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Research article

Clinical evaluation of effect of aloe Vera gel formulation for healing following gingival depigmentation

Naina Pattnaik[1]*, Sangram Patro[2], Abhitosh Debata[3], Subash Chandra Nayak[4], Monalisa Panda[5], Monalisa Das[6], Anasuya Sahoo[7]

[1]Department of Periodontics, Hi-Tech Dental College and Hospital, Bhubaneswar, Odisha, India
[2]Department of Oral and Maxillofacial Surgery, Hi-Tech Dental College and Hospital, Bhubaneswar, Odisha, India
[3]Department of Oral and Maxillofacial Surgery, Hi-Tech Dental College and Hospital, Bhubaneswar, Odisha, India
[4] Department of Orthodontics Dentofacial Orthopaedics, Hi-Tech Dental College and Hospital, Bhubaneswar, Odisha, India
[5]Department of Periodontics, Hi-Tech Dental College and Hospital, Bhubaneswar, Odisha, India
[6]Department of Orthodontics Dentofacial Orthopaedics, Hi-Tech Dental College and Hospital, Bhubaneswar, Odisha, India
[7]Sri Jayadev College of P'ceutical Sciences, Bhubaneswar, Odisha, India

ABSTRACT

Gingival hyperpigmentation is of cosmetic concern for many individuals, particularly while smiling. Gingival depigmentation has been evolved as enchanting method for hyper pigmented gingiva. Surgical wound healing attaints an important role in the surgical field. There are various topical medicaments and antibiotics available to expedite the healing process. Out of this Aloe vera showed numerous therapeutic benefits. The objective of the study was to prepare a Aloe vera gel containing Carbopol 934 and to evaluate its efficacy on the healing following Gingival Depigmentation.Total thirty patients with gingival depigmentation were included in this double-blinded, randomized, and controlled clinical trial. The test area received an application of Aloe vera gel preparation postoperatively. Postoperative healing was assessed using HI after first, second, and third weeks following therapy by a blinded examiner.Total 48 patients were enrolled in the study and out of this 30 patients fulfilled the criteria. Test sites showed better healing compared to control sites. The healing in patients in test sites showed statically significant with gradual progress in time. However, control sites did not showed statistically significant results. Anova analysis was done and Spss v.20 was used. Results showed prepared Aloe vera gel had showed significant results towards surgical wound healing after gingival depigmentation.

Keywords: Gingival Depigmentation, Aloe vera, Healing Index, Randomized Clinical trial.

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Correspondence: Naina Pattnaik* ✉ drnainapattnaik@gmail.com

Department of Periodontics, Hi-Tech Dental College and Hospital, Bhubaneswar, Odisha, India

