Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(1), 230-236 | ISSN:2251-6727

Comparative Analysis of C-Reactive Protein Levels: Evaluating the Impact of 0.12% And 0.2% Chlorhexidine Mouthrinses in Non-Surgical Periodontal Therapy

[1]Dr. Padam Singh, [2]Dr. Vikram Bali,

[1] PhD scholar Professor Department Of Periodontolgy & Oral Implantology, Desh Bhagat University, Mandi, Gonindgarh.Punjab

[2]Professor & Head, Deptt Of Periodontolgy & Oral Implantology, Desh Bhagat University, Mandi, Gonindgarh.

Corresponding Author

Dr. Padam Singh

PhD scholar Professor Department of Periodontolgy & Oral Implantology, Desh Bhagat University, Mandi, Gonindgarh.punjab

(Received: 27 October 2023 Revised: 22 November 2023 Accepted: 26 December 2023)

KEYWORDS

inflammation,mouthrinse,Plaque,parameters.

ABSTRACT:

Background: C-reactive protein (CRP) serves as an inflammation indicator naturally found in plasma, with levels that can elevate in response to inflammatory activities. This increase is linked to an elevated risk of cardiovascular events, such as acute myocardial infarction. The immune-inflammatory response triggered by periodontal disease plays a role in elucidating its connection with cardiovascular issues.

Methods: For the proposed study, a total of thirty participants were selected and randomly assigned to three groups: the Control group, Test group A, and Test group B. In Test group A, consisting of 10 patients, plaque control was implemented using chlorhexidine 0.12% mouthrinse as a supplementary measure after one month of non-surgical periodontal therapy (NSPT). Follow-up assessments were conducted at baseline, 1 month, and 2 months. Similarly, Test group B, also comprising 10 patients, underwent plaque control with chlorhexidine 0.2% mouthrinse following one month of NSPT, with evaluations conducted at the same intervals. This design allows for a comparative analysis of the effectiveness of different chlorhexidine concentrations as adjuncts to NSPT in managing periodontal health.

Results: The study assessed mean percentage reductions in Plaque Index (PI) across three groups. In Group A (n=10), reductions were 12.86 ± 1.10 (0-1 month), 6.75 ± 0.97 (1-2 months), and 20.64 ± 2.01 (0-2 months). Group B (n=10) showed reductions of 12.41 ± 1.10, 7.27 ± 1.40, and 20.94 ± 2.38 for the same intervals. The Control Group's (n=10) reductions were 13.08 ± 1.70, 6.40 ± 0.88, and 21.10 ± 2.22. These results highlight intervention variances, providing insights into Plaque Index changes over the study periods.

Conclusion: Significantly greater improvement in clinical parameters was observed with the use of 0.12% and 0.2% chlorhexidine mouthrinses compared to non-surgical periodontal therapy alone.

INTRODUCTION:

Periodontitis, a condition characterized by the infectious assault on the periodontium, arises from the activity of specific microorganisms, leading to the progressive degradation of the supportive structures surrounding teeth.[1] The pivotal trigger for this cascade is the accumulation of plaque, setting off a complex host response. Within the realm of periodontal infections, a reservoir is established for Gram-negative anaerobic organisms, lipopolysaccharides, and inflammatory mediators, whose repercussions extend far beyond the confines of the periodontal tissues.The acute phase of inflammation introduces marked alterations, notably an escalation in the concentration of specific blood proteins. These proteins, detectable at baseline, serve as invaluable diagnostic indicators,

