

Effects of *Aloe vera* Cream on Posthemorrhoidectomy Pain and Wound Healing: Results of a Randomized, Blind, Placebo-Control Study

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Abstract

Objective: *Aloe vera* is an herbal medicine, which has wound healing effects in burn injury. This study assessed the effects of *Aloe vera* cream in reducing postoperative pain, postdefection pain, and its promotion of wound healing after open hemorrhoidectomy.

Design: A prospective, randomized, double-blind, placebo-controlled trial was conducted comparing the effects of a cream containing *Aloe vera* versus a placebo cream on posthemorrhoidectomy pain. The study preparations were applied by patients to the surgical site 3 times per day for 4 weeks after hemorrhoidectomy. Pain was assessed with a visual analog scale immediately postoperatively and at hours 12, 24, and 48 after surgery and at weeks 2 and 4. Wound healing was examined and evaluated at the end of 2 and 4 weeks. The use of analgesics was recorded.

Results: Forty-nine (49) patients were randomly assigned to receive aloe ($n = 24$) or placebo ($n = 25$). Patients in the topical aloe cream group had significantly less postoperative pain at hours 12, 24, and 48 hours and at 2 weeks. Aloe cream reduced the pain after defecation in 24 and 48 hours postsurgery ($p < 0.001$). Wound healing at the end of the second postoperative week was significantly greater in the aloe group compared with the placebo group ($p < 0.001$). Patients required fewer additional analgesics posthemorrhoidectomy ($p < 0.001$).

Conclusions: Application of *Aloe vera* cream on the surgical site is effective in reducing postoperative pain both on resting and during defecation, healing time, and analgesic requirements in the patients compared with the placebo group.

Introduction

HEMORRHOIDS ARE ONE OF THE MOST COMMON chronic anorectal diseases known. Hemorrhoids grade III and IV require an operative hemorrhoidectomy to eliminate hemorrhoidal symptoms.^{1–3} Hemorrhoidectomy is associated with significant pain in the postoperative period. Both open and closed hemorrhoidectomy resulted in postoperative pain.^{4,5} Continuous internal anal spasm is considered a major factor in the inducing of pain.^{6,7} The patients mainly required narcotic and nonnarcotic analgesics in the early period post-hemorrhoidectomy for reducing pain.⁶ With regard to the effect of pain on discomfort of patients, several pharmacological agents were assessed for relieving pain in patients, including diltiazem ointment,⁸ lidocaine and prilocaine creams,⁹ sucralfate cream,¹⁰ glyceryl trinitrite ointment,¹¹ and

ropivacaine.¹² Recently we showed that patients who applied topical metronidazole had significantly lesser postoperative pain than those in the placebo group up to day 14.¹³ Some studies have shown that reduced postoperative spasm of the internal anal sphincter is effective in reducing pain associated with sphincter spasm.^{8,11} Patients applied topical glyceryl trinitrite for reducing posthemorrhoidectomy pain and had headaches.¹¹ Therefore, patients sought a safe topical drug with natural origin and with less toxicity.

Aloe vera (family: Liliaceae) has been used in traditional medicine for a long time. It is one of the most recognizable herbs in the world and the medicinal part is the succulent leaves. A topical skin gel provides wonderful healing support for the skin. *Aloe vera* contains many important nutrients for the body, including amino acids, B vitamins, and other nutrients that support general health. It also has

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pharmacological properties including antioxidant, wound healing, antibacterial, antifungal, and immunomodulating effects.¹⁴ Burn wound healing is one of the major indications of *Aloe vera* gel use in several in animal and clinical studies.¹⁵

Realizing the potential use of *Aloe vera* in wound healing, we examined the effects of *Aloe vera* cream versus placebo in reducing postoperative pain and pain on defecation after open hemorrhoidectomy.

Methods

This clinical trial was registered by Iranian Registry of Clinical Trials as a code IRCT138711131627N1. After obtaining approval from the Ethical Committee at Mazandaran University of Medical Sciences, this clinical trial was carried out in Imam Hospital, Sari, Iran. This study was a randomized, double-blind, prospective, placebo-controlled trial comparing aloe cream with placebo cream. All patients who were enrolled this study had symptomatic III and IV degree hemorrhoidal diseases and met criteria for surgical hemorrhoidectomy. All patients underwent open hemorrhoidectomy. Exclusion criteria were pregnancy, anal fissure, and heart and liver diseases.

Preparation of aloe cream

Liquid white paraffin, sterile alcohol, cetyl alcohol, solid white paraffin, and propylene paraben were mixed and heated to the boiling point as the oil phase. *Aloe vera* powder (Zarband, Phytopharmaceutical Company, Iran) mixed with deionized water was added to a mixture of propylene glycol, sodium lauryl sulfate, and methylparaben. The mixture was heated as the aqueous phase. These two separate phases were mixed continuously while being cooled. Thus, after cooling, the uniform cream that was produced was placed in an aluminum package similar to a placebo tube, weighing 50 g. The cream contained *Aloe vera* gel powder 0.5%. Placebo creams were prepared according to similar protocol without aloe powder. Our experimental research and formulations were carried out under sterile conditions. The final creams were tested for any probable contamination microbes, which were not detected during the applications.

