

Comparative Clinical Evaluation of Chlorhexidine and Hyaluronic Acid Gel in the Management of Plaque-Induced Gingivitis

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Abstract

Background: Gingivitis is a reversible inflammatory disease primarily caused by dental plaque. Chlorhexidine is considered the gold standard antiplaque agent, its prolonged use is associated with adverse effects. Hyaluronic acid has recently emerged as a promising adjunct because of its anti-inflammatory and wound-healing properties.

Aim: To compare the clinical efficacy of hyaluronic acid gel and chlorhexidine gluconate gel in the treatment of chronic generalized gingivitis.

Materials and Methods: Sixty patients with chronic generalized gingivitis were randomly allocated into two groups. Following scaling and polishing, Group I received Gingicare® (0.3% hyaluronic acid gel) and Group II received Hexigel® (1% chlorhexidine gluconate gel) twice daily for four weeks. Plaque Index (PI), Gingival Index (GI) and bleeding on Probing (BOP) were

recorded at baseline, 2, 4, and 8 weeks. Data was analyzed using repeated measures ANOVA and independent t-test ($p < 0.05$).

Results: Both groups demonstrated significant improvement in PI, GI, and BOP throughout the study ($p < 0.001$). However, the Gingicare group showed significantly greater reductions in gingival inflammation and bleeding than the Hexigel group at 4 and 8 weeks ($p < 0.05$), with fewer adverse effects.

Conclusion: Hyaluronic acid gel was more effective than chlorhexidine gel as an adjunct to mechanical plaque control in the management of chronic generalized gingivitis.

Keywords: Gingivitis, Hyaluronic Acid, Chlorhexidine Gel, Gingicare, Hexigel, Periodontal Therapy.

Introduction

Gingivitis is a reversible inflammatory condition of the gingival tissues initiated primarily by the accumulation of

microbial dental plaque at the gingival margin. It is characterized clinically by gingival erythema, edema, bleeding on probing, and tenderness without loss of periodontal attachment. Despite its reversible nature, persistent untreated gingivitis may progress to periodontitis in susceptible individuals, ultimately resulting in irreversible destruction of periodontal supporting tissues and tooth loss. Therefore, early diagnosis and effective management of gingivitis remain essential components of preventive periodontal care.^{1,2} Mechanical plaque control through tooth brushing, interdental cleaning, and professional scaling remains the cornerstone of gingivitis management. However, inadequate patient compliance and limited accessibility of oral hygiene measures often result in incomplete plaque removal, necessitating the use of adjunctive chemotherapeutic agents. Topical antimicrobial gels have gained considerable attention because they provide prolonged contact with gingival tissues while minimizing systemic exposure and adverse effects associated with systemic medications.³ Chlorhexidine gluconate has long been regarded as the gold standard antiplaque and antigingivitis agent because of its broad-spectrum antimicrobial activity and high substantivity. It effectively inhibits plaque formation by disrupting bacterial cell membranes and reducing bacterial colonization on tooth surfaces. Numerous clinical studies have demonstrated significant reductions in plaque accumulation and gingival inflammation following topical chlorhexidine therapy. Nevertheless, prolonged use is frequently associated with undesirable side effects including tooth staining, tongue discoloration, taste alteration, mucosal irritation, and increased supragingival calculus formation, which may adversely affect patient compliance.^{4,5} Hyaluronic acid (HA) is a naturally occurring, high-molecular-weight glycosaminoglycan

that constitutes a major component of the extracellular matrix of connective tissues. It plays a pivotal role in tissue hydration, cellular migration, angiogenesis, collagen synthesis, and modulation of inflammatory responses. In periodontal tissues, hyaluronic acid contributes to wound healing by regulating leukocyte migration, scavenging reactive oxygen species, promoting fibroblast proliferation, and enhancing epithelial regeneration. These biological properties have stimulated growing interest in its use as an adjunctive therapeutic agent in periodontal therapy.^{6,7} Recent randomized clinical trials and systematic reviews have demonstrated that topical hyaluronic acid significantly reduces gingival inflammation, bleeding on probing, and periodontal tissue edema when used as an adjunct to conventional nonsurgical periodontal therapy. In addition to its anti-inflammatory and wound-healing effects, hyaluronic acid has been shown to exhibit bacteriostatic activity against several periodontal pathogens while maintaining excellent biocompatibility and patient tolerance. Unlike chlorhexidine, hyaluronic acid is not associated with clinically significant tooth staining or taste disturbances, making it an attractive alternative for long-term management of gingival inflammation.^{8,9} Gingicare® (Oradox), containing 0.3% hyaluronic acid gel, has been introduced as a topical oral formulation designed to enhance gingival healing and reduce inflammation. Conversely, Hexigel® (ICPA), containing 1% chlorhexidine gluconate, is one of the most commonly prescribed topical antiseptic gels for plaque-induced gingivitis. Although both agents have independently demonstrated clinical benefits, direct comparative evidence evaluating their relative efficacy in managing plaque-induced gingivitis remains limited. Therefore, the present randomized clinical trial was undertaken to compare the effectiveness of 0.3%

hyaluronic acid gel (Gingicare®) and 1% chlorhexidine gluconate gel (Hexigel®) as adjuncts to professional mechanical plaque control in patients with chronic generalized gingivitis.¹⁰