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(1), 230-236 | ISSN:2251-6727

providing insight into the presence and extent of infectious and inflammatory processes.[2] The acute phase response, characterized by a distinctive pattern of changes in plasma protein concentrations, unfolds in the wake of various forms of inflammation. These acute phase proteins, inherent in humans at baseline, exhibit a capacity to surge during instances of tissue trauma or infectious events, such as sepsis. Notably, these responses wield a dual influence, manifesting as both pro-inflammatory and anti-inflammatory effects.Beyond the confines of periodontal tissues, the implications of this intricate interplay extend to systemic health.[3] Periodontitis, in particular, has been implicated in connections with various systemic diseases, including cardiovascular diseases, cerebrovascular ischemia, and respiratory conditions. However, the precise mechanisms underpinning these associations remain shrouded in complexity and warrant further exploration. The intricate interplay between periodontitis, the acute phase response, and systemic health underscores the need for a comprehensive understanding of the multifaceted dynamics at play in the realm of periodontal and systemic health.[4]The compelling association between periodontitis and coronary artery disease (CAD) is substantiated by a network of inflammatory factors, among which C-reactive protein (CRP) emerges as a pivotal player in elucidating the intricate interplay between these two health conditions. CRP, classified as an acute-phase reactant, is synthesized in response to a diverse array of inflammatory stimuli, including but not limited to heat, trauma, infection, and hypoxia. This multifaceted protein serves as a valuable biomarker, offering crucial insights into the diagnosis, monitoring, and therapeutic management of inflammatory processes and associated diseases.One distinctive feature of CRP is its rapid response kinetics. Following acute tissue damage, CRP levels escalate in serum or plasma within a remarkably short timeframe, typically within 24 to 48 hours.[5,6] During the acute stage of inflammation, CRP concentrations can surge dramatically, sometimes reaching levels as high as a thousand-fold. This surge, a hallmark of the acute-phase response, provides clinicians with a dynamic marker to gauge the intensity of the inflammatory process. Importantly, as inflammation or trauma subsides, CRP levels follow suit, diminishing with the resolution of the underlying condition.CRP's significant role in the innate immune response is underscored by its extended plasma half-life, ranging from 12 to 18 hours. This characteristic makes CRP easily measurable, further enhancing its utility as a clinical marker. In individuals without underlying health issues, CRP is typically present in trace amounts, maintaining levels below 0.3 mg/l. However, in the presence of a severe systemic infection, CRP levels can surge dramatically, exceeding 100 mg/l. This substantial elevation serves as a crucial indicator, allowing healthcare professionals to track the progression and severity of the infection.The versatility of CRP as a marker extends beyond infectious diseases, finding relevance in conditions characterized by inflammatory components, such as periodontitis and CAD. Its responsiveness, dynamic nature, and ease of measurement make CRP an invaluable tool for clinicians seeking to understand, monitor, and manage inflammatory processes, offering a nuanced perspective on the intricate relationship between oral health and systemic well-being.[7]Chlorhexidine (CHX) has found widespread use in both medical and dental applications, and its positive adjunctive effects in conjunction with routine mechanical plaque control have been well-established through both short-term and long-term clinical trials. The chlorhexidine gluconate product, maintaining a near-neutral pH range of 5-7, is a salt comprising chlorhexidine and gluconic acid. Notably, two commonly used concentrations of CHX are available: 0.2% CHX, administered in a 10 ml volume, and 0.12% CHX, administered in a 15 ml volume. The rationale behind the variance in concentration is to mitigate potential side effects while preserving comparable efficacy. It is noteworthy that, despite the differing concentrations, the total amount of CHX is approximately equivalent, with 10 ml of 0.2% CHX containing 20 mg and 15 ml of 0.12% CHX containing 18 mg per volume.[8,9]Following successful non-surgical periodontal therapy (NSPT) coupled with diligent mechanical and chemical plaque control by the patient, a significant reduction in bacterial load is achieved. While destructive periodontal diseases are treatable, some studies suggest that effectively managing these conditions may lead to a decrease in C-reactive protein (CRP) values and subsequently reduce the associated risk of atherosclerotic complications.The primary aim of this study is not only to reconfirm the impact of NSPT on CRP reduction levels, thereby mitigating or eliminating periodontal inflammation, but also to explore the influence of different concentrations of CHX mouthrinses (0.12% and 0.2%) when used as adjuncts to NSPT. This investigation aims to assess their effects on clinical and hematological parameters, specifically CRP, in patients suffering from generalized chronic periodontitis. By delving into the nuanced relationship between CHX, NSPT, and CRP levels, the study seeks to contribute valuable insights into optimizing therapeutic strategies for managing periodontal health and potentially mitigating systemic risks associated with inflammatory processes.

