

THE LOCAL EFFECT OF CHLORHEXIDINE AGENTS IN THE TREATMENT OF CHRONIC PERIODONTITIS PATIENTS

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ABSTRACT

Background: Periodontitis is an immuno-inflammatory disease of the tissues surrounding the teeth. Various treatment modalities like mechanical debridement and use of antimicrobials have been followed in the treatment of such conditions. Introduction of local drug delivery system in the periodontal pocket is a promising therapeutic modality for achieving better clinical outcomes when used as an adjunct to conventional non-surgical periodontal therapy.

objectives: To evaluate clinical effect of different local delivery chlorhexidine Periochips and solution agents as adjuncts to SRP as combined therapy in patients with chronic periodontitis.

Materials and methods: A Clinical comparative study was conducted on 45 patients of both gender (male and female) with an age of 30-50 years and with chronic moderate to severe periodontist, all patients are being undergone full-mouth mechanical debridement by using ultrasonic scaler and universal and Gracey curettes. Periododontal pockets are to be irrigated by distillate water. Then the subjects were divided into two main group; first group consist of 15 patients with chronic periodontitis treated by chlorhexidine periochips, second group consist of 15 patients with chronic periodontitis treated by chlorhexidine Solution In addition to control group consist of 15 patients which were treated by SPR only. The criteria for chronic periodontitis was defined by the presences of $PPD \geq 5\text{mm}$ and $CAL \geq 3$, in two or more different sites for each patient of at least two teeth in each quadrant, and then the results were analyzed statistically.

Results: The most significant improvements were found concerning CAL, PI and GI in the group treated with CHX solution over CHX periochips ($P < 0.05$), over three months. Regarding PPD, there were no significant differences in PPD reduction gain in between the two agents ($P > 0.05$).

Conclusion: Results of this study favor combination therapy using CHX solution as an adjunct to SRP due to greater improvement in periodontal condition of patients with chronic periodontitis, compared to those obtained by SRP alone or with SRP and CHX periochips.

KEY WORDS: Chronic periodontitis, Chlorhexidine gluconate.

Abbreviation: Chlorhexidine (CHX), Scaling root planning (SRP). Gingival index (GI), Plaque index (PI), Clinical Attachment loss (CAL), Probing pocket depth (PPD).

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INTRODUCTION

Chronic periodontitis is an inflammatory disease caused by infection with periodontopathic bacteria that results in the progressive destruction of the tooth-supporting tissues and eventually tooth loss (Ren *et al.*, 2017).

It has been associated with a number of systemic diseases and conditions (Scannapieco *et al.*, 2010),

Such as cardiovascular disease and diabetes, and interactions may contribute to

these systemic diseases. Chronic periodontitis has a complex etiology dependent on the bacterial community residing in the gingival sulcus. Bacteria may be directly pathogenic or may stimulate damaging host inflammatory responses. The core oral microbiome appears to consist of <1000 species-level taxa (Dewhirst *et al.*, 2010).

Although any number of species may appear transiently in a site so open to the environment (Ann *et al.*, 2012).

Socransky *et al.* in 1998 described the subgingival microflora plaque formation as a

series of successive waves of colonization by increasingly periodopathogenic clusters of bacteria. The microflora shifts from Gram positive to Gram negative microbes and rods. The most pathogenic microbial cluster is the red complex which consists of the *P. gingivalis*, *T. Forsythia* and *T denticola* species (Socransky *et al.*,1998).

The microbial- inflammatory response interface plays a major role in the occurrence of the disease. According to data from the World Health Organization (WHO), advanced disease with deep periodontal pockets (≥ 6 mm) affects approximately the 10 to 15% of the adult population worldwide (Petersen and Ogawa.,2005).

Chlorhexidine Gluconate (CHX), a cationic bisbiguanide compound with high antibacterial activity, is one of the most commonly used chemotherapeutic agents against oral diseases. This is because of its wide spectrum of activity against yeasts, Gram positive, and Gram-negative bacteria including many anaerobic pathogens (Young *et al.*,2002).

