Does adjunction of *Melaleuca alternifolia* to periodontal treatment protocol improve clinical outcome?

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Abstract

Objective To assess the evidence on possible clinical periodontal benefits of tea tree oil (TTO) as an adjunct in the management of periodontal disease.

Methodology Systematic research was carried out using ResearchGate, PubMed and Cochrane library databases. Specific terms with applied Boolean operators and truncators completed. A total of seven papers met the criteria and were critically appraised using the Critical Appraisal Skills Programme (CASP).

Results This literature review (LR) includes: two papers with TTO gel, one paper looked at TTO subgingival film application, two papers discussed mouthwash and two were systematic reviews. Appraised papers addressed TTO properties in clinical outcomes and summarised these into tables.

Conclusion Further longitudinal and high Hierarchy of Evidence (HoE) studies are required. The clinical methodologies periodically present uncertainty in results due to a wide range of TTO applications, delivery protocols, and the duration of interventions.

Introduction

Periodontal disease (PeDi) is a complex multifactorial inflammatory oral disease, caused by anaerobic periodontopathic bacteria, categorised by loss of clinical attachment and destruction of periodontal tissues.[1] Following diagnosis confirmation, PeDi is categorised by the process of staging and grading using specific decision-making algorithms to confirm the diagnosis, assess risks, and complexity management of PeDi.[2]

Conventional non-surgical periodontal therapy to manage PeDi involves mechanical

debridement, and is a widely used approach, however, debridement alone may not eliminate causative bacteria and recurrence can take place.

Systemic antimicrobials have been used as an adjunctive method to suppress periodontal pathogens. However, antibiotic resistance and side effects are rising, so their use has been reduced.

There are a variety of antibiotic systems of local delivery available, though their indications for use are limited.[3] Moreover, the Scottish Dental Clinical Effectiveness Programme (SDCEP) view on the use of adjuncts is limited to chlorhexidine (CHX) and locally delivered antibiotics.[4] A study suggests that long-term use of CHX presents a range of reported adverse reactions (AR): numbness and pain in the tongue and mouth; taste alterations; xerostomia and discoloration.[5]

The General Dental Council (GDC) advise to: 'Provide good quality care based on current evidence and authoritative guidance'.[6] With relevance to this statement, Sanz *et al.*[7] reported on recent guidelines by the British Society of Periodontology that support the use of adjuncts. Furthermore, Herrera *et al.*[8] concluded that the use of a local adjunctive in patients with periodontal disease results in statistically beneficial clinical outcomes, exclusive of relevant side effects.

It has been suggested that tea tree oil (TTO) can be used as alternative to CHX. TTO is derived from *Melaleuca alternifolia* (MA) *(Myrtaceae),* a plant native to Australia. It is considered to have antioxidant, antifungal, antiviral, anti-inflammatory, and broad-spectrum antimicrobial effects.[9] The main antimicrobial components of TTO are terpinen-4-ol and 1,8-Cineole. These phytoconstituents are able to disrupt the membrane integrity of bacteria, and inhibit the growth of *Escherichia coli, Staphylococcus aureus* and adhesion of *Porphyromonas gingivalis.*[10]

Being a dental therapist student, I treat patients of different backgrounds, views, and medical statuses. I noticed that patients are frequently on multiple medications, have sensitivities and allergies to products. With antibiotic resistance on the rise and CHX side effects, I wanted to explore how a herbal agent can be effective to manage PeDi. MA is an adjunct of interest. Existing literature claims TTO could have beneficial properties as a successful adjunct in the management of PeDi. In this review, my emphasis will be on the periodontal aspect and restricted to clinical research.

Methodology

A scoping review and background reading on TTO through September–December 2022, using a specific combination of MeSH terms and Boolean operators (AND, OR). PubMed, Cochrane Library and ResearchGate for academic search.

An additional papers search was conducted manually through all reference lists in the articles of interest. Several authors were contacted regarding their published work with only one response obtained.

- 444 prospective papers identified through database search
- 313 papers excluded after filters applied and duplicates removed
- 131 screened papers
- 7 papers met criteria
- 5 randomised controlled trials (RCTs)
- 2 systematic reviews (SRs).

> *'Tea tree oil is considered to have antioxidant, antifungal, antiviral, anti-inflammatory, and broad-spectrum antimicrobial effects.'*

Results

A total of seven studies, two SRs and five RCTs, published between 2013–2022 were selected. The RCTs discussed TTO gel applications, mouthwashes and TTO film while the SRs described TTO applications with various modes of delivery, duration of trials, and calibration instruments. Most studies supported the use of TTO in management of PeDi, however they presented several limitations, therefore the intervention outcomes should be carefully considered.

