

Comparative Evaluation of Effectiveness of Hyaluronic Acid and Chlorobutanol Along With 0.20% Chlorhexidine as a Subgingival Irrigation Following Periodontal Flap Surgery- A Split Mouth Study

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Abstract

Introduction: There are various pharmacologic agents widely used in dentistry with different purpose and in different form. (e.g., mouthwashes, gels and varnishes). Literature has stored scientific evidence that these agents are used as an adjuvant for various dental treatments applied in dentists to improve therapeutic response. Both chlorhexidine and hyaluronic acid has its own unique properties and has been advocated as monotherapy or as an adjunct to non-surgical and surgical periodontal treatment.

Aim and Objective: To compare and evaluate the effectiveness in terms of pain perception and soft tissue healing in patients treated with Hyaluronic acid and Chlorobutanol along with 0.20% Chlorhexidine (Curasept) as a subgingival irrigation following periodontal flap surgery.

Materials And Methods: A total of 5 patients within the age group of 20-50 years diagnosed with stage II/III with grade B or C periodontitis with probing pocket depth ≥ 5 mm were randomly selected and divided into 2 groups: Group 1- 5 Patients assigned with surgical periodontal therapy along with subgingival irrigation with Curasept (0.20% chlorhexidine and chlorobutanol) as soothing treatment on the day of surgery and Curasept (0.20% chlorhexidine and hyaluronic acid) as regenerative treatment on 3rd day of surgery Group 2- 5 Patients were assigned with surgical periodontal therapy alone. All the patients were evaluated for clinical parameters such as Plaque Index, Bleeding on Probing and Probing Pocket Depth at baseline and after 3 months. Numeric rating Scale for pain perception was also analysed at 3 days and after 7days.

Results: Both the groups revealed a statistically significant difference with meaningful reduction from baseline to 3 months when comparing intragroup clinical measures (PI, GI, and BOP). On Intergroup comparison of all the clinical parameters there was a statistically non-significant difference in between group 1 and group 2.

Conclusion: The result obtained from the study showed that subgingival irrigation with chlorobutanol and hyaluronic acid with 0.20% chlorhexidine positively influence the soft tissue healing and post operative pain after periodontal surgery. Curaspet can be used as an adjunctive treatment for improvement in wound healing process and reduction in post-operative pain. P

Keywords: Hyaluronic Acid, Chlorobutanol, Chlorhexidine, Subgingival Irrigation, Periodontal Flap Surgery

1. Introduction

Periodontitis is an inflammatory disease resulting from the complex interaction between subgingival biofilm and host immune inflammatory process that may involve the periodontal attachment apparatus. Progression of periodontitis caused by gram negative anaerobic microflora leads to soft tissue destruction and loss of alveolar bone. The aetiology of periodontal disease is multifactorial especially periodontal pathogens play an important role in the initiation and progression of disease process. The success rate of periodontal therapy depends upon environmental and behavioural factors along with the reduction or elimination of periodontal pathogens [1].

The effectiveness of periodontal treatment may be evaluated by its ability to control either by reduction or elimination of periodontal pathogens [2]. Mechanical therapies that include scaling root planing (Phase I therapy) and periodontal surgery (Phase II therapy) are aimed to improve the clinical conditions by lowering microbial load either by physical removal of plaque or by radical alteration of the sub gingival habitat. Antimicrobial approaches, including the use of systemically and locally administered antibiotics, application of pharmaceutical agents sub gingivally in the form of local drug delivery agents or irrigation with antimicrobial agents directly targeted subgingival species residing in the plaque biofilm or in the adjacent epithelial tissues lining the periodontal pocket [3]. Various chemotherapeutic agents can be used as an adjunct to mechanical therapy to eradicate the sub gingival microbes and thereby creating a healthy sub gingival environment. Anti-bacterial agents such as chlorhexidine, metronidazole, tetracyclines and povidone iodine have been attempted for their usage in the past years and proven to be effective as sub gingival irrigating agents in the management of shallow periodontal pockets [4, 5]. There are number of antimicrobials and biomaterials with less known and less used at present and at the same time have the potential to augment the results of periodontal therapy.