INTRODUCTION

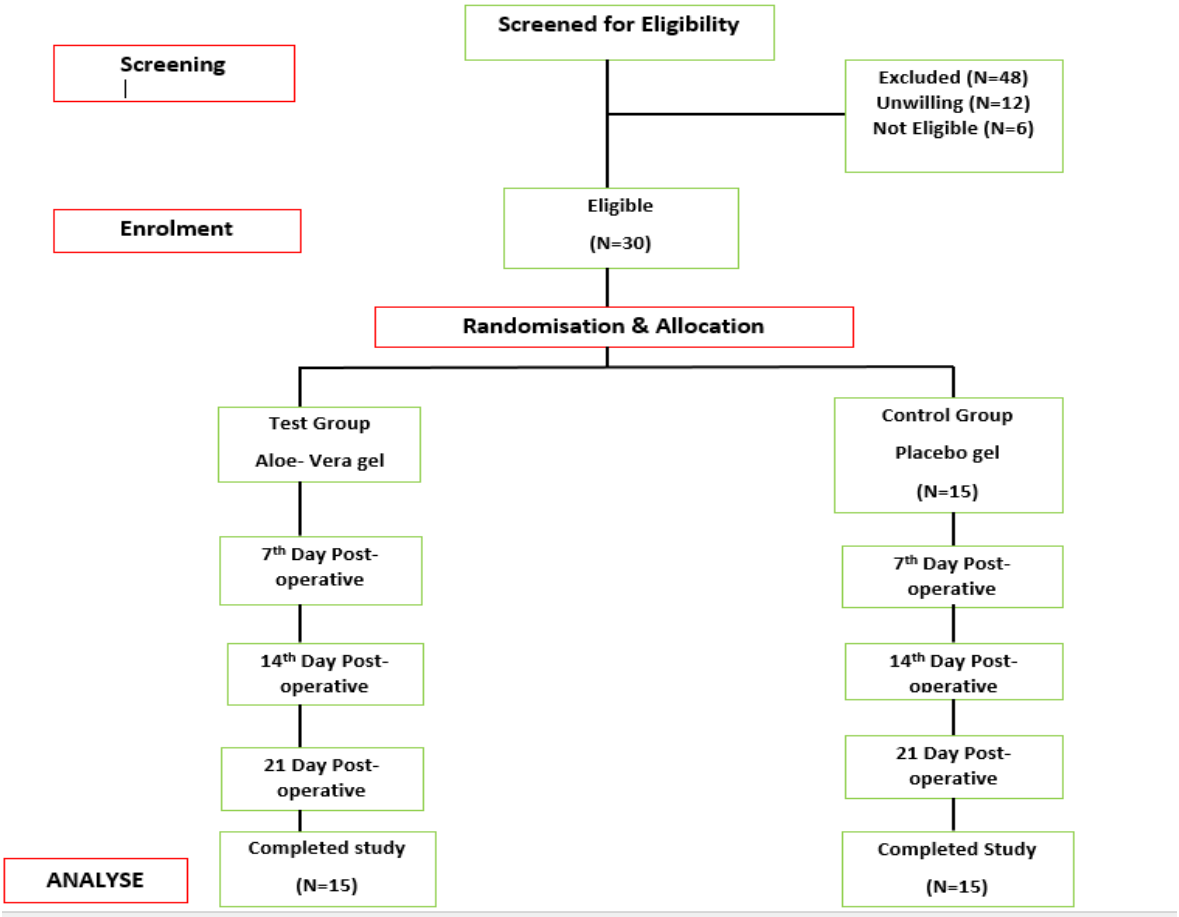
In society, dental esthetics represents as one of the major factors in the quality of life. This new generations seeks to enhance their personality in every respect and wanted to be sounding high in social platform. Now a days patients are more concerned with their appearance and social acceptance towards society. Also, esthetics helps in building- up their self- confidence and personality. Its not only include alignment of teeth, smile corrections but also involves jaw correction and facial profile enhancement [1]. Gingival tissue is usually pale pink in colour, however many people have hyperpigmented gingiva. Mostly the hyperpigmentation of gingiva is due to the presence of excessive melanin in the epithelium [2]. It is usually light to dark brown in colour and distributed as ribbon like dark band uniformly or as molded patches intermittently in the gingival area [2, 3]. Dark pigmentation of gingiva is of cosmetic concern for many patients [2] .There are various method for depigmentation ranging from scalpel method to laser [3]. Early healing of wound along with decreased patient discomfort will led to faster rehabilitation of surgical patient [4].Wound healing is a complex process that can take place by the interaction of various cell, extracellular matrix proteins, mediators such as cytokines and growth factors [5].Despite of various advances in technology and research, sometimes healing takes a lot of time [6].When we compared the healing process, oral cavity healing occurs much faster than skin. Also, saliva has antimicrobial and anti-inflammatory properties as it consist of various growth factors, lysosomes, lactoferrin which aids in wound healing process. Fibroblast also plays a pivotal role in wound healing process. However, sometimes the saliva and oral microorganisms present in oral environment can also affect the wound healing process [6]. Thus, adjunctive use of various topical medicaments and antibiotics has been administered to expedite the healing process [7].Also newer intervention should be employed which ensures quick healing. There are various commercially

available gels which were widely used however, they sometime exhibit various disadvantages such as unpleasant taste, discoloration of teeth [8].Various medicinal plants such as tulsi, aloe vera, neem, turmeric etc have been used in medical and dental fields in various forms and it has a wide application in dentistry [9]. Aloe vera has attracted the attention of many researchers because of its various booming properties such as anti-inflammatory, antifungal, antioxidant, anti-microbial [10]. Aloe vera has already been proved to have a positive effect on infection, inflammation, wound healing [11]. Aloe vera reduce inflammation of wound, keeps the wound moist, increases epithelial migration and helps in rapid maturation of collagen[11].Aloe vera has prospered so much in each corner of human's life, from medicine, to cosmetics, to healthy food. So, everywhere it imprints its footsteps for the human benefits. Thus, this study represents to prepare Aloe vera gel containing Carbopol 934 and to evaluate its efficacy on the healing following Gingival Depigmentation.