Discussion

Casarin *et al*[11] conducted SR through October 2016 with participants from 15 to 49 people per study. Interventions included a wide range of TTO applications in the forms of toothpaste (0.5%), gel (2.5%, 5%), solutions (0.2%, 1.5%), and duration of use from five days to six months. Periodontal outcomes were assessed in only two studies, tested similar interventions using 5% TTO gel. A significant reduction in periodontal pocket depth (PPD) and clinical attachment loss (CAL) was reported. Casarin *et al.*[11] reported ARs of unpleasant taste, similarly to Taalab *et al.*[12] and Elgendy Ali Zineldeen.[13] Only clinical studies were included in this review; laboratory studies were excluded under exclusion criteria. Findings are to be interpreted with caution due to differences in the studies.

Singh *et al.*[14] presented SR explored in March 2021, four studies with CHX and TTO of various concentrations and delivery systems were studied. The variation of assessment between day one and six months. With the wide variety of TTO and CHX concentrations, it was a challenging task to obtain an accurate results assessment. Some studies had considerable clinical heterogeneity in PPD, CAL, gingival index (GI), and bleeding on probing (BOP). No Statistical Significance (SS) or Confidence Interval (CI) stated. CAL and PPD were not assessed. Thus, this can be explained by the difference in concentrations of agents being used. Results indicated TTO is superior to CHX in reducing gingival inflammation (Gin). Likewise, Casarin *et al.*[11] reported a positive effect of TTO on the gingival outcome. In this SR, results suggest CHX is superior in plaque formation inhibition than TTO. TTO may be used as alternative to CHX for Gin reduction with effective plaque control.

Relatedly, Casarin *et al.*[11] disclosed varied modes of administration, TTO dosage, with the use of multiple indices, and follow-up periods. Both SRs are high-evidence papers with a weak power of recommendation.

TTO gel application

Taalab *et al.*[12] conducted a six-month, parallel RCT between November 2019 and August 2020 with a total of 30 patients of either sex with periodontitis. The diagnosis was confirmed as per CAL 3–4 mm, BOP, and radiographic bone loss. Participants were divided into Control and Test groups, randomly assigned using

a computer-generated list of random numbers. RCT analysis was limited to clinical assessment only.

Similar to Elgendy, Ali and Zineldeen[13] this study used 5% TTO gel.

Periodontal parameters were recorded at baseline, three and six-month post-intervention, including: PPD, CAL, GI, and BOP. William's probe was used to record the measurements by a single-blinded clinician. Intraexaminer reliability for probing depth and CAL were stated for both groups. TTO gel 5% was locally prepared and delivered subgingivally with a bent, blunt-ended needle syringe to ensure the deepest point of delivery. Sample size estimation was explained with alpha error = 5% and study power 80%. All participants completed the study. Random assignment with a computer-generated list of a random number allocation was completed by a blinded assistant. Sequentially numbered opaque envelopes were used for allocation. Qualitative data shown in percentages. The Kolmogorov-Smirnov test measures distribution and normality. Age and gender comparison was done by chi-square and Student t-test.

PPD, CAL, GI, and BOP showed SS improvement from the baseline and follow-up periods in two groups. PPD no significant difference (NSD) noted in both groups from the baseline and follow-up periods. CAL NSD in both groups at baseline and three months, but significant difference (SD) at six months. GI NSD at baseline, but three and six months SS noted. BOP NSD in both groups at baseline and three months, but SS at six months. The superior results of the test group over the control group could be due to TTO's anti-inflammatory and antimicrobial properties. Intrapocket TTO gel application improves clinical outcomes for up to six months.

The current study results indicate TTO gel as an adjunct to Scaling and root planing (SRP) proved to be effective in the treatment of periodontitis; this supports the findings of Elgendy *et al.*[13] Both authors demonstrated TTO gel significantly reduces gingival bleeding and Gin in patients with periodontitis. Comparably, Mohamed *et al.*[15] reported an improved reduction in Gin and enhanced healing of periodontal tissues, when using TTO gel subgingivally in patients with periodontitis.

Elgendy, Ali and Zineldeen[13] conducted RCT from February 2011 to January 2012 with 40 patients. This study lacks credibility, due to the unreported sample data. Additionally, the wide age gap among participants could reflect on the severity of PeDi amongst different age groups and significantly differ in older participants.

The patients were randomly divided by a random number table and drawn into two groups. The blinding of participants, investigators or assessor were not declared; this is deemed an allocation concealment.