Chlorhexidine is a cationic bis-biguanide broad spectrum antimicrobial agent which reduces dental biofilm penetration. It has a proteolytic activity for certain periodontal pathogens and antioxidative activity for inhibition of superoxide anion generation in white blood cells. It also scavenges nitrogen-chlorine oxidants which degrade the sulphhydryl groups associated with endogenous autoactivation of neutrophil collagenase. Based on the concentration it may be bactericidal or bacteriostatic. Chlorhexidine is a gold standard broad antimicrobial agent with several advantages as an irrigating agent such as low systemic toxicity to humans, no reported resistance among oral microflora and lack of teratogenic effects [6]. However, its long-term use may cause an issue such as mucosal desquamation, tooth staining and altered taste sensation.

Recently, a new biomolecule hyaluronic acid (HA) has a clinical application to facilitate soft tissue healing, and regeneration of bone, surgical wounds and periodontal tissue. It also has an anti-inflammatory and anti-bacterial effect in periodontitis therapy. It has functions like cell proliferation,

recognition and locomotion that contributes to its tissue healing properties. Hyaluronic acid contains hyaluronan as a scavenger by draining prostaglandins, metalloproteinases and other bio active molecules [7]. Hyaluronan also regulate the inflammatory response, acting as an antioxidant by scavenging ROS. Thus, hyaluronan may help to stabilize the granulation tissue matrix [8]. Low molecular weight HA has a marked angiogenic effect whereas higher molecular weight has the opposite effect. It has been proposed that an accelerated wound healing in the bone matrix will occur due to stimulation of angiogenesis by HA [9]. Hyaluronan always seems to surround proliferating and migrating cells in repair, remodelling and healing tissues [10]. Hyaluronan is further involved in the activation of inflammatory cells, such as polymorphonuclear leukocytes and macrophage functions, including their migration to the wound site, adherence at the wound site, phagocytosis and killing of invading microbial pathogens in order to counteract the colonization and proliferation of anaerobic pathogenic bacteria in the gingival crevice and adjacent periodontal tissues.

HA has been investigated as a drug delivery agent through topical route or through sub gingival irrigation. It exhibits the property of bio-adhesion resulting in increased bioavailability in mucosa owing to its viscoelastic property. As a result, it retains the drug at the site of action/absorption or to modify the in vivo release/absorption rate of the therapeutic agent it is used with [11]. Hyaluronic acid has an extensive action in various periodontal therapies such as topical application in subgingival regions resulting in reduction of microbial activity, bone regeneration in deep periodontal bony defects, and nonsurgical treatment of peri implantitis pockets. HA is biocompatible and intrinsically safe to use, with no evidence of cytotoxicity. The data available in the literature for subgingival irrigation with hyaluronic acid and chlorobutanol with 0.20% Chlorhexidine following periodontal flap surgery is very scant.

Therefore, the study was conducted with an aim and objective to compare and evaluate the effectiveness in terms of pain perception and soft tissue healing in patients treated with Hyaluronic acid and Chlorobutanol along with 0.20% Chlorhexidine (Curasept) as a subgingival irrigation following periodontal flap surgery.

2. Material and Methods

2.1. Study Population

For the proposed study, a total of 5 patients within the age group of 20-50 years diagnosed with stage II/III with grade B or C periodontitis with probing pocket depth $\geq$ 5mm were randomly selected from the outpatient department of Periodontics and Oral Implantology. An ethical approval for the study was obtained from the Institutional Ethical Board Committee and a detailed verbal and written consent was taken from each of the patient.

