

CLINICAL EFFECT OF A TRICLOSAN CONTAINING DENTIFRICE ON GINGIVITIS DURING PREGNANCY AND POST-PARTUM

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Abstract. One hundred forty pregnant women 3 months gestation were enrolled in a 9 month, double-blind clinical study to evaluate the effect of 0.3% triclosan/copolymer dentifrice on gingivitis, compared to a placebo dentifrice. Women were stratified into two balanced groups according to their baseline gingivitis scores. They then received oral prophylaxis and were assigned to use either a placebo or the triclosan dentifrice for the next 9 months. The 3, 5 and 9 month results of this study showed that the triclosan dentifrice provided statistically significant reductions in gingivitis of 19.73, 27.91 and 38.45%, respectively, compared to the placebo dentifrice.

INTRODUCTION

Within a few hours of tooth cleaning, oral bacteria colonize the tooth surface. This developing bacterial biofilm (dental plaque) releases a variety of biologically active products which diffuse into the gingival epithelium to initiate the host response that results in gingivitis (Kornman *et al*, 1997; Kolenbrander, 2000). Clinically, gingivitis is seen as redness, swelling and bleeding upon probing (Armitage, 2003). With appropriate intervention, gingivitis can be reversed and the periodontium returned to a healthy state. Unfortunately, many people, especially pregnant women, fail to maintain adequate hygiene, and the process of inflammation goes unchecked and untreated for years. In some individuals, for reasons that remain unknown, the chronic inflam-

mation of established gingivitis spreads to involve the destruction of the periodontal ligament and alveolar bone, resulting in periodontitis. The presence of gingivitis and periodontitis may have far greater implications for systemic health than imagined before. Recent evidence indicates associations between gingival and periodontal inflammation and systemic diseases, such as cardiovascular disease, stroke, respiratory disease and adverse pregnancy outcomes (Loesche, 1994; Madianos *et al*, 2002; Scannapieco, 2003, 2004; Dave *et al*, 2004; Moreu *et al*, 2005).

Several studies have shown that pregnant women have a higher incidence of gingivitis than non-pregnant women (L e and Silness, 1963; Jensen *et al*, 1981; Nuamah and Annan, 1998). The prevalence of gingivitis in pregnant women has been reported to range from 36-100% (Jensen *et al*, 1981; Ferris, 1993; Chanchareonsook and Sukprome, 1999). Hormonal and vascular changes during pregnancy can exaggerate the response of the gingiva to bacterial biofilm (Zachariassen, 1993; Raber-Durlacher *et al*, 1994). There is increas-

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ing evidence that periodontal disease is a significant risk factor for pre-term birth and low birth weight (Offenbacher *et al*, 1996, 1998; Lopez *et al*, 2002; Scannapieco *et al*, 2003; Radnai *et al*, 2004; Moreu *et al*, 2005). It is obvious that oral health and dental care of women during pregnancy are important for both the mother and the baby. A number of approaches have been considered for the prevention and treatment of pregnancy gingivitis.

Several clinical studies have shown that dentifrice containing triclosan and copolymer provides anti-plaque and anti-gingivitis clinical benefits (Palomo *et al*, 1989; Garcia-Godoy *et al*, 1990; Triratana *et al*, 1993, 1994). However, there have been no studies to assess the antigingivitis benefits of triclosan/copolymer dentifrice in pregnant women. This study was thus undertaken to determine the effects of a dentifrice containing 0.3% triclosan and 2.0% copolymer on gingivitis over a period of 9 months during pregnancy and 3 months post-partum, compared to a placebo dentifrice.

MATERIALS AND METHODS

Healthy pregnant women 3 months gestation, aged 19-40, were evaluated by a dental examiner while receiving routine prenatal care at Taksin Hospital, Thailand for the presence of gingivitis (except third molars and those teeth with prosthetic crowns or cervical restorations) and given gingivitis score. This initial gingivitis score was considered a woman's baseline gingivitis score. The scoring procedure used to assess gingivitis was the Löe-Silness Gingival Scoring Index as modified by Talbott *et al* (1977). This Index scores gingivitis on a numerical scale according to the following criteria: 0 = absence of inflammation; 1 = mild inflammation: slight change in color and texture. There is no bleeding upon probing; 2 = moderate inflammation: moderate glazing, redness, edema and hypertrophy. There is bleeding upon probing; 3 = severe inflammation: There is marked redness

and hypertrophy, a tendency to spontaneous bleeding and ulceration.