MATERIALS AND METHODS:

In this proposed study, a total of thirty patients were meticulously selected for participation. The subjects

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(1), 230-236 | ISSN:2251-6727

were then randomly assigned to three distinct groups: the Control group, Test group A, and Test group B.Test group A, consisting of 10 patients, underwent a specific treatment regimen where plaque control was implemented using chlorhexidine 0.12% mouthrinse. This intervention was introduced as an adjunct after one month of non-surgical periodontal therapy (NSPT). Follow-up assessments were conducted at key intervals, including baseline, 1 month, and 2 months, enabling a comprehensive evaluation of the treatment's effectiveness over time.Similarly, Test group B, comprising another 10 patients, followed a slightly different protocol. In this case, plaque control was executed using chlorhexidine 0.2% mouthrinse as an adjunct, also introduced after 1 month of non-surgical periodontal therapy (NSPT). Subsequent follow-up evaluations took place at baseline, 1 month, and 2 months, offering insights into the comparative effectiveness of different chlorhexidine concentrations when used in conjunction with NSPT.This meticulous grouping and systematic follow-up structure not only facilitate a robust comparison of treatment outcomes but also contribute valuable data to the understanding of the impact of varying chlorhexidine concentrations on plaque control and periodontal health after non-surgical periodontal therapy.The inclusion criteria for this study encompass a specific demographic, targeting individuals between the ages of 30 and 50 years. A diagnosis of chronic generalized periodontitis is a key prerequisite, ensuring that participants exhibit the specified periodontal condition under investigation. Furthermore, the inclusion criteria specify certain clinical parameters, including a probing depth of at least 4mm and clinical attachment loss of 5mm or more. Radiographic evidence demonstrating horizontal bone loss is also deemed essential for inclusion. Additionally, a crucial aspect involves patients being cooperative and willing to adhere to prescribed oral hygiene instructions, fostering compliance with the proposed treatment plan.Conversely, the exclusion criteria serve to refine the participant selection process by excluding individuals with systemic diseases or those undergoing medication and treatment that could potentially influence the healing process, with diabetes serving as an exemplar regardless of its control status. Pregnancy is also considered an exclusion criterion due to the hormonal changes associated with this condition that may impact periodontal health. Furthermore, smokers are excluded from participation, acknowledging the well-established adverse effects of smoking on periodontal tissues. By delineating these inclusion and exclusion criteria, the study aims to create a cohort that is not only representative of the target population but also controlled to isolate the specific factors under investigation.

Methodology

a. **General Measurement Techniques:** Employing proper techniques is crucial to minimize the impact of instrument variables, stray light, and air bubbles. Turbidity measurements are conducted promptly to prevent alterations due to temperature changes, particle flocculation, or sedimentation. In cases where flocculation is observed, aggregates are broken up through agitation. Dilution is avoided whenever feasible, as particles in the original sample may undergo changes when exposed to temperature variations or dilution. Prior to measurement, air or other entrained gases are removed from the sample.

b. **Nephelometer Calibration:** Adhering to the manufacturer's operating instructions, calibration of the nephelometer is a meticulous process. At least one standard is run in each instrument range to ensure stability in all sensitivity ranges. The reliability of the nephelometer is verified through stable readings.

c. **Measurement of Turbidity:** The sample is gently agitated, and measurement is conducted once air bubbles dissipate. Well-mixed samples are preferred, and in some cases, an ultrasonic bath or vacuum degassing is applied to release all bubbles. Turbidity readings are obtained directly from the instrument display.

d. **Calibration of Continuous Turbidity Monitors:** For low turbidities, continuous turbidity monitors are calibrated by determining the turbidity of the outflowing water. This is achieved using a laboratory-model nephelometer or by following the manufacturer's instructions, utilizing formazin primary standard or an appropriate secondary standard. Calibration ensures accurate and reliable monitoring of turbidity levels over time.