Patients were randomly selected and divided into 2 groups: Group 1- 5 Patients assigned with surgical periodontal therapy along with subgingival irrigation with Curasept (0.20% chlorhexidine and chlorobutanol) as soothing treatment on the day of surgery and Curasept (0.20%

chlorhexidine and hyaluronic acid) as regenerative treatment on 3rd day of surgery and
Group 2- 5 Patients were assigned with surgical periodontal therapy alone.

2.2. Inclusion Criteria

- Patients between the age group of 20-50 years.
- Patients were diagnosed with stage II/III with grade B or C periodontitis with probing pocket depth ≥ 5 mm
- Patients of both genders and were having minimum of 20 teeth present.
- Absence of any systemic illness.
- Patients who had not received any kind of periodontal treatment in the last 6 months.

2.3. Exclusion Criteria

- Pregnant or lactating females.
- Patients suffering from known systemic disease.

- Patients with known allergy to hyaluronic acid
- Any surgical or non- surgical therapy 6 months before the start of the study.
- Antibiotic therapy in last 6 months.
- Chemotherapeutic mouth rinses past 6 months.
- Habits- smoking, tobacco and pan chewing.
- Patient undergone periodontal plastic surgery in the selected area in the last 1year

2.4. Methodology

2.5. Clinical Procedure

The surgical procedure was carried out in all the patients under local anaesthesia of 2% lignocaine hydrochloride with 1:80,000 adrenaline.

Group 1- Surgical Periodontal Therapy Along with Subgingival Irrigation with Curasept as Soothing Treatment and as Regenerative Treatment



Figure 1: At Baseline



Figure 2: Subgingival Irrigation with Curasept as Soothing Treatment on The Same Day of Periodontal Surgery



Figure 3: Subgingival Irrigation with Curasept as Regenerative Treatment on 3rd Day of Periodontal Surgery

**Figure 4: After 3 Months**

Conventional periodontal flap was performed in all the patients. A full thickness muco-periosteal flap was reflected with crevicular incision followed by blunt elevation with periosteal elevator. The root surface was thoroughly scaled and planned. This was followed by osseous re-contouring if needed, removal of unhealthy granulation tissue and removal of specks of calculus. Flap closure was done by 3.0 silk suture by means of direct loop suture. This was followed by sub

gingival irrigation with Curasept (0.20% chlorhexidine and chlorobutanol) as soothing treatment on the day of surgery. A periodontal dressing was placed and left for seven days. Patient was recalled after 3rd day of the surgery for sub gingival irrigation with Curasept (0.20% chlorhexidine and hyaluronic acid) as regenerative treatment.

Group 2- Surgical Periodontal Therapy Alone

**Figure 5: At Baseline****Figure 6: After 3 Months**

A full thickness muco-periosteal flap was reflected with crevicular incision followed by blunt elevation with periosteal elevator. The root surface was thoroughly scaled and planned. This was followed by osseous re-contouring if needed, removal of unhealthy granulation tissue and removal of specks of calculus. Flap closure was done by 3.0 silk suture

by means of direct loop suture. A periodontal dressing was placed and left for seven days. Post-operative instructions were given regarding oral hygiene maintenance and warm saline gargles were given to all the patients. Antibiotic amoxycillin 500mg three times a day and analgesic Ibuprofen 550mg were prescribed for 5 days.

2.5. Assessment of Clinical Parameters

Clinical parameters included the assessment of probing pocket depth (PPD), Plaque index (PI). Bleeding on Probing (BOP) were measured at baseline and after 3 months. Numeric Rating Scale (NRS) for pain perception was also analysed after 3 days and after 7 days.

2.6. Statistical Analysis

The parameters were tabulated and put to statistical analysis.

The data for the present study was entered in the and analyzed using the SPSS statistical software 23.0 Version. The descriptive statistics included mean and standard deviation. The level of the significance for the present study was fixed at 5%. The intergroup comparison for the difference of mean scores between independent groups was done using unpaired/ independent t test.