MATERIALS AND METHODS

The objective of the study was to prepare a Aloe vera gel containing Carbopol 934 and to evaluate its efficacy on the healing following Gingival Depigmentation. This study was a randomized, double blinded, placebo – controlled, parallel group study. This study was approved by the ethical committee of Hi–Tech group of Institutions (No. HMCH/IEC/202115). All the subjects were briefed about the surgical procedures and signed the consent form. The patient included in the study were aged 15 to 30 years with moderate to severe physiologic gingival melanin hyperpigmentation according to Gupta et al.,(1964)[12]. All the subjects were systemically healthy, having highly concerned towards esthetics with well-maintained oral hygiene. The subjects having systemic disease associated with pathological hyperpigmentation or any uncontrolled diabetes or autoimmune diseases etc. which may led to delayed healing were excluded in the study. Also any periodontal disease and smokers were also exclude. (Figure 1: Study Design).

Figure 1: Consort flow chart



Process of Aloe vera gel preparation

The thick succulent leaves of Aloe vera (*Aloe Barbadensis*) plant was obtained from herbal garden of Sri Javadev College of Pharmaceutical Sciences, Bhubaneswar, Odisha. The Plant was authenticated by Prof. K.B. Satapathy, Department of Botany,Utkal University, VaniVihar, Bhubaneswar, Odisha.The following ingredients were used for gel preparation carbopol 934, methylparaben sodium and prooylparabensodium, sodium metabisulphite were procure from Burgoyne Laboratory ltd., Mumbai, India.

Preparation of Aloe vera extract

After thoroughly cleaning the leaves, it was cut into pieces transversely. The inner gel was collected from the centre of leaf was removed with spoon thoroughly and grinded [13].

Choosing and enhancement of gelling Agent

In order to optimize the gelling agent to achieve proper consistency of the gel formulation. With the Carbopol 934 of different concentration of viscosity enhancer via 1.0, 2.0, 3.0 and 4.0 percent were tired and finally gel that showed good Spreadability and consistency was selected [14].

Method of Aloe Vera Gel preparation

The ingredient such as sodium metabisulphite, methyl paraben sodium and propyl paraben sodium were used. First add all the ingredients in water followed by adding of gelling agent. Then stirred continuously with simultaneously adding of Vitamin E. Now, the Aloe extract was added and mixed till a uniform gel was formed [14].

Gel Evaluation

The 1.0g of the gel was accurately weighed and dispersed in 100 ml purified water. The measurement of pH were done in triplicate and average values were then calculated [14, 15].

Spreadability

The curative efficacy of the gel was also based on its spreading value. The gel's spreadability was done by keeping 0.5 g of gel within 1cm diameter in between two glass slab. After placing a weight of 500g over the glass plate its increasing diameter was noted [14-16].

Viscosity

The viscosity of the formulation was determined without dilution by DV-I- Prime Digital Viscometer (Brookfield Engineering Laboratory, Inc., Middleboro, MA,USA) using spindle No.3, at 50 rpm having diameter of 35mm. Viscosity was noted when it appears on the DV-I- Prime Viscometer display.

Homogeneity

The homogeneous nature of the gel was done by their appearance and accumulation of aggregates. Following that it was filled in the dark brown bottles.

Composition of gel

Table 1: Varying composition of gel

Batch No	Aloe Extract (g)	Sodium-meta bisulphite (g)	Carbopol 934(g)	Methyl Paraben Sodium (g)	Propyl Paraben Sodium(g)	Purified water(g)
B1	75	0.200	1	0.020	0.002	Qs to 100
B2	75	0.200	2	0.020	0.002	Qs to 100
B3	75	0.200	3	0.020	0.002	Qs to 100
B4	75	0.200	4	0.020	0.002	Qs to 100

Methods

Total 48 subjects were selected out of which 30 fulfilled the inclusion criteria. A single examiner assessment of subject's eligibility for the study and enrolment of the subjects into the trial. The subjects were preceded by thorough oral prophylaxis by the same examiner. The lottery method was used for the randomization. A code number was allocated to all the subjects and were maintained to identify with these codes only throughout the study. Then the first clinical coordinator (from other Department of Hi- Tech Dental college and hospital, Bhubaneswar) marked the subject's code on the neutral bottles containing the test gels. All the tested gels were dispensed in identical amber colour bottles which were indistinguishable in terms of labelling and packaging. The bottles were labelled to indicate the subject's code, the study period, instructions and a code for the product. The bottles were distributed in two groups. Each group consist of 10 bottles consisting of 15 gram of Aloe vera gel in group A and Control group B.

