotic agents, antimicrobial mouthrinses, and topical anesthetics (Ismail et al. 2007). Although some patients obtain symptomatic relief, a systematic review concluded that there is only circumstantial evidence for the superiority of various interventions over placebo for the palliation of symptomatic OLP (Zakrzewska et al. 2005).

In the paper by Corrocher et al. (2008) evidence is provided that builds on previous work indicating that topical tacrolimus 0.1% ointment may provide symptomatic relief for patients suffering from erosive lichen planus (Hodgson et al. 2003, Thomson et al. 2004, Lozada-Nur & Sroussi 2006). It is intriguing that the results of this small, short-term, randomized trial showed that while all patients reported severe or moderate pain and burning sensation at baseline, a substantial percentage of patients treated with tacrolimus ointment reported complete remission of pain (43.7%) and burning sensation (93.7%). Moreover, 56.3% of patients using tacrolimus

ointment had complete remission of mucosal lesions. In comparison, none of the patients treated with clobetasol ointment reported complete remission of these symptoms (Table 1, Corrocher et al. 2008).

Based on the results of this trial and results reported by others (Hodgson et al. 2003, Thomson et al. 2004, Lozada-Nur & Sroussi 2006), it would be tempting to recommend use of topical tacrolimus ointment for symptomatic relief of erosive oral lichen planus. However, all trials of this drug have been very limited in terms of sample size and duration. As with many other clinical trials of oral diseases, small clinical trials may have adequate statistical power to detect differences between various interventions, but they are very different than the typical large sample, multicenter clinical trials involving hundreds or even thousands of subjects that have the necessary power and generalizability to change standards of clinical practice, inform public health policy, or gain marketing approval from regulatory agencies.

The dental literature is replete with small clinical trials that show promising results regarding the effectiveness of new or widely used treatments for oral diseases. However, because these trials have been conducted in relatively small numbers of subjects in single centers involving homogeneous populations, they have done relatively little to change clinical practice or inform public health policy.

Well-designed, large, multicenter, randomized clinical trials are required if treatment of oral disease is to be based on the highest level of scientific evidence. Before such trials can be undertaken, the oral health research community and those who financially support oral health research must be prepared to seriously address major issues such as appropriate trial design, pre-trial registration, governmental regulatory standards and guidelines (e.g. European Union, United States), standards of care, sample size, trial management and most significantly, cost. All must be addressed before large multicenter trials can be implemented that truly have the potential to globally change clinical practice or inform public health policy. If the oral health research community is to address these issues seriously and in a manner that is consistent with standards of the larger medical community, there is a pressing need for increased industrial or government support for oral health clinical trials.

Because oral diseases are globally among the most common diseases known to mankind and because costs for such trials are unlikely to come from any one government, perhaps funding for pivotal oral disease trials could be accomplished by collaborative funding from health research agencies in participating countries. For example, it might be possible to fund trials by having each country support its own portion or center in a multicenter trial. In one possible

scenario, support for the central data coordinating center could be shared among participating countries and each trial enrollment site (center) could be supported by the country in which the enrollment site located. Undoubtedly, there would be many logistic and cultural hurdles that would need to be resolved in such an arrangement but, combined with modern electronic means of communication, increased international standardization and harmonization of clinical trial standards and regulations should make such collaboration possible. International multicenter trials are becoming very common in medicine and with increasing societal and medical recognition of the importance of oral health, the time has arrived for innovative international collaboration and funding of oral health clinical trials.

In view of the limitations of their trial, Corrocher et al. (2008) appropriately take a conservative approach and conclude that other studies are needed to confirm the effectiveness of tacrolimus ointment for treatment of erosive oral lichen planus. This is but

one example of the need for significant industrial or governmental support of large, multicenter clinical trials that are needed to address treatment of oral disease. Perhaps it is too much to hope for, but as the importance of oral health continues to be recognized by the medical community and by society as a whole, such funding will be forthcoming. Quite simply put, such funding is essential; our patients and society demand the best scientific evidence for care and they should get it.

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