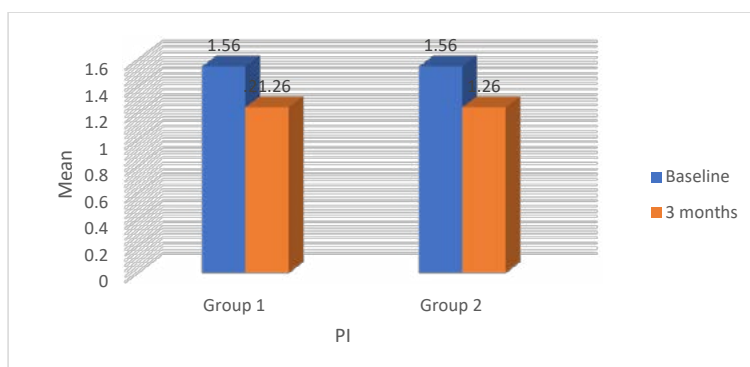
3. Results

	PLAQUE INDEX (Mean $\pm$ SD)		BLEEDING ON PROBING (Mean $\pm$ SD)		PROBING POCKET DEPTH (Mean $\pm$ SD)	
	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2
BASELINE	1.56 $\pm$ 0.36	1.56 $\pm$ 0.36	1.87 $\pm$ 0.59	1.15 $\pm$ 0.26	4.80 $\pm$ 0.76	4.70 $\pm$ 0.76
AFTER 3 MONTHS	1.26 $\pm$ 0.31	1.26 $\pm$ 0.31	1.90 $\pm$ 0.66	1.32 $\pm$ 0.32	2.00 $\pm$ 1.00	2.60 $\pm$ 0.55
P value	0.09**	0.09**	0.02*	0.06**	0.01*	0.02*
*P value <0.05 (statistically significant)						
**P value >0.05 (non-statistically significant)						

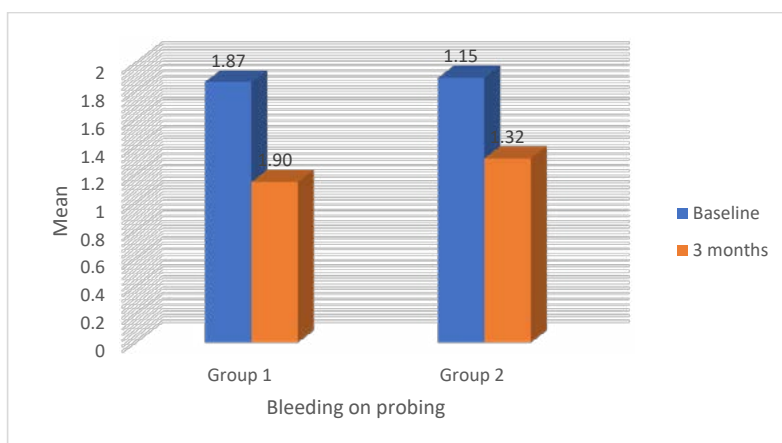
Table 1: Intragroup Comparison of all Clinical Parameters at Various Time Interval

The intragroup comparison of probing pocket depth between the time intervals i.e. at Baseline and after 3 months was statistically significant for both groups i.e. Group 1 (Surgical periodontal therapy along with subgingival irrigation) and Group 2 (Surgical periodontal therapy alone). However,

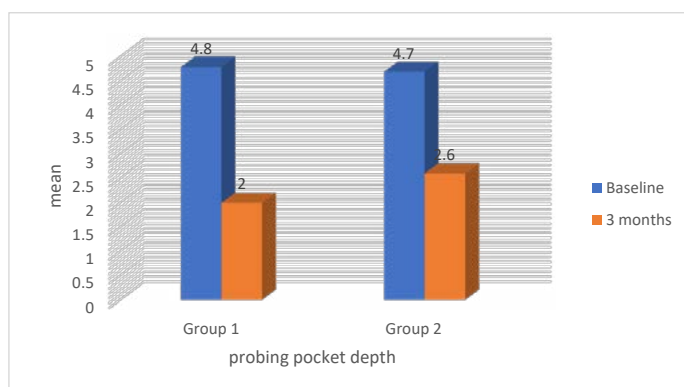
Plaque Index was found to statistically non-significant for both groups. The intragroup comparison of Bleeding on probing in group 1 was found to statistically significant and for group 2 it was found to statistically non-significant at time interval i.e. baseline and after 3 months.