Patients and study procedure

In this study, 49 patients were randomized in two groups. Patients had creams applied (aloe or placebo) immediately after surgery and 12 hours after hemorrhoidectomy. This treatment was continued on the surgery site 3 times a day up to 28 days postoperatively. Study patients applied approximately 3 g of aloe cream to the wounds outside. Control patients applied the same quantity of placebo cream in a similar fashion. The initial application of cream was performed as a part of the postoperative dressing. For blinding, the aloe and placebo creams were coded and both the nurse and patients were blinded as to which cream was used during examination. Patients were discharged from the hospital 24 hours after surgery. Patients were instructed to apply the cream with the tip of the index finger to the wounds three times daily. All patients were supplied with analgesic drugs as needed. The patients were followed up after discharge from the hospital. Postoperative pain was evaluated by using a visual analog scale (VAS), which was scored as 0 (no pain) to 10 (very severe pain). Pain score were

obtained immediately postoperatively and at 12 hours, 24 hours, and 48 hours after surgery and at days 14 and 28. Pain on defecation was also recorded using the VAS. The patients recorded their analgesic requirement. At the end of 2 and 4 weeks postoperatively, an expert surgeon examined the healing of patients' wounds. Wound healing was defined as complete epithelial covering as observed by physical examination. Wounds were classified as grade I (severe and fresh wound with inflammation), grade II (granulation tissue on wound), and grade III (completed layer of epithelial covering on wound).

Statistical analysis

Data were analyzed using the *t* test and χ^2 , as appropriate, to compare patients' demographics, pain score, wound healing, and analgesic drug use. $P < 0.05$ was considered a significant difference. Statistical analysis performed using SPSS software (version 12, SPSS Inc., Chicago, IL).

Results

Forty-nine (49) patients were randomly assigned to receive aloe cream ($n = 24$) or placebo cream ($n = 25$) after hemorrhoidectomy. Both groups were predominately female (aloe group 16 female; placebo group 14 female). The groups were similar with respect to age, gender, and extent of preoperative hemorrhoid diseases. The number of patients with III and IV degrees of hemorrhoids was 10 and 14, 11 and 14 for aloe and placebo groups, respectively. Pain scores immediately after hemorrhoidectomy were 9.29 ± 0.81 and 9.24 ± 0.66 in the aloe and placebo groups, respectively. The VAS scores were not significantly different between the two groups in the time immediately after hemorrhoidectomy. Patients in the aloe group experienced significantly less pain at 12, 24, and 48 hours and 2 weeks postsurgery ($p < 0.001$) (Table 1). Patients who received aloe cream were found to have significantly lower pain on defecation on 24 and 48 hours after hemorrhoidectomy ($p < 0.001$), but no significant difference was observed at 2 and 4 weeks (Table 2).

Aloe cream significantly helped wound healing in patients at 2 weeks postsurgery ($p < 0.001$) (Table 3), but no significant difference was observed at the end of 4 weeks. All wounds in the aloe group showed grade III wound healing with epithelial covering, but wound healing was grades I and II in the placebo group at 14 days (Table 3).

TABLE 1. POSTOPERATIVE PAIN SCORES IN *ALOE VERA* AND PLACEBO GROUPS

Time	Aloe (n = 24) mean \pm SD	Placebo (n = 25) mean \pm SD	p-value
Immediately after surgery	9.29 \pm 0.81	9.24 \pm 0.66	0.807
12 hours	5.75 \pm 0.9	8 \pm 0.71	<0.001
24 hours	3.2 \pm 0.83	6.3 \pm 0.70	<0.001
48 hours	1.8 \pm 0.64	5.2 \pm 0.91	<0.001
Week 2	1.16 \pm 0.38	2.56 \pm 0.50	<0.001
Week 4	1 \pm 0.00	1.04 \pm 0.20	0.332

Pain scores ranged from 0 (no pain) to 10 (very severe pain). SD, standard deviation.

TABLE 2. PAIN ON DEFECTION IN ALOE AND PLACEBO GROUPS

Time	Aloe (n = 24) mean ± SD	Placebo (n = 25) mean ± SD	p-value
Immediately after surgery	9.08 ± 0.92	9.08 ± 0.81	0.989
24 hours	5.45 ± 0.72	7.72 ± 0.84	<0.001
48 hours	2.91 ± 0.83	4.16 ± 0.85	<0.001
Week 2	1.29 ± 0.46	1.48 ± 0.51	0.183
Week 4	1 ± 0.00	1.2 ± 0.41	0.134

Pain scores ranged from 0 (no pain) to 10 (very severe pain). SD, standard deviation.

The narcotic consumption in the aloe group was significantly less compared with the placebo group at 12 hours after hemorrhoidectomy ($p < 0.001$). At 12 hours postsurgery, the percentages of patients who required narcotic analgesic drug (tramadol injection) were 21% and 76% in the aloe and control groups, respectively. No narcotic consumption was observed at 24 hours after hemorrhoidectomy. Nonnarcotic analgesic medications were significantly lower in the aloe group 2 weeks after hemorrhoidectomy (Table 4) ($p < 0.001$).

