Original Article

Anti-Inflammatory Effects of 1% Aspirin Gel and Mouthwash on Clinical Parameters and on Salivary PGE_2 Conc. in Periodontal Diseases: A Clinical Study

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ABSTRACT

Objective: The objective of this study was to develop 1% aspirin gel and mouthwash to determine its local effects in patients with periodontal diseases in order to prevent the systemic adverse effects associated with its oral use.

Study Design: Randomized control trial study.

Place and duration of study: This study was conducted at the Department of Pharmacology, University of Karachi and also Crown Dental Clinic, Karachi from July 2015 to December 2015.

Materials and Methods: 40 patients were included and divided into four groups. 1) Control group received no treatment, 2) Standard treatment group received only scaling and root planning.3) Gel treated group,1% gel was applied into the periodontal pocket of patients after scaling and root planning. 4) Mouthwash treated group, 1% mouthwash was given to the patients after scaling and root planning. The clinical parameters and the level of PGE_2 were measured at day 0 and after 30 days of treatment in the all groups. Analysis was done by one way ANOVA followed by Bonferroni test where $p \leq 0.05$ was considered significant.

Results: Both the gel and mouthwash were very effective in reducing the clinical parameters and PGE_2 level as compared to standard and control group. The mouthwash in comparison to gel was more effective in reducing the level of PGE_2.

Conclusion: We concluded from this study that local drug preparations produced significant effects in the treatment of periodontal diseases and can prove an alternate to the systemic treatment.

Key Words: Periodontal diseases, clinical parameters,PGE_2, scaling, root planning.

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INTRODUCTION

The two diseases that usually affects the periodontium are gingivitis and periodontitis. Both these diseases have similar clinical features of inflammation, including erythema, edema, bleeding and enlargement of gingival tissues but in periodontitis there is clinical attachment loss, periodontal pocketing and alveolar bone loss. The most common cause of these diseases is the bacterial plaque and calculus as well as variable microbial pattern [1].

The periodontologist generally treat these diseases by conventional standard treatment which includes scaling and root planning. Sometimes oral drugs in which NSAIDs are usually combined with antibiotics are given in combination with standard treatment. The long term uses of these drugs have been associated with several systemic adverse effects[2].

In periodontal diseases, the level of COX-2 is increased which in turn are responsible for the production of PGE_2 that is associated with inflammation[3].

Aspirin is an analgesic, anti-inflammatory and anti-pyretic agent commonly used in toothache and other inflammatory diseases of oral cavity[4].In the stomach and intestine PGE_2 and$PGF_{2-\alpha}$ stimulate the synthesis of protective mucosal barrier. Aspirin decreases gastric acid and mucous secretion which may cause epigastric distress, ulceration, hemorrhage, and iron-deficiency anemia[5, 6].

New researches are now focusing to treat the periodontal diseases locally rather than systemically in order to avoid the adverse effects associated with the systemic administration. Although it is a time consuming procedure and required proficiency but the advantages of local delivery system are that less dose is required for the treatment and the possibility of emergence of resistant microorganisms is decreased.

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The drug is also maintained at the site of action for a longer period of time at appropriate levels[7].

The aim of this study was to develop and compare the local formulation of 1% aspirin gel and mouthwash with standard treatment in patients with gingivitis and periodontitis to prevent the systemic adverse effects associated with its oral use. The clinical parameters and the level of PGE_2were also measured before and at the end of 30 days treatment. In this study we also compared the efficacy of 1% aspirin gel with 1% aspirin mouthwash.

MATERIALS AND METHODS

Acetylsalicylic acid (Aspirin) from Kaizen Pharmaceutical (Pvt) Limited, Karachi was used. The other chemicals were obtained from Nigheban Pharmacy, Karachi for the preparation of 1% aspirin gel and mouthwash.

Preparation of 1% aspirin gel Acetylsalicylic acid was dissolved in between 80 on basic magnetic stirring hot plate (IKA Works Inc.) between 100°C to 150°C with continuous stirring until a clear solution was obtained[8].Then this clear solution was added to 2% carboxy-methylcellulose gel containing methylparaben sodium, propylparaben sodium and EDTA at room temperature with continuous stirring to prevent lump formation. Triethanolamine was finally added to adjust the pH of the solution[9].Gel was then evaluated for its physicochemical properties.

Preparation of 1% aspirin mouthwash: Aspirin was dissolved in parts in propylene glycol with the help of mechanical stirrer at 500 RPM for30 minutes. Then sodium benzoate was added as a preservative, and glycerin as a sweetener. Finally, triethanolamine was added to adjust the pH of the solution. After the mouthwash preparation it was evaluated for its physicochemical properties.

Procedure including the application of intra-crevicular gel and mouthwash

Subjects participated in the study: 40 patients were included in this study. The complete clinical procedure was explained to each patient and consent was also signed from each patient before starting the procedure.