Graph 1: Intragroup Comparison of Plaque Index at Baseline and After 3 Months



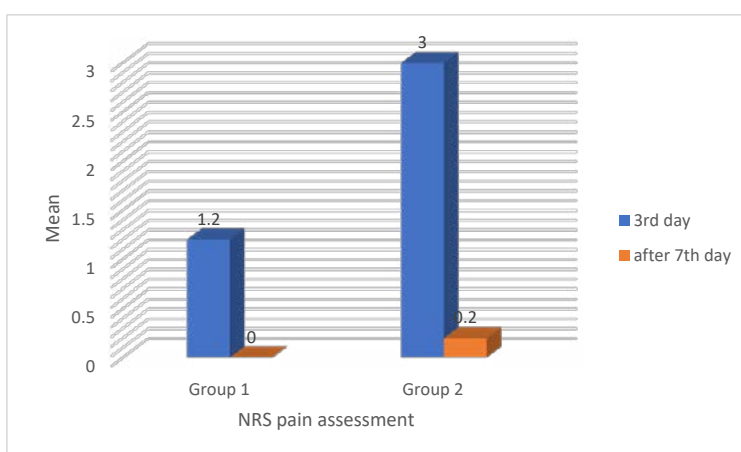
Graph 2: Intragroup Comparison of Bleeding on Probing at Baseline and After 3 Months



Graph 3: Intragroup Comparison of Probing Pocket Depth at Baseline and After 3 months

	NUMERIC RATING SCALE (NRS) (Mean ± SD)	
	Group 1	Group 2
AFTER 3 DAYS	1.2±1.30	3±1.58
AFTER 7 DAYS	0.00±0.00	0.2±0.44
P value	0.109	0.009
*P value <0.05 (statistically significant)		
*P value >0.05 (non-statistically significant)		

Table 2: Intragroup comparison of Numeric Rating Scale (NRS) for pain perception



Graph 4: Intragroup Comparison of Numeric Rating Scale (NRS) for Pain Perception After 3 Days and After 7 Days

The intragroup comparison of the Numeric Rating Scale (NRS) for pain perception between the time intervals after 3 days and after 7 days was statistically non-significant for Group 1 (Surgical periodontal therapy along with subgingival irrigation) and was statistically significant for Group 2 (Surgical periodontal therapy alone).

	PLAQUE INDEX (Mean ± SD)		BLEEDING PROBING (Mean ± SD)		PROBING POCKET DEPTH (Mean ± SD)	
	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2
BASELINE	1.56±0.36	1.56±0.36	1.86±0.59	1.90±0.66	4.80±0.76	1.56±0.36
AFTER 3 MONTHS	1.56±0.36	1.56±0.36	1.15±0.26	1.32±0.32	2.60±1.00	2.60±0.55
P value	1.00	1.00	0.934	0.38	0.84	0.27
*P value >0.05 (non-statistically significant)						

Table 3: Intergroup Comparison of all Clinical Parameters at Various Time Interval

The intergroup comparison of the plaque Index, bleeding on probing and probing pocket depth between the time intervals i.e. at Baseline and after 3 months was found to

be statistically non-significant for both groups i.e. Group 1 (Surgical periodontal therapy along with subgingival irrigation) and Group 2 (Surgical periodontal therapy alone).