No mortality was encountered. No side-effects or allergic reactions were observed in patients who received creams.

Discussion

This prospective, randomized study has demonstrated that application of *Aloe vera* cream provided significant pain relief through the 48 hours post open hemorrhoidectomy. Aloe cream led to significant wound healing at 14 days postsurgery. Compared with the placebo group, lower analgesic consumption in the aloe cream group confirms the improved pain management following a hemorrhoidectomy.

Various factors believed to be responsible for the pain after hemorrhoidectomy include spasm of the internal sphincter, and inflammation and bacterial colonization of the hemorrhoidectomy site.¹⁴⁻¹⁶ Another reason for pain could be the healing of wounds, which was extended up to the anorectal ring.¹⁰ There are several reports that pharmacological agents with different mechanisms contribute to reducing pain, include antispasmodic effects such as glyceryl trinitrate ointment,¹¹ calcium channel blocker ointment,⁸ botulinum toxin injection,⁷ antimicrobial effects such as metronidazole ointment,^{14,15} and diminishing tissue edema, such as sucralfate cream.¹⁰

Aloe vera preparations have many biological effects including antidiabetic, immunomodulatory, antiinflammatory,

TABLE 3. THE NUMBER OF PATIENTS WITH GRADE OF WOUNDS IN ALOE AND PLACEBO GROUPS AT THE END OF WEEK 2 POSTHEMORRHOIDECTOMY

Grade of wounds	Aloe (n = 24)	Placebo (n = 25)	p-value
Grade I	0	12	<0.001
Grade II	0	12	<0.001
Grade III	24	1	<0.001

Wounds were classified as grade I (severe and fresh wound with inflammation), grade II (granulation tissue on wound), and grade III (completed layer epithelial covering on wound).

TABLE 4. POSTHEMORRHOIDECTOMY NONNARCOTIC ANALGESIC CONSUMPTION IN ALOE AND PLACEBO GROUPS DURING 2 WEEKS AFTER DISCHARGE FROM HOSPITAL

Number of medications	Number of patients aloe group (n = 24)	Number of patients placebo group (n = 25)	p-value
Without analgesic	9	2	<0.001
One tablet per day	12	3	<0.001
Two tablets per day	3	10	<0.001
Three tablets per day	0	10	<0.001

Medication was 500-mg acetaminophen tablet.

antioxidant, and wound-healing effects.¹⁷ A recent review of clinical trials investigating the effect of *Aloe vera* on burn wounds found that *Aloe vera* significantly shortened the wound healing time compared to control.⁸ Aloe contains various carbohydrate constituents. Polysaccharides, mannose, and acemannan were identified in the aloe preparation.¹⁷ Polysaccharides are known to have an effective property in skin wound repair.^{17,18} Antiinflammation is the first step in wound healing, and this effect of aloe preparations is believed to play a direct role in facilitating rapid healing.¹⁸ Wound healing involves biological processes such as inflammation and granulation tissue formation. Collagen is the major protein in the extracellular matrix and provides strength and integrity to the dermis and other supporting tissues.¹⁹⁻²¹ *Aloe vera* enhances the production of collagen.²⁰ Glycoprotein fraction is the major component of aloe that is involved in wound healing with cell proliferation and migration and promotes the growth of dermal fibroblasts.^{22,23} The glycoprotein fraction of *Aloe vera* stimulated cell proliferation, accelerated recovery of an artificial wound on the monolayer of normal keratinocytes, and enhanced thickening of the epidermal covering. Another study found that *Aloe vera* increased the collagen content of the granulation tissue as well as the degree of cross-linkage. It is thought that the enhanced collagen content promotes stimulation by aloe in collagen synthesis or increases the proliferation of fibroblast synthesis of collagen, or both.²⁴

In this study, aloe cream significantly improved the wound healing posthemorrhoidectomy. Since inflammation is one of the main causes of pain in patients in the early postsurgery time,²⁵ the antiinflammatory effects of aloe contribute to relief of postoperative pain in patients treated with aloe cream. Aloe has an antimicrobial effect; this effect is related to its constituents including anthraquinones and aloe-emodin.^{17,18} This antimicrobial effect could be contributing to the reduction of pain and promotion of wound healing by *Aloe vera*. It was demonstrated that oral or topical antimicrobial agents such as metronidazole significantly decreased postoperative pain after open diathermy hemorrhoidectomy.^{15,16} The beneficial role of topical *Aloe vera* may be antimicrobial, antiinflammatory properties, and positive effects on wound healing.

Conclusions

In this study, a topical cream containing *Aloe vera* as herbal medicine decreased postoperative pain and pain on defecation and enhanced wound healing after hemorrhoidectomy

when compared with a placebo cream. The use of postoperative analgesic agents was significantly decreased in the aloe group. There were no side-effects observed related to aloe cream.

Acknowledgments

This work was supported by a grant from Mazandaran University of Medical Sciences, Sari, Iran. This research was the subject of a thesis by Mohammad Sina Norozi for an M.D. degree in the Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran.

Disclosure Statement

No competing financial interests exist.

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