Materials and Methods

Study Design and Participants

This randomized, parallel-group, single-center clinical trial was conducted at Triveni Institute of Dental Sciences, Bilaspur after obtaining approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants before enrollment. The study included 60 systemically healthy patients aged between 18 and 50 years who were diagnosed with chronic generalized plaque-induced gingivitis according to the 2017 World Workshop Classification of Periodontal Diseases. Patients presenting with generalized gingival inflammation, bleeding on probing, and a Plaque Index (PI) and Gingival Index (GI) score ≥ 1.0 , without clinical attachment loss or radiographic evidence of alveolar bone loss, were included. Patients with periodontitis, systemic diseases affecting periodontal health, smokers or tobacco users, pregnant or lactating women, individuals who had received periodontal therapy or antibiotics within the previous three months, patients with known hypersensitivity to hyaluronic acid or chlorhexidine, and those using anti-inflammatory or immunosuppressive medications were excluded from the study.

Sample Size

A total sample size of 60 participants (30 per group) was considered adequate to detect a clinically significant difference between the two treatment groups with a confidence level of 95% and a study power of 80%.

Randomization and Allocation

Eligible participants were randomly allocated into two equal groups (n = 30 each) using a computer-generated

randomization sequence. Allocation concealment was achieved using sequentially numbered, opaque, sealed envelopes that were opened only after completion of baseline clinical examination and professional oral prophylaxis.

- **Group I (Hyaluronic Acid Group):** Patients received Gingicare® gel containing 0.3% hyaluronic acid.
- **Group II (Chlorhexidine Group):** Patients received Hexigel® containing 1% chlorhexidine gluconate.

Clinical Procedure

At baseline, all participants underwent professional scaling and polishing using ultrasonic scalers and hand instruments to remove plaque and calculus deposits. Standardized oral hygiene instructions, including the Modified Bass brushing technique, were provided to all patients. Following oral prophylaxis, participants were instructed to apply a pea-sized amount of the allocated gel over the gingival margin using a clean finger twice daily (morning and night) after tooth brushing for a period of 8 weeks. Patients were advised not to eat, drink, or rinse for at least 30 minutes following gel application. Compliance was assessed at each recall visit through patient interviews and evaluation of the returned gel tubes.

Clinical Parameters

Clinical examinations were performed by a single calibrated examiner at baseline, 2 weeks, 4 weeks and 8 weeks. The following periodontal parameters were recorded:

- **Plaque Index (PI)** according to Silness and Löe (1964)
- **Gingival Index (GI)** according to Löe and Silness (1963)

- **Bleeding on Probing (BOP)** recorded as the percentage of bleeding sites after gentle periodontal probing.

Any adverse effects, including tooth staining, taste alteration, mucosal irritation, burning sensation, or allergic reactions, were also recorded during each follow-up visit.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics software (Version 31.0; IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean $\pm$ standard deviation (SD). Normality of data distribution was assessed using the Shapiro–Wilk test. Intragroup comparisons over different time intervals were performed using repeated measures analysis of variance (ANOVA) followed by Bonferroni post hoc analysis where appropriate. Intergroup comparisons were carried out using the independent samples t-test. Categorical variables were analyzed using the Chi-square test. A p-value <0.05 was considered statistically significant.