Moreover, they are agents that kill oral microorganisms that cause gingivitis, periodontitis, and caries (Ryan.,2005).

The mechanism of action is due to its cationic nature which binds to anionic compounds on the bacterial surface such as phosphate groups of teichoic acid in Gram positive and lipopolysaccharide in Gram negative bacteria and disrupts bacterial integrity (Estrela *et al.*,2003).

This leads to leakage of the cell constituents and ultimately cell death (Siqueira *et al.*,2007).

The significant effects of chlorhexidine on plaque and gingivitis have been well documented and the effects were attributed to the reduction of pellicle formation and attachment of bacteria on the tooth surface. (Lorenz *et al.*,2006), (Sandhu and Grewal.,2011).

However, prolonged use of chlorhexidine carries with it several side effects including teeth staining, disturbances in taste sensation and increased calculus accumulation (McCoy *et al.*,2008), (Turkoglu *et al.*,2009).

Over the year's chlorhexidine available in gels, chips, sprays, and mouth- washes has been developed. Of these, mouth-wash is the most commonly used (Stoeken *et al.*,2007).

METHOD OF THE STUDY

1.Design of study

A Clinical comparative study was conducted on 45 patients of both gender (male and female) with an age of 30-50 years and with chronic moderate to severe periodontist. The subjects were divided into two main group; first group consist of 15 patients with chronic periodontitis treated by chlorhexidine periochips, second group consist of 15 patients with chronic periodontitis treated by chlorhexidine Solution; In addition to control group consist of 15 patients which were treated by SPR only. The criteria for chronic periodontitis was defined by the presences of $PPD \geq 5$ mm and $CAL \geq 3$ (Xiong *et al.*,2009), in two or more different sites for each patient of at least two teeth in each quadrant.

The study was reviewed and approved by institutional ethical committee of the University of Duhok College of Dentistry and informed consent was signed by all participants before conduction of the study.

In addition, during the first visit, patients are going to be motivated and educated towards self-performed oral hygiene measures. Furthermore, all patients are being undergone full-mouth mechanical debridement by using ultrasonic scaler and universal and Gracey curettes. Periododontal pockets are to be irrigated by distillate water. According to the applied treatment protocol, patients are going to be divided into three group as follows

Group	Materials	Procedure
1st Group	3.6% Chlorhexidine chip (Perio Products, Dexcel, Germany).	<p>Baseline: patients are being treated with 2.5 mg Chlorhexidine chip (Perio Products, Dexcel, Germany) will be applied, to the periodontal pocket by using tweezer after SRP then seal it by suture (Lecic et al., 2016). And in control sites at the same patient periodontal pockets will be thoroughly irrigated by distilled water after SRP, using a syringe with blunted needle located in the area of the bottom of the pocket</p> <p>One month later: Clinical examination (PI, GI, PPD, CAL)</p> <p>Three month later: Clinical examination (PI, GI, PPD, CAL)</p>
2 nd Group	2% solution of chlorhexidine gluconate (Gluco-CHEX).	<p>Baseline: The experimental group of periodontal pockets will be thoroughly irrigated with 0.12% solution of chlorhexidine, after SRP, using a syringe with blunted needle located in the area of the bottom of the pocket. Irrigation will be performed once a day in five days (Lecic et al., 2016). And in control sites at the same patient periodontal pockets will be thoroughly irrigated by distilled water after SRP, using a syringe with blunted needle located in the area of the bottom of the pocket</p> <p>One month later: Clinical examination (PI, GI, PPD, CAL)</p> <p>Three month later: Clinical examination (PI, GI, PPD, CAL)</p>

2. Clinical periodontal examination

All participants underwent a full-mouth periodontal examination at the baseline before periodontal therapy and after one month of scaling and root planing (SRP) and three months later including clinical periodontal parameters:

2.1. Plaque index (PI): Measurement the thickness of plaque according to plaque index PI (Silness and Loe, 1964); the plaque index was performed by using periodontal probe and measure the amount of plaque on all teeth for four surfaces, mid labial (buccal), disto labial(buccal), mesio labial(buccal) and mid lingual(palatal) surfaces and given a score from 0-3.2

2.2 Gingival index (GI): The extent and severity of gingival inflammation was measured according to (Loe and Silness, 1963), inspection by naked eyes and by gentle probing throughout using graduated periodontal probe (UNC-15 probe) for four gingival surfaces of all examined teeth; mid labial (buccal), disto labial(buccal), mesio labial(buccal) and mid lingual (palatal) surfaces, and giving a score from 0-3.