This study used 5% TTO gel which is similar to 5% TTO gel in Taalab *et al.*'s[12] trial; despite both TTO gels being produced in Germany and having the same sterilisation method, the process of gelling agent preparation differed amongst studies. Plaque index (PI), GI, PPD, CAL were recorded at baseline, one, three, and six months respectively. No calibration instrument was indicated. Results were statistically analysed using independent sample t-test and paired t-test. SS $p < 0.05$ for group one, and $p < 0.01$ for group two. Results suggest that local delivery of TTO may have benefits and potential therapeutic value as an anti-inflammatory agent; further human research is recommended.

its chromatographic profile. The included recommendations relating to Terpine-4-ol 35%–48%, and 1,8-Cineole up to 10%.[17] The percentage of TTO active components included in the clinical intervention were not specified. Clinical parameters (CP) PI (Silness and Loe), and GI (Loe and Silness) taken at baseline and after three weeks. $P < 0.05$ as significant. Statistical analysis with the use of paired *t*-test and one-way analysis of variance. SS Reduction $P < 0.001$ occurred in three groups of PI, GI at baseline to three weeks. After three weeks, group A and B had a significant reduction in PI and GI. In contrast, group C had no significant reduction in PI and GI. Results found EO MW was effective as an adjunct to scaling.

Bharadwaj *et al.*[18] conducted a single-centre, parallel-arm design, double-blind RCT, between November and December 2019. All participants completed the study with no withdrawal. Randomisation was conducted via the lottery method. The principal investigator was blinded. SS $p < 0.05$. Participants were split into three groups:

'Tea tree oil could be used as an adjunct or alternative to periodontal treatment and offers a greater opportunity to treat PeDi than a single allopathic drug.'

Mouthwash (MW)

Madhavi and Prasanna[16] presented a double-blind RCT completed in April 2018, amongst participants with severe gingivitis. They were allocated into three groups. The study sample was calculated at 95% CI. The sample size was explained. Power of the study was 90% for a sample size of 12, and 80% for a sample size of ten. Randomisation was completed by computerised allocation, participants and intervention conductor were blinded.

The Essential oil (EO) mouthwash presented as mixture of TTO, peppermint oil (PO), and water. The study used 10 ml of MW trice daily. According to the standards of the International Organization for Standardization (ISO), TTO contains certain characteristics for quality assessment in TTO MW, chloride dioxide (CD) MW and CHX. The plaque and GI were assessed with the modified Silness and Loe plaque index and the Loe and Silness GI at baseline and follow-up (21 days). TTO MW was prepared locally. Interestingly, 21.7% of smokers were included in this RCT, however, their group allocation was not indicated. The statistical analysis assessed with the Shapiro-Wilk test. The paired *t*-test and Wilcoxon matched-pair signed-rank test for comparison of mean PI and GI and post MW use. Kruskal-Wallis test used for difference evaluation.

Plaque was assessed with mouth mirrors and dental explorers. GI noted with mouth mirrors and periodontal probes. At the baseline and follow-up 21 days for plaque and GI. Results revealed a SS reduction in plaque

and mean gingival scores in three groups after 21 days. TTO MW and CHX demonstrated a greater reduction in plaque than CD. TTO can be used to reduce plaque and gingivitis.

TTO Film

Siddabasappa and Vandana[19] completed a split-mouth, triple blind RCT. Thirty participants with periodontitis. TTO films were inserted in pockets at baseline and reinserted on day seven. PI, Gingival bleeding index (GBI), PPD, CAL recorded by a single investigator. CP at 6–7 sites with 5–7 mm or greater pocket depth at baseline and day 21 documented. SRP performed with ultrasonic (Cavitront BOBCAT PRO) and hand instruments (Universal Gracey Curettes, 2R/2L and 4R/4L). Groups were split as follows: No Treatment, SRP, TTO, SRP + TTO. SS $p < 0.05$. At baseline CP showed NSD amongst groups. PI maximum reduction observed in SRP +TTO (0.87) was SS, and there was GBI reduction 96.67%. Interestingly, TTO alone demonstrated 94.7%. GBI reduction in contrast to SRP alone 39.43%. Following 21 days, PPD and CAL showed reductions, however, maximum reduction was observed in SRP +TTO (6.07 mm to 5.26 mm).

The current study suggests PI and GBI significantly reduced within each group; this can be explained by a simple consequence of demonstrated oral hygiene to participants. Notably reduced plaque scores can be explained by TTO films releasing the active agent *in situ,* over a period of time, unlike other TTO agents, that are deficient in this action. TTO could be used as an adjunct or alternative to periodontal treatment and offers a greater opportunity to treat PeDi than a single allopathic drug.

Conclusion

I conclude that there is not enough evidence of a sufficient level and quality to introduce tea tree oil within clinical settings at this stage. More meticulous and consistent protocols developed with longer follow-up period are necessary for additional analysis of TTO. The potency of TTO was not specified amongst the studies leading to further method discrepancies.

Recommendations

Further longitudinal, human studies of robust quality are required to investigate TTO to augment intervention modalities for PeDi. A standardised study protocol along with identical pharmaceutical grade formulation of TTO is needed for an accurate comparison.

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