Each tooth was scored in six areas: 1. mesio-facial, 2. mid-facial, 3. disto-facial, 4. mesio-lingual, 5. mid-lingual, and 6. disto-lingual. A gingivitis index for each woman was determined by adding all the individual scores (6/ tooth) and dividing this sum by the total number of measurements (number of teeth scored multiplied by six), thus yielding the woman's mean.

A total of 140 pregnant women with a modified Löe-Silness Gingival Index score of 1.0 or greater at baseline examination participated in the clinical study. All women received a complete and thorough oral prophylaxis, including the removal of both supragingival and subgingival plaque and calculus deposits. Women were then stratified into two balanced groups on the basis of their pre-prophylaxis Löe-Silness Gingival Index (Talbott-Mandel-Chilton modification) scores. Each group was randomly assigned to use either 0.3% triclosan/copolymer dentifrice or a placebo dentifrice. All women were instructed to brush their teeth twice daily (morning and evening) for 1 minute each time in their usual and customary manner. They were instructed to use only their assigned dentifrice and provided a soft-bristle toothbrush for the entire 9 month duration of the study.

After 3, 5 and 9 months of using their assigned dentifrice, the women were evaluated for gingivitis by the same dental examiner using the same methodology.

RESULTS

Of the 140 pregnant women (3rd month of pregnancy) participating in the study, 136 (6th month of pregnancy) were available for the 3 month examination, 130 (8th month of pregnancy) were available for the 5 month examination, and 120 (3 months post-partum) completed the entire 9 month study. The subjects that did not complete the study did so for rea-

sons unrelated to the use of any of dentifrices.

The baseline characteristics for the 136, 130, and 120 women examined for gingivitis at 3, 5 and 9 months, respectively, are presented in Table 1. The pre-prophylaxis mean Löe-Silness Gingival Index score for the placebo dentifrice group were 1.771, 1.768, and 1.797, respectively. For the triclosan/copolymer dentifrice group, the scores were 1.755, 1.749 and 1.778, respectively. The Student's *t*-test confirmed that there were no statistically

significant differences between the two dentifrice groups with regard to pre-prophylaxis gingivitis scores at baseline ($p > 0.05$).

A comparison of the mean Löe-Silness Gingival Index scores for the two dentifrice groups after 3 months, 5 months and 9 months of use, respectively, are presented in Table 2. The placebo dentifrice group had a mean Löe-Silness Gingival Index scores of 1.125, 0.849 and 0.684, respectively while the triclosan dentifrice group had a mean Löe-

Table 1
Baseline characteristics and pre-prophylaxis mean Löe-Silness Gingival Index scores for women completing the first 3 months, 5 months, and the entire 9 months of study.

Dentifrice group	Number of women	Age		Mean pre-prophylaxis L-S Gingival Index score
		Mean	Range	
Women completing the first 3 month study				
Placebo	68	25.95	19-40	1.771 ± 0.431
Triclosan	68	26.45	19-37	1.755 ± 0.429
Total	136			
Women completing 5 month study				
Placebo	65	26.03	19-40	1.768 ± 0.437
Triclosan	65	26.72	19-37	1.749 ± 0.436
Total	130			
Women completing the entire 9 month study				
Placebo	60	25.90	19-40	1.797 ± 0.432
Triclosan	60	26.97	19-37	1.778 ± 0.432
Total	120			

Table 2
Comparison of the mean Löe-Silness Gingival Index scores for the two dentifrice groups after 3 months, 5 months, and 9 months.

Dentifrice group	Mean L-S Gingival Index scores	Percent reduction	Statistical significance
After 3 months			
Placebo	1.125 ± 0.582		
Triclosan	0.903 ± 0.497	19.73%	$p < 0.05$
After 5 months			
Placebo	0.849 ± 0.609		
Triclosan	0.612 ± 0.476	27.91%	$p < 0.05$
After 9 months			
Placebo	0.684 ± 0.612		
Triclosan	0.421 ± 0.443	38.45%	$p < 0.05$

Silness Gingival Index scores of 0.903, 0.612 and 0.421, respectively. The triclosan dentifrice was thus associated with a 19.73, 27.91 and 38.45% statistically significant reduction in gingivitis, respectively, compared to the placebo dentifrice ($p < 0.05$).