	NUMERIC RATING SCALE (NRS) (Mean $\pm$ SD)	
	Group 1	Group 2
AFTER 3 DAYS	1.20 $\pm$ 1.30	3.00 $\pm$ 1.58
AFTER 7 DAYS	0.00 $\pm$ 0.00	0.20 $\pm$ 0.44
P value	0.085	0.347
*P value >0.05 (non-statistically significant)		

Table 4: Intergroup Comparison of Numeric Rating Scale (NRS) for Pain Perception

The intergroup comparison of the Numeric Rating Scale (NRS) for pain perception between the time intervals after 3 days and after 7 days was statistically non-significant for both the groups i.e., Group 1 (Surgical periodontal therapy along with subgingival irrigation) and Group 2 (Surgical periodontal therapy alone).

4. Discussion

Patient with stage II/III with grade B or C periodontitis are generally treated by phase II therapy (surgical therapy) with an aim to arrest the inflammatory disease process through removal of subgingival biofilm and to establish a local environment as well as microflora which is consistent with periodontal health. The primary outcome of periodontal surgical therapy is satisfactory healing and regeneration of the periodontal tissue. Treatment of periodontal disease is based on the root debridement, adjunctive use of antimicrobials in the form of local drug delivery agents or sub gingival irrigation, oral hygiene maintenance of the results which are obtained after the treatment. Sub gingival irrigation with chemotherapeutic agent when delivered as an adjunct to surgical therapy may be beneficial as treatment modality. Sub gingival irrigation allows the individual to actively engage in self-therapy specifically at the problem site and also potentially have a direct effect on the reduction of microflora.

Several studies in the literature indicated that sub gingival irrigation with anti-microbial agents have beneficial outcome and improvement in periodontal health as compared to placebo. Some studies are in the favour of placebo with equivalent and similar results. American Academy of Periodontology published the guidelines for subgingival irrigants, according to which the subgingival irrigants must have:

- A noticeable and long-lasting effect on the composition of the subgingival plaque.
- A speculative and sustained effect on the clinical parameters of periodontitis.
- An improved effect on periodontitis than SRP alone.
- In addition to these all the subgingival irrigants used and the techniques used to deliver them must be safe [12].

Subgingival irrigation has a nonspecific action of flushing the periodontal pocket and can effectively alter the quality and

quantity of subgingival plaque associated with periodontitis. the commonly used irrigants are normal saline, hydrogen peroxide, povidone iodine, ozonised water, chlorhexidine, metronidazole, tetracycline and Hyaluronic acid. In the present study, Curasept was used for subgingival irrigation. Curasept have the formulation of 0.20% chlorhexidine and chlorobutanol and Hyaluronic acid. Professionally subgingival irrigation with 1% or 2% chlorhexidine during root debridement have shown to reduce the number of P. gingivalis more as compared to scaling and root planning alone.

In the present study Hyaluronic acid with combination of chlorhexidine was used for subgingival irrigation. Hyaluronic acid contains hyaluronan which decreases prostaglandin types and inflammatory processes, moreover, it improves collagen disposition, causing better tissue healing and reparation [13]. It participates in the process of tissue repair and healing. It has a marked angiogenic property which in turn helps in proliferation of mesenchymal cells. It may be speculated that the biological and physiological nature has contributed to the significant results in the study. In the present study the subgingival irrigation of chlorobutanol and Hyaluronic acid was done immediately after the periodontal flap surgery and after the 3rd day of intervention. The subgingival irrigation with chlorobutanol was done for soothing treatment and with Hyaluronic acid was done for regenerative treatment.

Plaque Index provides an assessment of plaque thickness on gingival third which represent the inflammatory status of gingiva that can be used to compare gingival status at recall visits. Intergroup comparison for both the group 1 and group 2 showed statistically non-significant at baseline and after 3 months of time interval. However, Intragroup comparison of plaque index score was reduced after 3 months from the baseline. This indicating that root debridement during periodontal flap surgery results in significant reduction in clinical signs of inflammation and reduction in microbial load with their endotoxins. There is a reduced severity of inflammatory infiltrate in the periodontal soft tissues, providing a beneficial environment for diseased gingival tissues to heal.