Results

A total of 60 patients diagnosed with chronic generalized plaque-induced gingivitis were enrolled in the study and completed the 8-week follow-up period. There were no dropouts during the study. Baseline demographic characteristics, including age and gender distribution, were comparable between the two groups ($p > 0.05$). Similarly, no statistically significant differences were observed in baseline Plaque Index (PI), Gingival Index (GI), or Bleeding on Probing (BOP) scores between the groups ($p > 0.05$), indicating homogeneity at baseline. Both treatment groups demonstrated significant improvements in all clinical parameters throughout the study period ($p < 0.001$). The mean Plaque Index

decreased progressively from baseline to 2, 4, and 8 weeks in both groups following professional scaling and adjunctive topical gel application. Although both groups exhibited marked plaque reduction, the hyaluronic acid group showed slightly lower PI values than the chlorhexidine group at the 4- and 8-week evaluations; however, the difference was not statistically significant ($p > 0.05$). The Gingival Index showed a significant reduction in both groups at each follow-up visit compared with baseline ($p < 0.001$). At 4 weeks, the mean GI score was significantly lower in the Gingicare® group than in the Hexigel® group ($p < 0.05$). This difference became more pronounced at the 8-week follow-up, suggesting greater resolution of gingival inflammation in patients receiving hyaluronic acid gel. Bleeding on probing also decreased significantly in both groups over time ($p < 0.001$). The reduction was significantly greater in the Gingicare® group at both the 4-week and 8-week evaluations compared with the Hexigel® group ($p < 0.05$), indicating superior control of gingival inflammation and improved periodontal tissue healing. Regarding safety, patients treated with Gingicare® reported excellent tolerance, and no adverse effects were observed throughout the study. In contrast, a few participants in the Hexigel® group reported mild tooth staining and transient taste alteration during the treatment period, although no participant discontinued the study because of these effects. Overall, both topical gels were effective as adjuncts to mechanical plaque control in the management of plaque-induced gingivitis. However, 0.3% hyaluronic acid gel (Gingicare®) produced significantly greater improvements in gingival inflammation and bleeding while demonstrating superior patient tolerance compared with 1% chlorhexidine gluconate gel (Hexigel®).

Table 1: Baseline demographic characteristics

Variable	Gingicare® (n=30)	Hexigel® (n=30)	p-value
Age (years)	32.8 ± 8.1	33.6 ± 7.5	0.71
Male/Female	17/13	16/14	0.79

Table 2: Intergroup comparison of clinical parameters between Gingicare® and Hexigel® groups

Clinical Parameter	Time Interval	Gingicare® (Mean ± SD)	Hexigel® (Mean ± SD)	p-value
Plaque Index (PI)	Baseline	2.10 ± 0.24	2.08 ± 0.22	0.82
	2 Weeks	1.36 ± 0.21	1.41 ± 0.24	0.46
	4 Weeks	0.82 ± 0.16	0.90 ± 0.18	0.08
	8 Weeks	0.54 ± 0.13	0.61 ± 0.15	0.06
Gingival Index (GI)	Baseline	2.01 ± 0.19	2.03 ± 0.18	0.74
	2 Weeks	1.28 ± 0.20	1.36 ± 0.22	0.18
	4 Weeks	0.69 ± 0.15	0.87 ± 0.17	0.02*
	8 Weeks	0.33 ± 0.10	0.52 ± 0.12	0.001*
Bleeding on Probing (BOP %)	Baseline	86.2 ± 6.4	85.7 ± 5.8	0.77
	2 Weeks	54.8 ± 5.2	58.3 ± 5.7	0.09
	4 Weeks	24.5 ± 4.8	33.6 ± 5.1	0.01*
	8 Weeks	10.8 ± 3.6	18.9 ± 4.2	<0.001*

Table 3: Comparison of adverse effects between Gingicare® and Hexigel® groups

Adverse Effect	Gingicare® (n = 30)	Hexigel® (n = 30)	p-value*
Tooth staining	0 (0%)	4 (13.3%)	0.038
Taste alteration	0 (0%)	3 (10.0%)	0.076
Oral mucosal irritation	1 (3.3%)	2 (6.7%)	0.554
Burning sensation	1 (3.3%)	2 (6.7%)	0.554
Allergic reaction	0 (0%)	0 (0%)	—
Discontinuation due to adverse effects	0 (0%)	0 (0%)	—

Discussion

The present randomized clinical trial compared the clinical efficacy of 0.3% hyaluronic acid gel (Gingicare®) and 1% chlorhexidine gluconate gel (Hexigel®) as adjuncts to professional mechanical plaque control in the management of chronic generalized plaque-induced gingivitis. Both treatment modalities produced significant reductions in plaque accumulation, gingival inflammation, and bleeding on probing during the 8-

week follow-up period. However, the hyaluronic acid group demonstrated significantly greater improvement in gingival inflammation and bleeding on probing, together with superior patient tolerance. These findings indicate that hyaluronic acid can serve as an effective host-modulating adjunct in the treatment of plaque-induced gingivitis. Mechanical plaque removal remains the gold standard for the management of gingivitis, but complete plaque control often depends on patient compliance with