3-Probing pocket depth (PPD): the distance from the free gingival margin to the base of the pocket and clinically normal gingival sulcus in human is 2-3mm. Pocket probing depth was assessed by insert calibrated periodontal probe (UNC-15 probe) from gingival margin to the base of pocket at four surfaces of each tooth see figure 2.5, no pressure was used and the probe was allowed to fall by its own weight (Lindhe et al., 2008). The examination was done by three reading for the labial/buccal site (mesiobuccal, mid buccal, distobuccal) and one reading for the lingual/palatal site(mid-palatal). Then these reading was re-evaluated after one month of non-surgical periodontal therapy (scaling and root planing).

4. Clinical attachment loss (CAL): the distance from the free gingival margin to the cemento-enamel junction and the distance from the free gingival margin to the bottom of the gingival sulcus are measured in millimeters with a periodontal probe. If the free gingival margin is on the cementum, its distance from the cemento-enamel junction is recorded as a negative number.

Slight (mild) periodontitis: Periodontal destruction is generally considered slight when no more than 1 to 2mm of clinical attachment loss has occurred.

Moderate periodontitis: Periodontal destruction is generally considered moderate when 3 to 4 mm of clinical attachment loss has occurred.

Severe periodontitis: Periodontal destruction is considered severe when 5 mm or more of clinical attachment loss has occurred (Ramfjord.,1959).

3. Scaling and root playning

Scaling and root planing (SRP) were performed for each patient after periodontal clinical parameters examination by using an ultrasonic device, (Acteon,Satelec,France) and hand instrument (universal and gracy curette). SRP was carried out until the root surface was felt smooth with the tip of a metallic probe (Newman et al., 2012), then the teeth were polished with rubber cup.

RESULTS

The changes in clinical parameters throughout the study period for CAL, PPD, GI

and PI for the first group of patients that treated with SRP and CHX Perio-chips and the second that were treated with SRP and CHX- solution are shown in Table 1 and Table 2 respectively.

At one month, both two groups showed improvement in periodontal conditions as revealed by significant reductions of PPD, GI and PI gain ($P < 0. 05$).

After three months visit, changes were observed between the two groups. However, at that time, the change in CAL gain was not significant in the first group, while in the second group, the reduction was significant. While PPD, PI and GI all showed significant reduction in both groups ($P < 0. 05$) (Table 1 and Table 2).

As shown in Table three, the higher reduction and better improvement in the periodontal condition was observed in the group treated with CHX solution.

Independent t-test was performed for statistical analyses, the result showed that, there were significant difference between the two agents over the three months period in relation to CAL, PI and GI ($P < 0. 05$). However, there were no significant differences in PPD reduction gain in between the two agents ($P > 0. 05$) Table 3.

Table (1): Comparison of clinical parameters of chronic periodontitis among time period for CHX Periochips agent

Dependent Variable	(I) Time	(J) Time	Mean Difference (I-J)	Std. Error	P-value
CAL	Baseline	1 Month	0.74	0.69	0.86
		3 Months	0.91	0.69	0.58
	1 Month	3 Months	0.17	0.68	1.00
PPD	Baseline	1 Month	1.46 [*]	0.38	0.00
		3 Months	1.62 [*]	0.38	0.00
	1 Month	3 Months	0.17	0.37	1.00
GI	Baseline	1 Month	0.73 [*]	0.12	0.00
		3 Months	1.07 [*]	0.12	0.00
	1 Month	3 Months	0.34 [*]	0.12	0.02
PI	Baseline	1 Month	0.53 [*]	0.11	0.00
		3 Months	0.77 [*]	0.11	0.00
	1 Month	3 Months	0.25	0.10	0.07