The process was precede by topical anaesthesia (Lidocaine Topical Aerosol – LOX 10% Spray) in the affected area. The laser unit with the fibrotic laser tip having a 320UM diameter at 2.5 power was used for the procedure. The fiber was in contacted towards the affected area where laser was emitted in gated pulse mode with wavelength of 800 and 980 nm. Depigmentation was performed after wiped with saline gauze in horizontal direction and removing the epithelial lining. Periodontal pack were placed. However, antimicrobials and analgesic were given to all the subjects for five days.

Subjects were asked to apply the Aloe vera gel to apply over the surgical site after removal of coe-pak. Subjects were instructed that after tooth brushing and consumption of liquid and solid food was avoided for next 3 hours after application of tested gels for more efficient distribution and absorption as described by Jentsch et al., (2003) [16] . A blinded examiner explained the subjects to dab the gel gently and not to message it over the surgical site. And rinse it after 15 -20 minutes of application.

Data collection

The visual analog scale (VAS), the pain parameter was used on the subjects during intraoperative procedure; 24 hour post-operative , after 1 week followed by the Healing index and after first, second and third week of surgery by a blinded examiner [17].

RESULTS AND DISCUSSION

A total of patients had given consent to undergo the procedure. At. A 5 % percent significance level, with 95% confidence interval and an effect size of 0.5 estimated the total sample to be 20%, the desired sample size was estimated to be at 30.These patients were again subdivided into two groups of 15 number each.

The results in (Table 2) showed no significant difference in the VAS scores of 1st week between group A and Group B. The VAS scores in 24hrs post-operative amongst the groups also did not show any significant difference. The healing index showed there was a greater healing factor observation at day 7, day 14 and day 21 in comparison to patients administered in group B medicaments. Unpaired t test was done and Spss v20 was used.

Table 2: No significant difference in the VAS scores of 1st week between Group A and Group B

		Mean	N	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference	Sig. (2-tailed)	
1st week post-operative	A	0.20	10	0.42	0.13	Lower	Upper	
	B	0.20	10	0.42	0.13	-.48	0.48	1.00
24 hr post-operative VAS	A	1.70	10	0.48	0.15	-.51	0.31	0.59
	B	1.80	10	0.42	0.13			
Healing Index Day 7	A	4.30	10	0.48	0.15	-.18	0.78	0.03
	B	3.00	10	0.47	0.15			
Healing Index Day 14	A	5.60	10	0.52	0.16	-.36	0.76	0.02
	B	4.40	10	0.52	0.16			
Healing Index Day 21	A	6.25	10	0.00	0.00	-0.45	0.85	0.04
	B	5.00	10	0.00	0.00			
Intra-operative VAS	A	0.70	10.00	0.48	0.15	-0.48	0.48	1.00
	B	0.70	10.00	0.48	0.15	-0.48	0.48	1.00

Table 3: Depicted the comparison of healing scores in day 7, day 14 and day 21 amongst the two groups

		Mean	N	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference		p	f	df
						Lower	Upper			
A	Healing Index Day 7	3.30	10	.48	.15	2.82	3.78	0.00	47.4	2
	Healing Index Day 14	4.60	10	.52	.16	4.08	5.12			
	Healing Index Day 21	5.00	10	.00	.00	-	-			
B	Healing Index Day 7	3.00	10	.47	.15	2.53	3.47	0.00	63.36	2
	Healing Index Day 14	4.40	10	.52	.16	3.88	4.92			
	Healing Index Day 21	5.00	10	.00	.00	-	-			

The results in (Table 3) depicted the comparison of healing scores in day 7, day 14 and day 21 amongst the two groups. Anova analysis was done and Spss v.20 was used. The healing index in the patients was statistically significant with gradual progress in time in group A. However, in group B the healing index was not statistically significant.