oral hygiene measures. Therefore, adjunctive topical agents are frequently recommended to improve clinical outcomes. In the present study, both treatment groups exhibited significant reductions in Plaque Index throughout the study period, confirming that adjunctive topical therapy following scaling and polishing effectively enhances plaque control. Similar improvements have been reported in recent randomized clinical trials evaluating adjunctive periodontal therapies.¹¹ Although both gels effectively reduced plaque accumulation, the hyaluronic acid group demonstrated significantly greater reductions in Gingival Index and bleeding on probing at the 4- and 8-week evaluations. These findings may be explained by the biological properties of hyaluronic acid, which extend beyond its antimicrobial activity. Hyaluronic acid is known to regulate inflammatory cytokines, promote fibroblast proliferation, enhance angiogenesis, facilitate collagen synthesis, and accelerate epithelial regeneration. Collectively, these actions promote faster resolution of gingival inflammation and tissue healing.^{12,13} The findings of the present study are consistent with those of Bertl et al., who demonstrated that repeated local delivery of hyaluronic acid gel significantly improved pocket closure and reduced bleeding on probing in patients receiving supportive periodontal therapy compared with conventional treatment alone. The authors attributed these improvements to enhanced connective tissue healing and prolonged anti-inflammatory activity of hyaluronic acid, observations that closely correspond with the greater reduction in gingival inflammation observed in the present study.¹¹ Similarly, Gündoğdu Ezer and Gunpinar reported that adjunctive application of 0.8% hyaluronic acid gel significantly enhanced both clinical and radiographic healing following minimally invasive nonsurgical treatment of periodontal intrabony

defects. They concluded that hyaluronic acid accelerates periodontal wound healing by stimulating extracellular matrix formation and improving soft tissue regeneration. Although their investigation involved periodontitis rather than gingivitis, the biological mechanisms responsible for enhanced tissue repair support the superior clinical outcomes observed in the present study.¹² Recent investigations have further demonstrated that hyaluronic acid exerts its beneficial effects through modulation of the host inflammatory response. By reducing oxidative stress and suppressing pro-inflammatory mediators while simultaneously promoting fibroblast migration and extracellular matrix remodeling, hyaluronic acid enhances periodontal tissue healing beyond the antimicrobial effects achieved by conventional antiseptics. Consequently, greater reductions in gingival inflammation and bleeding may occur even when plaque reduction is comparable between treatment groups.¹³ Chlorhexidine remains the most widely prescribed topical antiseptic because of its broad-spectrum antimicrobial activity and prolonged substantivity. In the present study, chlorhexidine gel significantly reduced plaque accumulation and gingival inflammation, confirming its established clinical efficacy. However, several patients experienced mild tooth staining and transient taste alteration, findings that are consistent with previous clinical reports evaluating chlorhexidine-containing oral antiseptics. These adverse effects may reduce patient compliance during prolonged use and support the search for safer adjunctive therapies such as hyaluronic acid. An important observation of the present investigation was the excellent safety profile of Gingicare®. None of the participants receiving hyaluronic acid gel reported clinically significant adverse reactions, whereas minor adverse effects were observed in the chlorhexidine group. Recent clinical trials have

similarly reported excellent biocompatibility and patient acceptance of topical hyaluronic acid preparations, making them suitable for repeated or long-term application in periodontal therapy.^{11,12} The present study has certain limitations. The relatively small sample size, single-center design, and short follow-up period limit extrapolation of the findings to larger populations. Furthermore, microbiological assessment and evaluation of inflammatory biomarkers were not performed, preventing detailed investigation of the biological mechanisms underlying the observed clinical improvements. Future multicenter randomized controlled trials with larger sample sizes, longer follow-up periods, and microbiological as well as immunological analyses are recommended to further establish the role of hyaluronic acid in the management of plaque-induced gingivitis.¹³

Conclusion

Within the limitations of the present randomized clinical trial, both 0.3% hyaluronic acid gel (Gingicare®) and 1% chlorhexidine gluconate gel (Hexigel®) were effective adjuncts to professional mechanical plaque control in the management of plaque-induced chronic generalized gingivitis, resulting in significant reductions in plaque accumulation, gingival inflammation and bleeding on probing. However, the hyaluronic acid gel demonstrated superior improvement in gingival health, particularly with respect to reduction in gingival inflammation and bleeding, while exhibiting excellent patient tolerance and an absence of common chlorhexidine-associated adverse effects such as tooth staining and taste alteration. These findings suggest that 0.3% hyaluronic acid gel may serve as a safe and effective alternative to chlorhexidine gel for the adjunctive management of plaque-induced gingivitis. Further multicenter studies with larger sample sizes and longer follow-up periods are recommended to validate

these findings and assess the long-term clinical benefits of hyaluronic acid in periodontal therapy.

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