Table (2): Comparison of clinical parameters of chronic periodontitis among *time period for CHX solution agent

Dependent Variable	(I) Time	(J) Time	Mean	Std. Error	P-Value
			Difference (I-J)		
CAL	Baseline	1 Month	1.33*	0.50	0.03
		3 Months	1.43*	0.50	0.02
	1 Month	3 Months	0.10	0.48	1.00
PPD	Baseline	1 Month	1.51*	0.35	<0.001
		3 Months	1.58*	0.35	0.00
	1 Month	3 Months	0.07	0.34	1.00
GI	Baseline	1 Month	0.77*	0.12	<0.001
		3 Months	0.98*	0.12	<0.001
	1 Month	3 Months	0.22	0.11	0.19
PI	Baseline	1 Month	0.25*	0.08	0.02
		3 Months	0.51*	0.08	<0.001
	1 Month	3 Months	0.27*	0.07	<0.001

Table 3: Comparison of clinical parameters of chronic periodontitis between CHX Periochips and Solution agents

Clinical Indicators	Agents		P-value
	CHX Periochips	CHX Solution	
	Mean \pm SD	Mean \pm SD	
CAL	5.08 \pm 1.86	4.27 \pm 1.44	0.02
PPD	4.31 \pm 1.23	4.16 \pm 1.17	0.56
GI	0.99 \pm 0.55	0.77 \pm .52	0.05
PI	0.75 \pm 0.42	0.55 \pm .27	0.01

Independent t-test was performed for statistical analyses.

DISCUSSION

Chronic periodontitis is an infectious disease resulting in inflammation within the supporting tissues of the teeth, progressive attachment loss, and bone loss, and is characterized by periodontal pocket formation and/or recession of the gingiva. The inflammatory periodontal diseases are widely accepted as being caused by bacteria associated with dental plaque (Vandana and Prakash .,2011)

Antimicrobials have been used as an adjunct with mechanical debridement in the management of periodontal infection. For the effective treatment, antimicrobial agent must reach the depth of the periodontal pocket and

produce gingival crevicular fluid concentration more than the Minimum Inhibitory Concentration of the suspected periodontal microbes (Kaplsh et al.,2013).

Perio-chips

PI scores reflect the oral hygiene status of the patient. In the present study the Ramfjord plaque index scores from baseline to one month and three months was taken into consideration. There was a reduction in PI scores, which was statistically significant ($p < 0.05$). These results are in agree with the results showed in studies conducted by (Soaskolne et al.,1997), (Jeffcoat et al.,1998), (Heasman et al.,2001). This reduction in the scores can be attributed to SRP

as well as adherence to oral hygiene instructions.

GI scores were reduced significantly from baseline till three months which were statistically highly significant the results are in agreement with the findings observed by (Soskolne et al.,1997), (Jeffcoat et al.,1998), (Heasman et al.,2001). This reduction in the scores can also be attributed to SRP as well as good education and motivation of the patient.

The result of the study showed that the use of CHX chip as an adjunct to SRP have led to significant decrease in PPD in comparison to SRP alone. This additional effect of CHX was observed 3 months after the baseline, and this agree with the study of (Soskolne et al.,1997)

The result of the study agree with The studies conducted by (Soskolne et al.,1997), (Jeffcoat et al.,1998), (Grisi et al.,2002) using SRP plus chlorhexidine chip. PPD reduction was greater This could be due to the additional antibacterial effects (cationic molecule binding to extra microbial complexes and negatively charged microbial cell walls altering the osmotic equilibrium), during the healing process of tissues that could have enhanced the effect of SRP (Hanes and Purvis., 2003). It also could bind to salivary bacteria thus interfering with their adsorption to teeth (Newmann et al.,2006)

The result of the study also agree with The study conducted by (Jeffcoat et al.,1998) (Heasman et al.,2001) that showed the PPD reduction was greater in SRP plus chlorhexidine chip. There was a significant reduction in probing pocket depth from baseline to 30 days. However, comparatively the reduction in probing depth from 30 days to 3 months was not as significant.