DISCUSSION

The main provoking factor that induces inflammation of gingival tissue is the presence of bacterial biofilm on the teeth/gingival interfaces (Teng, 2003). Dental biofilm is composed of numerous bacteria, comprising over 400 species, which release a variety of biologically active products, including lipopolysaccharides (endotoxins), chemotactic peptides, organic acids and protein toxins. These molecules are soluble and penetrate into the gingival epithelium and then signal the epithelium to produce and release inflammatory mediators, such as prostaglandins, interleukin-1 beta, interleukin-6, interleukin-8, tumor necrosis factor-alpha and interferon-gamma. These mediators induce the spectrum of periodontal response from mild gingivitis to severe destructive periodontitis (Kornman *et al*, 1997).

The etiological factors of gingivitis during pregnancy are complex and primarily related to hormonal changes and bacterial dental plaque (Raber-Durlacher *et al*, 1994; Zachariassen 1997). Hormonal changes due to increased levels of estrogen and progesterone during pregnancy cause an increase in the permeability of the blood capillaries in the gingiva and as a consequence bacteria and/or their products can diffuse through tissues more readily than normal and thereby increase susceptibility to gingival inflammation due to bacterial, chemical and physical irritation (Lindhe and Branemark 1967; Lindhe *et al*, 1968; Hugoson, 1970; Raber-Durlacher *et al*, 1994). High levels of progesterone also stimulate the production of prostaglandins, possibly increasing gingival inflammation and loss of gingival keratinization, proliferation of fibro-

blasts, chemotaxis and the phagocytic capacity of neutrophils (Zachariassen, 1993; Mariotti, 1994; Raber-Durlacher *et al*, 1994). The development of localized inflammation is affected by down-regulation of interleukin 6 production, rendering the gingival tissues less efficient in resisting the inflammatory challenges produced by bacteria (Lapp *et al*, 1995).

Hormonal and vascular changes during pregnancy are associated with the development and exacerbation of gingivitis. The results of this study show triclosan/copolymer dentifrice can reduce gingivitis both during pregnancy and post-partum. The antigingivitis effects of this dentifrice result from the dual antimicrobial and anti-inflammatory properties of triclosan.

Triclosan (2, 4, 4'-trichloro-2'-hydroxydiphenyl ether), a broad spectrum antimicrobial agent, has long been used in consumer products principally in deodorants, soaps and other dermatological preparations. The use of triclosan has recently been extended to oral health care products, such as dentifrices and mouthrinse. Safety information from pre-clinical and clinical studies, on the acute, subacute, subchronic and chronic toxicity, mutagenicity, carcinogenicity, reproduction/teratology and pharmacokinetics show that triclosan is well tolerated by a variety of species, including man, and can be considered safe for use in dentifrice and mouthrinse products (Desalva *et al*, 1989). Clinical pharmacokinetic studies show that triclosan at concentrations up to 0.3% in toothpaste do not accumulate in the human body. The elimination of the daily dose is complete and no accumulation of triclosan was observed even after three times daily tooth brushing with 1.25 grams of dentifrice and full ingestion of the dentifrice (Bagley and Lin, 2000).

Triclosan, by itself, does not readily adhere to plaque or oral tissue and is not retained at antimicrobial concentrations for extended time periods. However, when triclosan

is combined with a copolymer (polyvinyl methyl ether maleic acid), the retention of an effective concentration of triclosan in the oral cavity is increased (Nabi *et al*, 1989; Gaffar *et al*, 1990, 1994; Volpe *et al*, 1996). This triclosan copolymer formulation has been proven to prevent and treat gingival inflammation in 2 important ways by providing 12 hour antibacterial action and directly inhibiting potent mediators responsible for gingival inflammation. Triclosan interrupts inflammatory pathways by inhibiting both cyclooxygenase and lipoxygenase pathways of arachidonic acid metabolisms that lead to the production of prostaglandins, leukotrienes and lipoxins. Triclosan has also been shown to inhibit the release of prostaglandin E₂ from interleukin-1 beta-stimulated gingival fibroblasts, as well as reduce the production of interleukin-1 beta and interferon gamma (Gaffar *et al*, 1995; Modeer *et al*, 1996; Volpe, 1996; Mustafa *et al*, 1998).

In conclusion, the results of this clinical study indicate that the use of a dentifrice containing triclosan and a copolymer provides long term antigingivitis benefits during pregnancy and post-partum.

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