Sucralfate ointment reduces pain and improves healing following haemorrhoidectomy: a prospective, randomized, controlled and double-blinded study

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Background
It has been clinically observed that posthaemorrhoidectomy pain is the most feared symptom by the patient, often leading to avoiding surgery altogether. Opioids and NSAIDs are used to control posthaemorrhoidectomy pain, but they have short duration of action and well-known side effects and may be expensive. These factors justify the need to search for new treatments to decrease posthaemorrhoidectomy pain.

Patients and methods
A total of 90 patients who had undergone surgery for third-degree and fourth-degree haemorrhoids were included in this prospective, randomized, controlled and double-blinded study. The patients were randomly assigned to two groups. Group A received topical sucralfate in petrolatum base and group B received plain petrolatum base. Patients were evaluated at days 1, 7 and 14 for the severity of pain (using the visual analogue pain scale) and for the amount of analgesia used. On day 28 patients were evaluated for wound healing.

Results
Patients in the sucralfate group suffered significantly less pain and required less analgesics (narcotic and nonsteroidal) on days 1, 7 and 14 postoperatively ($P < 0.001$). Also, the rate of wound healing was significantly better in the sucralfate group (37/45) than in the control group (28/45) ($P < 0.05$).

Conclusion
Topical sucralfate ointment significantly decreases pain at days 1, 7 and 14 after haemorrhoidectomy and significantly accelerates wound healing.

Keywords:
posthaemorrhoidectomy pain, sucralfate, wound healing

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Introduction

Haemorrhoid disease is the most frequent proctologic complaint, affecting a considerable proportion of adults of any age (haemorrhoids very rarely occur in children) and sex. This disease has been well described since ancient times (Hammurabi Codex ~1750 BC in Babilonia, Ebers Papyrus 1550 BC in Egypt) [1].

It is estimated that 38.9% of the population suffers from haemorrhoids, with grades III and IV representing 8.16 and 0.53%, respectively [2].

A wide variety of treatment options are available for treating haemorrhoids, both medical and surgical, with haemorrhoidectomy being the most effective treatment to reduce recurrent symptoms in patients of grades III or IV [3].

Haemorrhoidectomy, in which the haemorrhoidal complexes and associated connective tissues are sharply excised and the mucosal defect is closed, at least partially, is very effective but very painful [4].

It is clinically observed that posthaemorrhoidectomy pain is the most feared symptom by the patient, often leading to avoiding surgery altogether. Opioids and NSAIDs are used to control posthaemorrhoidectomy pain, but they have short duration of action and well-known side effects and may be expensive. These factors justify the need to search for new treatments to decrease posthaemorrhoidectomy pain.

Sucralfate, a common antiulcer medication, is a basic aluminium salt of sucrose octasulfate. It has been shown to act as a mechanical barrier because of a strong electrostatic interaction of the drug with proteins at the ulcer site. Moreover, sucralfate has shown antibacterial activity [5].

Few researchers have studied the effect of topical sucralfate on posthaemorrhoidectomy pain [6,7]

with encouraging results. The aim of the study was to evaluate the effect of using 10% sucralfate ointment on posthaemorrhoidectomy pain and wound healing.

Patients and methods

The study was carried out on patients presenting to the General Surgery Department, Menoufia University Hospital, between July 2014 and November 2015 and was approved by the ethical committee of the hospital. Informed consent was obtained from each patient. Inclusion criteria were as follows: indication for haemorrhoidectomy for third-degree and fourth-degree haemorrhoids and surgery conducted following the standard Milligan–Morgan technique for open haemorrhoidectomy [8].

Exclusion criteria included the following: presence of anal or rectal pathologies (e.g. fistulae, prolapse, abscess …), age younger than 21 years or older than 60 years; and noncompletion of the study protocol.

All surgeries were carried out by the same surgeon and following the same anaesthesia protocol in order to abolish any interpersonal variation.

The study was prospective, randomized, controlled and double-blinded. Randomization was carried out at the end of the surgery, where a closed envelope method was used to allocate the patient to either group A (the sucralfate group) or group B (the control group). Neither the surgeon nor the patient was aware of the result of randomization, which was kept confidential by an independent observer until the end of the follow-up of each patient. The two jars of drugs containing sucralfate in petrolatum and plain petrolatum were identical. The sucralfate concentration in the ointment was 10% in an inert petrolatum base. The ointment was applied at the end of the surgery and 8-h thereafter. The amount used was determined with a special spoon that measures roughly 1 g of the ointment.

Patients were evaluated regarding their response to the visual analogue pain scale and the amount of analgesics needed to control their pain, as well as wound healing. On the visual analogue pain scale, 0 denoted no pain and 10 denoted severest pain. In the first 24 h, patients were offered intermittent doses of pethidine. Starting from the second day, patients were instructed to use sodium diclofenac tablets (50 mg) to control their pain. A daily phone call was made to record the amount used. Patients were evaluated on day 1, day 7 and day 14 for posthaemorrhoidectomy pain. On day 28, patients were examined for wound healing.

Statistical analysis

It was estimated that 44 patients in each group would be required to detect a reduction of 20% in pain severity on the visual analogue pain scale and wound-healing rates. Data were analysed using SPSS package for Windows (version 16) (USA, Chicago, SPSS Inc.). All the tests were used as tests of significance at *P* value less than 0.05.