RESULTS:

TABLE - 1A :Mean % reduction of PI in all the three group

Duration (month)	Mean % reduction of PI		
	Group A (0.12%)	Group B (0.2%)	Control
0 – 1	12.86±1.10	12.41±1.10	13.08±1.70
1 – 2	6.75±0.97	7.27±1.40	6.4±0.88
0 – 2	20.64±2.01	20.94±2.38	21.1±2.27

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(1), 230-236 | ISSN:2251-6727

The table illustrates the mean percentage reduction of plaque index (PI) over distinct time intervals (0-1 months, 1-2 months, and 0-2 months) for three distinct groups: Group A (0.12%), Group B (0.2%), and the Control group. In the initial month (0-1), both Group A and Group B demonstrated notable reductions, with Group A achieving 12.86% ± 1.10 and Group B showing 12.41% ± 1.10, while the Control group achieved a slightly higher reduction of 13.08% ± 1.70. Over the subsequent month (1-2), Group A exhibited a reduction of 6.75% ± 0.97, Group B showed 7.27% ± 1.40, and the Control group demonstrated a reduction of 6.40% ± 0.88. Over the cumulative duration of 0-2 months, Group A and Group B displayed similar reductions at 20.64% ± 2.01 and 20.94% ± 2.38, respectively, while the Control group maintained a reduction of 21.10% ± 2.27.These findings suggest comparable efficacy between the two treatment groups and the Control group in terms of plaque reduction. The data emphasizes the potential effectiveness of the interventions (0.12% and 0.2% formulations) in managing plaque accumulation over a two-month period. Understanding these trends is crucial for dental professionals and researchers in optimizing oral health strategies and tailoring interventions for effective plaque control.

TABLE - 1B : Percentage Difference in PI

	GROUP	N	Mean % reduction	Std. Deviation	Sig. (2-tailed)
Percentage Difference in PI from 0 to 1 month	0.12%	10	12.86	1.1	0.372
	0.20%	10	12.41	1.1	
Percentage Difference in PI from 0 to 2 month	0.12%	10	20.64	2.01	0.759
	0.20%	10	20.94	2.38	
Percentage Difference in PI from 1 to 2 month	0.12%	10	6.75	0.97	0.071
	0.20%	10	7.27	1.4	
Percentage Difference in PI from 0 to 1 month	0.20%	10	12.41	1.1	0.307
	Control	10	13.08	1.7	
Percentage Difference in PI from 0 to 2 month	0.20%	10	20.94	2.38	0.885
	Control	10	21.1	2.27	
Percentage Difference in PI from 1 to 2 month	0.20%	10	7.27	1.4	0.114
	Control	10	6.4	0.88	
Percentage Difference in PI from 0 to 1 month	0.12%	10	12.86	1.1	0.734
	Control	10	13.08	1.7	
Percentage Difference in PI from 0 to 2 month	0.12%	10	20.64	2.01	0.637
	Control	10	21.1	2.27	
Percentage Difference in PI from 1 to 2 month	0.12%	10	6.24	0.97	0.698
	Control	10	6.4	0.88	

Table2:Percentage reduction in CRP

Duration (month)	Mean%reductionofCRP		
	GroupA(0.12%)	Group B(0.2 %)	Control
0–1	4.00±3.78	-0.15±18.08	11.02±11.09
1–2	19.99±19.92	29.23±39.25	-4.68+30.01
0–2	18.67±17.52	18.88±35.16	-3.90+41.22

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(1), 230-236 | ISSN:2251-6727

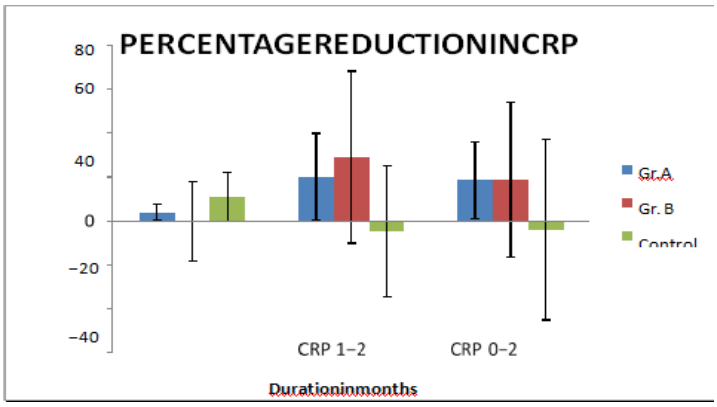

Figure1:Percentage reduction in CRP

DISCUSSION:

Periodontal disease emerges as a widespread infectious condition in humans, characterized by the inflammatory degradation of connective tissues within the periodontium—the supporting structures of the teeth.[10] This inflammatory response goes beyond local consequences, leading to both tissue damage and the resorption of bone. However, its impact extends significantly to the systemic level, presenting a formidable challenge attributable to the adverse effects triggered by microorganisms and their byproducts.The consequences of periodontal disease are multifaceted.[11] Firstly, there is a notable increase in procoagulant activity, contributing to the potential for abnormal blood clotting. Concurrently, there is a decrease in fibrinolysis, the process that dissolves blood clots, which further complicates the overall circulatory dynamics. The heightened adhesion of leukocytes, or white blood cells, exacerbates the inflammatory response and contributes to the progression of the disease.The impact on the cardiovascular system is particularly noteworthy. The inflammation induced by periodontal disease has implications for cardiovascular health, as it fosters conditions conducive to the deposition of lipids, such as low-density lipoprotein (LDL) and cholesterol, within arterial walls. This, in turn, poses a risk for atherosclerosis—a condition characterized by the narrowing and hardening of arteries.At a molecular level, the release of bacterial lipopolysaccharides and peptidoglycan fragments into the bloodstream prompts an increase in the production of inflammatory cytokines. These signaling molecules, including prostaglandin E2, tumor necrosis factor alpha, and interleukin-1β, play pivotal roles in the inflammatory cascade, further amplifying the systemic repercussions of periodontal disease.Moreover, the body's acute phase response is activated, leading to an elevation in acute phase reactants such as C-reactive protein (CRP), fibrinogen, alpha-1 antitrypsin, and beta-2 macroglobulin. These markers are indicative of the body's acute inflammatory reaction to the ongoing infection.In some instances, an increase in leukocyte count and the formation of the factor VIII-von Willebrand's factors complex are observed.[12] These changes underscore the systemic impact of periodontal disease, implicating not only the oral cavity but also intertwining with broader physiological processes, particularly those associated with inflammation, coagulation, and cardiovascular health.Understanding these intricate connections between periodontal disease and systemic manifestations underscores the importance of comprehensive oral health care not only for the preservation of dental structures but also for the overall well-being of the individual.The study conducted with Test groups A and B revealed a statistically significant reduction in C-reactive protein (CRP) values, demonstrating a potential link between periodontal treatment and systemic inflammation. Test groups A and B exhibited decreased CRP values (19.99 ± 19.92 and 29.23 ± 39.25, respectively) compared to the control group (-4.68 ± 30.01) over a 1–2 month duration. Although Test group B showed a slightly higher reduction in CRP compared to Test group A, this difference was not statistically significant.The investigation aligns with existing evidence proposing that periodontal disease may act as a trigger for systemic inflammation, leading to elevated levels of systemic inflammatory markers.[13] The study highlights the higher plasma levels of CRP in patients with periodontal disease compared to periodontally healthy subjects. Furthermore, the reduction in CRP levels following periodontal treatment supports the concept that periodontitis contributes to the overall inflammatory burden throughout the body. The findings also reinforce the hypothesis that controlling local inflammation can lead to a reduction in the systemic acute-phase response.In a study by Bokhari et al (2009), mechanical therapy resulted in a significant reduction in circulating levels of CRP, fibrinogen, and white blood cell (WBC) counts one month after