Bleeding on probing provides an objective and an easily reproducible assessment of gingival status. It is useful for detection of an early inflammatory changes and presence of inflammatory lesions located at the base of the periodontal pocket. When compared to baseline, a statistically significant reduction in Bleeding on probing scores were observed in group 1 as compared to group 2 from baseline to 3 months. The improvement is possibly due to the beneficial effects of periodontal surgical therapy along with subgingival irrigation of hyaluronic acid. Hyaluronic acid enhanced the formation of extracellular connective tissue matrix resulting in non-inflamed and healthy periodontal tissue that is less susceptible to bleeding on probing. The results of the study were in accordance with other studies who investigated the application of hyaluronic acid. Investigated the hyaluronic acid with anti-inflammatory and anti-edematous properties and found a similar reduction in papillary and sulcus bleeding index score [14,15].

Periodontal pockets are characteristic sign of periodontal disease and therefore attain critical status in diagnosis of periodontitis. When compared from baseline to 3 months a statistically significant reduction in probing pocket depth was observed at both group 1 and group 2. No statistically significant differences were observed in PPD values between group 1 and group 2 at baseline and after 3 months' time interval. Conducted a systematic review, which demonstrated that HA offers beneficial effects in pocket depth reduction, CAL gain and reduction in bleeding on probing during both surgical and non-surgical periodontal therapy [16]. evaluated the effect of local application of hyaluronan gel in conjunction with periodontal surgery. The adjunctive application of HA yielded statistically significantly higher clinical improvement evidenced by PD reduction and CAL gain compared with open flap debridement alone which suggests that HA has an added beneficial effect when used as an adjunct to periodontal surgery [17].

Pain perception was also recorded based on Numeric rating Scale. It measures the pain intensity on a scale from 0 to 10 representing "No pain" to "Worst possible pain". On intergroup comparison Numeric Rating Scale (NRS) for pain perception between the time intervals after 3 days and after 7 days was statistically non-significant for both the groups. i.e., Group 1 (Surgical periodontal therapy along with subgingival irrigation) and Group 2 (Surgical periodontal therapy alone). An improvement in reduction of pain may increase the postoperative comfort of the patients. Chlorbutanol have an analgesic and sedative effects along with the antiseptic action of the chlorhexidine might be responsible for pain reduction when used as a sub gingival irrigation. Chlorbutanol has been used therapeutically as a mild sedative and local analgesics.

There were very scant data and studies in the literature which supported the positive result or significant improvement in terms of clinical parameters. Within the limitation of study in terms of very short sample size and limited follow up time period that is 3 months is the major and important limitation to reach at significant conclusion. Since this study has shown

a positive result in terms of clinical parameters further research needed to be carried out on large sample size. To prove the efficacy and positive outcome of subgingival irrigation of Curasept with 0.20% chlorhexidine and chlorobutanol as soothing treatment and hyaluronic acid as regenerative treatment following periodontal flap surgery, further research needs to be carried out on large sample size. Also, histological and microbiological evaluation needed to check the use of Curasept as a sub gingival irrigation agent in surgical and non-surgical therapy.

5. Conclusion

Within the limitation of present study, it can be concluded that the adjunctive use of subgingival irrigation of Curasept with 0.20% chlorhexidine and chlorobutanol as soothing treatment and hyaluronic acid as regenerative treatment following periodontal flap surgery provided a favourable result in terms of clinical parameters. It has a positive influence on the soft tissue healing and post operative pain reduction after periodontal flap surgery. There is a paucity of data in the literature indicating insufficient evidence for the routine use of subgingival irrigation as adjunct to periodontal treatment. Histological evaluation is also needed to investigate the effect of hyaluronic acid on soft tissue healing. Future studies are required to evaluate long term effects of subgingival irrigation agents when used as an adjunct to surgical and non-surgical periodontal therapy.

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