Gingival hyperpigmentation is of cosmetic concern for many individuals, particularly while smiling [18]. Gingival depigmentation has been evolved as enchanting method for hyperpigmented gingiva [17, 19]. Rapid healing after gingival depigmentation is a great attainment in the surgical field [20, 21]. A secondary wound healing takes place after gingival depigmentation, based on various sequences of healing such as haemostasis, inflammation, proliferation and remodelling that takes place in a proper course and time period [20]. Sometime unpleasant taste, burning sensation or discoloration of teeth caused by the commercially available topical gel [8, 25]. Thus, usage of herbal products has enormously taken place. Many herbal plants have been traditionally used in folk medicine and their valuable by-products showed to have a boon effect on oral diseases [22]. One of such agent is aloe vera which is a medicinal plant with enormous therapeutic benefits [22].

Aloe vera is best known for its anti-inflammatory, antibacterial, antifungal, antioxidant and anti-healing effect [23]. It is also highly effective in anticancer, anti-diabetic and anti-hyperlipidemic [23]. The present study showed favourable results towards the healing effect of Aloe vera gel containing Carbopol 934 following Gingival Depigmentation. After application of the aloe vera gel on the gingival surface it helps the wound to keep moist, increases epithelial migration and maturation of collagen. This further reduces the inflammation of the wound and enhances gingival circulation. There was a significant change in the colour of gingiva from inflammatory red to pink in the test group with aloe vera gel when compared with the control group. There was also an early change in the colour of gingiva of many subjects in the test group compared to the control group. There was no bleeding on palpation of the wound area on the 14th and 21 day after surgery in the test group than control group. After a week of surgery there was exposed connective tissue in the wound area of the control group which improved gradually after 21 days. However in the test group epithelisation started occurring within a week after surgery and complete epithelisation of the wound can easily be seen with subjects using aloe vera gel from the 14th day onwards.

Aloe vera contains more than 75 different compounds, including vitamins (vitamin A, C, E, and B12), enzymes (i.e., amylase, catalase, and peroxidase), minerals (i.e., zinc, copper, selenium, and calcium), sugars (monosaccharides such as mannose-6-phosphate and polysaccharides such as glucomannans), anthraquinones (aloin and emodin), fatty acids (i.e., lupeol and campesterol), hormones (auxins and gibberellins), and others (i.e., salicylic acid, lignin, and saponins)[24] . Aloe vera is a natural product in which inner layer contain eight essential ammino acids [25].

Our study is in accordance with the study by Shamim et al., (2016)[26] and Hudemukar et al., (2019)[27] which showed aloe vera gel is highly effective in improving post-operative healing following periodontal flap surgery. Also Davis et al., (1989)[28] showed aloe vera increased the fibroblast and collagen proliferation which aids in wound healing. It contain gibberellins, auxin and mannose phosphate which bind to insulin like growth factor which is responsible in

achieving healing [29]. Acemannan is an active ingredient in aloe vera, which stimulates the macrophage and further enhances the cross linkage of collagen and thus favour healing [29]. Also it contains tryptophan and phenylalanine that aids in anti-inflammatory action. It also reduces vasodilation and decreases vascular effects of histamine, serotonin other inflammatory mediators by preventing the biosynthesis of prostaglandin from arachnoid acid [30]. It blocks prostaglandins and modulates the production of lymphocytes and macrophage derived mediators (lymphokins) including interleukins and interferons [30]. Also the carboxy peptidase in aloe vera inactivates 67 percentage of bradykinins and thus reduces pain [30]. Aloe vera acts as a scavenger as the vitamin c present in it inhibits inflammation by affecting the oxygen radicles to block the inflammatory process [31]. Thompson et al., (1991) [32] found that the topical application of aloe vera derived allotin gel stimulates fibroblast activity and collagen proliferation.

The gelling agent plays an important role in formation of gel. As it is of low concentration with low viscosity that leads to easy handling of solution. However if the concentration is high with high viscosity, an uneven gel formation will form and handling of gel will be difficult which further decreases the efficiency of drugs. This gel is of low consistency with easy handling properties while preparation and while application over the wound area. This prepared aloe vera gel had showed significant results towards surgical wound healing after gingival depigmentation. However further studies should be carried out for the various preparation of the aloe vera / herbal based products which will be highly efficient and effective in post-operative healings.

CONCLUSION

With the limitations of this study, it can be concluded that the prepared aloe vera gel containing Carbopol 934 has positive and favourable effects on the wound healing process following gingival depigmentation. Therefore, a gel containing aloe vera can be a natural alternative to chemically formulated gels. As it is highly effective and inexpensive and has favourable results towards healing, its usage should be encouraged.

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