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(1), 230-236 | ISSN:2251-6727

treatment. CRP, a sensitive marker for systemic inflammation and a predictor of coronary artery events, exhibited a consistent decrease after periodontal treatment, in line with other studies.Similarly, F. D. Aiuto et al reported a significant decrease in serum CRP in otherwise healthy individuals affected by severe, generalized periodontitis following periodontal treatment. The reduction in CRP levels was particularly significant in subjects who responded well to the therapy.[14,15]A study by Andrea M et al reinforced these findings, indicating that periodontal therapy led to a significant decrease in various clinical parameters. The data for high-sensitivity CRP (hs-CRP) showed a significant decrease in values after periodontal therapy, with a greater than 50% reduction in hs-CRP concentrations in the periodontal disease group three months after treatment.In summary, the study contributes valuable insights into the potential systemic impact of periodontal disease and the positive effects of periodontal therapy on reducing inflammatory markers, particularly CRP. These findings underscore the interconnectedness of oral health and systemic well-being.The study involving Test groups A and B investigated changes in oral health indicators over a 1-2 month interval, comparing them with a control group. While there was a slightly higher reduction in plaque index (PI) in Test groups A and B compared to the control group, the difference was not statistically significant. However, both Test groups A and B demonstrated a statistically significant reduction in gingival index (GI) at 1-2 months, indicating an improvement in gingival health.Specifically, Test group B exhibited a slightly higher reduction in GI compared to Test group A, although the difference did not reach statistical significance.[16] Additionally, Test group B showed a significant reduction in GI at 0-2 months compared to the control group. Despite a slightly higher reduction in pocket depth (PD) and clinical attachment level (CAL) in Test groups A and B at 1-2 months compared to the control group, these differences were not statistically significant.The study also references a definitive study by Löe and Schiøtt, which demonstrated the efficacy of a 0.2% chlorhexidine (CHX) mouthrinse in inhibiting plaque regrowth and gingivitis development when used twice daily for 60 seconds. The mouthrinse in the current study was formulated at a concentration of 0.12% CHX with a 15 ml rinse volume, maintaining the effective 20 mg dose present in the 0.2% rinses. The study suggests that concentrations of 0.12% CHX can be as effective as 0.2% when the volume of the rinse is increased.Moreover, the study highlights the importance of determining an optimum dose of CHX delivered by mouthrinse, balancing efficacy against potential local side effects. This balance is generally considered to be around 20 mg twice daily.In summary, while there were observable improvements in various oral health parameters in Test groups A and B compared to the control group, some differences were not statistically significant. The study also emphasizes the efficacy of CHX mouthrinse and the importance of optimizing the dose to achieve the desired balance between effectiveness and safety.

CONCLUSION:

The study's dual focus on chlorhexidine mouthrinse concentrations (0.12% and 0.2%) as adjuncts to non-surgical periodontal therapy (NSPT) illuminates noteworthy insights. Firstly, the investigation discerns no substantial disparity in efficacy between the two chlorhexidine concentrations concerning the reduction of key clinical parameters—plaque index (PI), gingival index (GI), pocket depth (PD), and clinical attachment level (CAL). Both concentrations exhibit comparable effectiveness in fostering improvements across these indices. Secondly, the study unveils a compelling narrative of heightened improvement when chlorhexidine mouthrinses are integrated with NSPT, surpassing outcomes achieved solely through non-surgical periodontal therapy. This not only underscores the proven efficacy of NSPT in reducing C-reactive protein (CRP) levels by mitigating periodontal inflammation but also accentuates the supplementary benefits derived from the concurrent use of chlorhexidine mouthrinses. The observed uniformity in clinical and hematological effectiveness between 0.12% and 0.2% chlorhexidine mouthrinses underscores their interchangeable utility. As the study provides a foundation for future investigations, its outcomes signal a compelling direction for larger-scale intervention trials, encouraging a deeper exploration of chlorhexidine mouthrinse's impact on CRP levels within the context of generalized chronic periodontitis and non-surgical periodontal therapy.