The result of the study disagree with study of (Rodriguez et al.,2007) came to different results. The authors did not find a significant improvement in PPD values after application of chlorhexidine chip when compared to SRP alone. In a study carried out by Rodriguez et al., biofilm was not removed prior to the placing of CHX chip. The complex structure of the biofilm prevents the diffusion of antimicrobial agents and protects its residents from internal and external influences (Walker et al.,2004) Removal or disruption of biofilm prior to the application of local antimicrobial agent leads to its greater efficiency against subgingival

microorganisms, which may explain the results different from ours.

The result of the study agree with (Carvalho et al.,2007) in which the study failed to observe CAL improvement after application sub gingivally chlorhexidine chips in comparison with scaling and root planing. The study has also reiterated the fact that time limitation may have affected the quality of root planing

The result disagrees when compared with pretreatment values, which is consistent with the findings of other researchers (Grisi et al.,2002), (Carvalho et al.,2007), (Rodrigues et al.,2007), (Paolantonio et al.,2008), showed Statistically significant improvement in CAL after application of CHX chip as an adjunct to SRP

CHX solution

The result of our study showed significant difference in GI ($p < 0.05$) and agree with the study of (Gottumukkala et al) showed significant difference in the effectiveness of multiple subgingival irrigation of periodontal pockets by 0.2% CHX gluconate and saline. One month and three months after the therapy, BI values were significantly decreased after both irrigation with CHX and saline. CHX group showed statistically significant decrease in BI values ($p < 0.01$) one month after the start of treatment compared to the group with saline. This reduction in BI values can be attributed to SRP as well as adherence to oral hygiene instructions.

The result of our study showed significant difference in GI ($p < 0.05$) and agree with the study of (Davies et al., 1954, Emisilon., 1977). It was shown that chlorhexidine can reduce the adherence of *Porphyromonas gingivalis* to epithelial cells. This effect is probably due to the binding of chlorhexidine to the bacterial outer membrane and therefore it could have similar results on the adherence of other plaque bacteria (Grenier., 1996). A study conducted on chlorhexidine for its "Substantivity" shown that chlorhexidine was associated with its ability to maintain effective concentrations for prolonged period of time and this prolongation of its action made it especially suitable for the inhibition of plaque formation (Bonsevoll et al., 1974).

The result of the study agree with the study of (Krishna et al.,2011) found similar improvements in CAL value after irrigation of periodontal pockets with both chlorhexidine and saline.

The result of the study also agree with the study of (MacAlpine et al.,1985) which is in accordance with the results of our study found similar improvements in CAL value after irrigation of periodontal pockets with both chlorhexidine and saline.

The result of the study agree with the study of (Gottumukkala et al.,2013) showed significantly higher reduction in PPD after irrigation of periodontal pockets with CHX gluconate solution over SRP baseline, three and six months after initial measurement.

The result of the study also agree with another study of (Walsh et al.,1992) which performed an irrigation of periodontal pockets with the aid of pulsating irrigator twice a day, for the period of 56 days after SRP, showed a significantly better reduction of PPD in the group that used 0.2% CHX solution as an irrigate over placebo solution.

The result of the study disagree with the study of (Braatz et al.,1985, MacAlpine et al.,1985) did not find statistically significant difference between groups of periodontal pockets irrigated by CHX solution as an adjunct to SRP and SRP alone

The result of the study also disagree with those, results obtained in the study conducted by (MacAlpine et al.,1985) did not confirm the benefit of periodontal pockets irrigation with CHX solution over saline, after SRP. Analyzing the results, authors did not find statistically significant difference in PPD values between observed groups, this explained to the large flow of gingival fluid that prevents the retention of chlorhexidine solution in the area of periodontal pocket and presents one of the limiting factors for the efficiency of the solution in the subgingival environment, affinity of CHX for serum proteins (R olla et al.,1970, Hjeljord et al.,1973).

CONCLUSION

Chlohexidine solution has higher impact on the treatment of patients with chronic periodontitis over CHX periochips, in relation to PPD, CAL, PI and GI variable measurments.

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