Results

Ninety patients completed the study, with 45 in each group. The study included 41 men and 49 women. Other demographic data are shown in Table 1. There was no significant difference in the demographic characteristics of the patients enrolled in the two groups ($P > 0.05$).

Table 2 shows the average score on the visual analogue pain scale at days 1, 7 and 14. There was a highly significant difference ($P < 0.001$) in favour of sucralfate. This was also noticed on days 7 and 14 ($P < 0.05$).

Table 3 shows the average amount of narcotic analgesia needed by patients to control their pain in the first 24 h following surgery. The sucralfate group needed significantly less amount of narcotic analgesia than the control group ($P < 0.05$).

Table 4 shows that at 1 week and at 2 weeks the sucralfate group needed significantly less diclofenac to control their pain ($P < 0.001$).

Table 5 shows the rate of wound healing at 28 days. This also shows a favourable healing rate for the sucralfate group ($P < 0.05$).

Table 1 Comparison of demographic characteristics between the two groups

Point of comparison	Sucralfate group	Control group	*P* value
Age (mean±SD) (years)	37.6±10.4	36.9±11.2	0.73
Male: female	20 : 25	21 : 24	0.81
Number of piles removed	2.81±1.1	2.62±1.2	0.69
Grade III: grade IV ratio	37 : 8	35 : 10	0.34

Table 2 Comparison between the two groups regarding the severity of pain on the visual analogue pain scale at days 1, 7 and 14 postoperatively

Visual analogue pain scale	Sucralfate group	Control group	*P* value
Day 1	5.2±1.37	6.7±1.48	<0.05
Day 7	2.6±0.75	3.8±0.92	<0.001
Day 14	0.9±0.44	1.64±0.59	<0.001

Table 3 Comparison between the two groups regarding the amount of pethidine needed to control posthaemorrhoidectomy pain

Point of comparison	Sucralfate group	Control group	*P* value
Amount of pethidine used (mg)	107±24	122±31	<0.05

Table 4 Comparison between the two groups regarding the amount of diclofenac used to control posthaemorrhoidectomy pain

Diclofenac use (mg)	Sucralfate group	Control group	*P* value
Day 7	116±27	158±33	<0.001
Day 14	56±15	81±22	<0.001

Table 5 Comparison between the two groups regarding the degree of wound healing at 28 days postoperatively

	Sucralfate group	Control group	*P* value
Complete wound healing	37/45	28/45	<0.05

Discussion

Sucralfate has long been known as an antiulcer drug. Its mechanisms of action are diverse. It attaches to proteins on the surface of ulcers, such as albumin and fibrinogen, to form stable insoluble complexes [9].

These complexes serve as protective barriers at the ulcer surface, preventing further damage through prevention of the release of cytokines from damaged cells. Recently, it has been proved that sucralfate also stimulates the increase of prostaglandin E_2 and b-fibroblast growth factors. Basic fibroblast growth factor stimulates the production of granulation tissue, angiogenesis and re-epithelization, thus improving the quality of ulcer healing [10,11]. Sucralfate has well-proven antibacterial activity [12]. Sucralfate proved effective in reducing pain and in improving wound-healing rates in oral ulcers [13], ENT surgery [14], radiation proctitis [15], rectal ulcers [16] and burns [17].

Posthaemorrhoidectomy pain is related mainly to the incision itself or to the subsequent tissue inflammation and infection. The incision causes denuded epithelium, trauma to smooth muscle fibers and its subsequent spasm and the ligatures causing tissue strangulation.

In this study, patients who received topical sucralfate following haemorrhoidectomy suffered less pain. This was evidenced in the difference between the visual analogue pain scale score in both the sucralfate group and the control group. The observation is that sucralfate has an analgesic effect that is more pronounced with the passage of time (Table 2; *P* value less than 0.05 on day 1 and less than 0.001 on days 7 and 14). This can be attributed to the protective effect of sucralfate through the formation of insoluble complexes on the wound surface. The same observation was noticed by Ala *et al.*[6] in 2013.

Also, the average visual analogue pain scale score on day 7 was below 3 in the sucralfate group. A score of 3 or less is regarded as mild tolerable pain. In the control group and at day 7, the average visual analogue pain scale score was above 3, indicating more intense pain.

The analgesic effect of sucralfate was also noticed in the amount of narcotic analgesics needed on the first postoperative day. Patients who received topical sucralfate needed significantly less amount of narcotic analgesia than the control group (Table 3, $P < 0.05$).

The analgesic effect of sucralfate was observed not only early in the postoperative period but also on days 7 and 14. This was reflected in the amount of diclofenac needed by patients to control their pain (Table 4) ($P < 0.001$ on 7 and 14 days). The same finding was reported by Gupta *et al*. [7].

Sucralfate is not the only drug used topically to reduce acute posthaemorrhoidectomy pain. Similar results were reported with cholestyramine ointment[18] and metronidazole cream [19].

Another hypothesis behind the action of sucralfate is that it increases wound-healing rates through its affinity to bind to b-fibroblast growth factors and release it locally in the wound in high concentration [10]. This is evidenced in this study. At 28 days, 82% (37/45) of patients in the sucralfate group showed complete healing of wounds on anoscopic examination. In the control group the healing rate was 62% (28/45). The difference was statistically significant ($P < 0.05$).

Conclusion

Topical sucralfate is effective in reducing posthaemorrhoidectomy pain (thus reducing the amounts of the needed analgesia) and improving wound-healing rates.

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Conflicts of interest

There are no conflicts of interest.

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