History taking and clinical examination: After taking history the patients were examined with dental examination instruments. The clinical parameters were measured when the patient was sitting on a dental chair by using WHO (CPITN) probe.

Inclusion criteria:

- Patients more than 20 years of age
- Patients of gingivitis and periodontitis with history of no systemic disease

Exclusion criteria:

- Patients on medicines since six months
- Patients with any known systemic disease
- Patients receiving any periodontal treatment since 2 years
- Pregnant women
- Lactating mothers

The patients were divided in to four groups

- Group 1: Control group received no treatment
- Group 2: Standard treatment group
- Group 3: Gel treated group
- Group 4: Mouthwash treated group

Sample collection and estimation of PGE_2 : The saliva samples of the patients were collected in sterilized vials at day 0 and after 30 days. The samples were collected in the morning between 11-12 am to prevent changes in antioxidants. The sample vials were coded and immediately centrifuged at 12,000 g for 10 minutes. The clear supernatant centrifuged fluid was shifted to -20°C refrigerator. The clear fluid was used to measure the level ofPGE_2at day 0 and at day 30 in patients by using enzyme-linked immunosorbent assay (Glory Science Co., Ltd, USA) kits[10].

Intra-crevicular gel application and estimation of clinical parameters: In gel treated group the gel was applied into the periodontal pocket of the patients by using 25 gauge syringe having blunted needle after drying the quadrant using air jet[11].

Probing depth: The measurement of probing depth was done using WHO probe also called as CPITN probe. In each tooth six sites were probed[11, 12].

Attachment level (CAL): The measurements were done using the WHO probe. In each tooth six sites were probed[11, 12].

Tooth mobility: Horizontaltooth mobility andvertical tooth mobility was measured [11, 12].

Bleeding on probing: Bleeding on probing was determined by probing gently along the wall of the gingival tissue of the sulcus [11, 12].

Plaque index: Four surfaces of tooth were examinedfor plaque index [11, 12].

Gingival index: Four surfaces of tooth were examinedfor gingival index [11, 12].

Statistical analysis: Data was analyzed by using SPSS 21using one way ANOVA. Post-hoc analysis using Bonferroni test was used for comparison among the groups. The p-value of ≤ 0.05 was considered significant.

RESULTS

Table 1a and 1b indicates that 1% aspirin gel and mouthwash showed highly significant reduction in all clinical parameters ($p\leq 0.001$) except tooth mobility as compared to standard and control group after 30 days. The standard treatment also showed reduction in bleeding ($p\leq 0.001$) as compared to control group. 1% aspirin mouthwash highly reduced the bleeding and plaque index ($p\leq 0.001$) as compared to 1% gel whereas 1% aspirin gel highly reduced the gingival index ($p\leq 0.001$) as compared to 1% mouthwash after 30 days.

Table 2 indicates that the level of PGE_2 was highly reduced by 1% aspirin gel and mouthwash($p\leq 0.001$) as

compared to standard and control after 30 days. 1% mouthwash showed highly significant reduction in PGE_2 level after 30 days as compared to 1% gel.

Table No. 1a: Clinical parameters after administration of 1% Aspirin Gel and 1% Aspirin Mouthwash

Groups	Periodontal Pocket Depth		Attachment Level		Bleeding on Probing	
	Day 0	Day 30	Day 0	Day 30	Day 0	Day 30
Control Group	3.69 ± 1.08	3.91 ± 0.83	3.96 ± 0.81	3.97 ± 0.81	1.00 ± 0.25	0.90 ± 0.32
Standard Group	3.90 ± 0.83	3.77 ± 0.95	3.79 ± 0.55	3.57 ± 1.00	0.90 ± 0.32	0.54 ± 0.25***
1% Aspirin Gel	3.89 ± 0.78	2.40 ± 0.84***###	4.28 ± 0.96	2.75 ± 1.00***###	1.00 ± 0.00	0.12 ± .14***###
1% Aspirin Mouthwash	3.87 ± 0.92	2.57 ± 1.12***###	4.07 ± 0.91	2.82 ± 1.17***###	0.98 ± 0.05	0.07 ± 0.12***###+++

n=10. Data is presented as Mean ± SD.
*** p≤ 0.001= highly significant with control group.
p≤ 0.001= highly significant with standard group.
+++ p≤ 0.001= highly significant between aspirin gel v/s aspirin mouthwash.