REFERENCES:

1. Marcaccini AM, Meschiari CA, Sorgi CA, Saraiva MCP, De Souza AM, Faccioli LH, Tanus-Santos JE, Novaes AB, and Gerlach RF. Circulating Interleukin-6 and High-Sensitivity C-Reactive Protein Decrease After Periodontal Therapy in Otherwise Healthy Subjects. J Periodontol 2009; 80:594-602.
2. Shimada Y, Komatsu Y, Ikezawa-Suzuki I, Tai H, Sugita N and Yoshie H. The effect of periodontal treatment on serum leptin, interleukin-6, and C-reactiveprotein. DOI: 10.1902/jop.2010.090741.
3. Solis C, Santos A, Nart N, Violant D. 0.2% chlorhexidine mouthwash with an antidiscoloration system versus 0.2% chlorhexidine mouthwash: a prospectiveclinical comparative study. J periodontal 2011; 82:80-85.
4. Pietruska M1, Paniczko A, Waszkiel D, Pietruski J, Bernaczyk A. Efficacy of localtreatment with chlorhexidine gluconate drugs on the clinical status of

periodontium in chronic periodontitis patients. Advances in Medical Sciences ·Vol.51 · 2006 · Suppl. 1.

5. Chew B, Cheng WL, Tay S and Fei YJ. Comparison of Two Commercially Available Mouth Rinses on Gingival Inflammation, Pain and Acceptability after Third Molar Surgery. Singapore Dent J 2007;29(1):34–40.
6. M.P.C. Van Leeuwen, D.E. Slot, and G.A. Van der Weijden. Essential Oils Compared to Chlorhexidine with Respect to Plaque and Parameters of Gingival Inflammation: A Systematic Review. J Periodontol 2011; 82:174- 194.
7. Neto CAF, Parolo CCF, Rösing CK, Marisa Maltz. Comparative analysis of the effect of two chlorhexidine mouthrinses on plaque accumulation and gingivalbleeding. Braz Oral Res 2008;22(2):139-44.
8. Bernstein D, Schiff G, Echler G, Prince A, Feller M and Briner W. In vitro Virucidal Effectiveness of a 0.12%-Chlorhexidine Gluconate Mouthrinse. J DENT RES 1990; 69; 874.
9. Borrajo JLL, L. Varela LG, Castro GL. Efficacy of Chlorhexidine Mouthrinses with and Without Alcohal: A Clinical Study. J Periodontol 2002; 73:313-321.
10. Porras R, Anderson GB, Caffesse R. Clinical Response to 2 Different Therapeutic regimens to Treat Peri-Implant Mucositis. J Periodontol 2002; 73:1118-1125.
11. Gu¨rgan CA, Bakirsoy EZ, and Soykan E. Short-Term Side Effects of 0.2% Alcohol-Free Chlorhexidine Mouthrinse Used as an Adjunct to Non- Surgical Periodontal Treatment: A Double-Blind Clinical Study. JPeriodontol 2006; 77:370- 384.
12. Saria E, Birincib I. Microbiological Evaluation of 0.2% Chlorhexidine Gluconate Mouth Rinse in Orthodontic Patients. Angle Orthodontist, Vol 77, No 5, 2007.
13. Zanatta FB, Antoniazzi RP, and Ro¨sing CK. The Effect of 0.12% Chlorhexidine Gluconate Rinsing on Previously Plaque-Free and Plaque- Covered Surfaces: A Randomized, Controlled Clinical Trial. J Periodontol 2007; 78:2127-2134.
14. Paraskevas S, Rosema NAM, Versteeg P, Van der Velden P, and G.A. Van der Weijden. Chlorine Dioxide and Chlorhexidine Mouthrinses Compared in a 3-Day Plaque Accumulation Model. J Periodontol 2008; 79:1395-1400.
15. Yévenes I, Alvarez SR, Jara MN, Wolfenson PM, Smith LP. Comparison of mouthrinses containing chlorhexidine and other active agents with chlorhexidine mouthrinse-gel: effects on de novo plaque formation. Rev. odontociênc. 2009;24(4):345-348.
16. Drisko CH. Nonsurgical periodontal therapy. Periodontology 2000, Vol. 25,2001, 77– 88