Table No. 1b: Clinical parameters after administration of 1% Aspirin Gel and 1% Aspirin Mouthwash

Groups	Tooth Mobility		Plaque Index		Gingival Index	
	Day 0	Day 30	Day 0	Day 30	Day 0	Day 30
Control Group	0.60 ± 0.70	0.80 ± 0.53	2.66 ± 0.21	2.67 ± 0.76	2.45 ± 0.36	2.47 ± 0.35
Standard Group	0.70 ± 0.67	0.70 ± 0.67	2.64 ± 0.18	2.31 ± 0.15	2.63 ± 0.37	1.89 ± 0.77
1% Aspirin Gel	0.60 ± 0.70	0.50 ± 0.53	2.79 ± 0.20	0.3[illegible] ± 0.29***###	2.60 ± 0.33	0.27 ± 0.08***###+++
1% Aspirin Mouthwash	0.60 ± 0.70	0.50 ± 0.53	2.57 ± 0.14	0.22 ± 0.17***###+++	2.46 ± 0.86	0.32 ± 0.21***###

n=10. Data is presented as Mean ± SD. *** p≤ 0.001= highly significant with control group.
p≤ 0.001= highly significant with standard group.
+++ p≤ 0.001= highly significant between aspirin gel v/s aspirin mouthwash.

Table No.2: Level of PGE_2 after administration of 1% Aspirin Gel and 1% Aspirin Mouthwash

Groups	Day 0	Day 30
Control group	90.83 ± 1.93	91.54 ± 1.76
Standard group	94.90 ± 2.26	92.9 ± 2.47
1% Aspirin Gel	91.51 ± 2.24	42.20 ± 2.42***###
1% Aspirin Mouthwash	118.91 ± 1.04	12.75 ± 1.14***###+++

n=10. Data is presented as Mean ± SD. *** p≤ 0.001= highly significant with control group.
p≤ 0.001= highly significant with standard group.
+++ p≤ 0.001= highly significant between aspirin gel v/s aspirin mouthwash.

DISCUSSION

Gingivitis and periodontitis are the two common diseases that affect the periodontium which is the supporting structure of the tooth. The main cause of these diseases is bacterial plaque which is responsible for the destruction of gingival tissues and periodontal attachment loss[13,14]. The collagen supporting the periodontium is affected, the alveolar bone is resorbed and there is a migration of gingival epithelium along the side of the tooth surfaces resulting in "pocket formation". This periodontal pocket provides an excellent environment for the growth of anaerobic bacteria. The anaerobic bacteria which gain access into the periodontal pocket causes the activation of neutrophils which results in increased production of pro-inflammatory cytokines. Continuous exposure to these pro-inflammatory cytokines leads to periodontal tissue destruction and may even cause the loss of the tooth[15, 16].

There are certain procedures through which these diseases are treated. The treatment includes surgical as well as non-surgical procedures. Nowadays local drug delivery systems are popular among the dentists to treat gingivitis and periodontitis in order to avoid the adverse effects associated with systemic use of drugs. However, regular visits are required by the patients for the complete treatment of the disease.

In this study we prepared 1% aspirin gel and mouthwash and applied into the periodontal pocket in the patients with periodontal disease. All the clinical parameters were highly reduced by both the gel and mouthwash preparation as compared to conventional treatment and control. 1% aspirin mouthwash reduced the bleeding and plaque index because the mouth rinse provides a good control on bacterial plaque in a very short time period[17].The effect of the mouthwash was not significant in reducing the gingival index as compared to 1% gel. This may be due to the muco-adhesive property[18] of 1% ASA gel which retained it in the dental pocket and attached to the oral mucous membrane directly, thus producing significant response. PGE_2 is a very important inflammatory biomarker in the diagnosis of periodontal disease[19].The use of the systemic aspirin reduces the inflammation by decreasing the level of PGE_2[20].In our study both the gel and mouthwash preparation significantly reduced the level of PGE_2 without altering the efficacy of the preparations in the environment of oral cavity. Our study also showed that the level of PGE_2 was not reduced by conventional treatment however; the use of 1% ASA mouthwash and gel showed a highly significant reduction in PGE_2 level.Thus, our study favors the use of gels and mouthwash administration after conventional scaling and root planning treatment.

The mouthwash has rapid absorption ability; it can remove plaque and lowers anaerobic bacterial count. This is in accordance to our results on clinical parameters where we observed reduction in the level of bleeding and plaque indices after the administration of 1% ASA mouthwash. This effect is also associated with the reduction in the level of PGE_2. The mouthwash also showed more reduction in the level of PGE_2 as compared to the gel formulation.

CONCLUSION

Thus we can conclude from this study that local drug preparations produce significant effects in the treatment of periodontal diseases and can prove an alternate to the systemic treatment. It also suggests that the local preparations retained all the effects of the drug and thedrug showed same efficacy in different local formulations.

Recommendations: Further researches are required to develop different local drug preparations to treat the periodontal diseases and to avoid systemic adverse effects associated with their long term oral use.

Author's Contribution:

Concept & Design of Study:	Faiza Hasan
Drafting:	Rahila Najam
Data Analysis:	Rahila Najam
Revisiting Critically:	Muhammad Usman
Final Approval of version:	Faiza Hasan

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Conflict of Interest: The study has no conflict of interest to declare by any author.

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