Study the effect of zinc oxide ointment on symptoms arising from hemorrhoids and anal fissure

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Abstract
Introduction: Anal fissure and hemorrhoids are the most common anorectal complaints. According to the prevalence of these diseases and the complications of their surgical treatments, attempts to relieve the symptoms of the disease with medical treatments, including the use of topical agents, are ongoing. This study was performed to study the effect of zinc oxide ointment on symptoms arising from hemorrhoids and anal fissure.

Materials and Methods: In a randomized clinical trial on patients with hemorrhoids and anal fissure referred to Amir al-Momenin hospital surgery clinic, 108 patients were examined in two groups. In the intervention group (n = 55) patients received zinc oxide ointment and in the control group (n = 53) placebo received vaseline in the anus area twice a day for one month. In addition, sitz bath and high fiber diet were recommended to all patients. At the end, the rate of pain reduction, bleeding and itching were compared between the two groups.

Results: The results showed that at the end of the study, the mean pain rate, mean bleeding per day and mean itching severity in all patients were significantly decreased in both groups. However, this difference was not significant in the case (control) and control (placebo) groups, and likewise in the fissure and hemorrhoid patients in the case and control groups.

Conclusion: Medical treatment helps relieve symptoms in most fissure and hemorrhoids patients. In this treatment, topical use of zinc oxide ointment is not superior to vaseline, and both zinc oxide ointment and vaseline are effective as a part of medical treatment.

Key words: Hemorrhoids, Anal fissure, Zinc oxide.

Introduction
Hemorrhoids are the most common anorectal complaints and over half of people experience symptoms of hemorrhoids at some point in time (1). Hemorrhoids are vascular cushions in the lower part of rectum and anus which help to close the anus completely and create stool maintenance. Primary treatment of hemorrhoids included dietary fiber supplementation; Topical agents such as: ointment and suppository are common and may help relieve symptoms. In hemorrhoids that do not respond to medical treatment, are used methods such as: elastic bandage; sclerotherapy; thermotherapy and surgery (1, 2, 3).

Anal fissure is also the most common cause of severe pain of anorectal. Anal fissure is a gap and crack below the dentition line, which usually presents with severe pain during stool disposal. The primary treatment for this disease is the use of sitz bath a high-fiber diet and topical treatments such as nitroglycerin ointment. Surgery is used in cases that do not respond to medical treatment, including internal sphincter anal sphincterotomy (1, 3). But hemorrhoids and fissure's surgical treatment is associated with complications such as urinary retention, wound infection, bleeding after surgery, incontinency, and anus stenosis (4, 5).

One of the medications used in the treatment of these two common diseases is zinc oxide ointment, which has been raised to reduce the itching and anus stimulation to reduce pain and swelling in hemorrhoids (4, 6).

The role of zinc in the anti-inflammatory response and create resistance to infection is well known (7). Zinc can accelerate wound healing by increasing skin cell generation (8, 9). Zinc as a main factor, has a big role in cellular activities including DNA production, bone construction and generation and wound healing. It has also been implicated in the function of more than 300 types of enzymes and biological reactions and in safety performance including regulation of TCD4 and interleukin 2 lymphocyte activity and antiviral activities (10,11,12,13). Recent studies represent the role of zinc in the cellular signaling path, and states that it can be used in antitumor drugs (14). In some studies, topical zinc has been used in wound management to promote wound healing (15,16,17), without increased pain, cellular abnormalities or other harmful effects (18).

Based on the broad array of role of zinc, the goal of this study was to evaluate the effect of zinc oxide ointment on hemorrhoids and anal fissure symptoms and to present an effective and low complicated method for the treatment of hemorrhoids and fissure and to reduce the need for surgery in patients who suffer from these diseases.

Materials and Methods
Patient selection and grouping
This study was performed as an interventional double-blind randomized clinical trial on 108 patients who referred to Amir al-Momenin hospital. Patients were entered in the study after checking exclusion and inclusion criteria. The patients were randomly divided into two groups of case (drug) and control (placebo) and received zinc oxide ointment an vaseline respectively.

Inclusion criteria
Patients were entered to the study, who referred to the surgical clinic of Amir al-Momenin Hospital and diagnosed with chronic anal fissure (Fissure dose not heal within 6-8 weeks) or grade 1 or 2 internal hemorrhoids. All selected samples should not have received specific treatment for at least the past 1 week.
Study the effect of zinc oxide ointment on symptoms arising from hemorrhoids and anal fissure

Exclusion criteria
Patients with acute fissure or external hemorrhoids or internal grade 3 or 4 hemorrhoids, and who had hemorrhoids and fissure at the same time, were excluded.

Study the effect of ointment
The usage of zinc oxide ointment (By eposink 20% brand of Caspian Supply Company of Iran) was that the patient was applied, into and around the anus twice a day. In the control group, patients taking the placebo completed the symptom registration form. If the patient could not complete the form, help was received from the closest family member. At the first visit, the patient was given a form to fill in on a daily basis based on their symptoms. In this method, the patient had to score its pain severity from zero to 10, zero for no pain and 10 for maximum degree of pain according to VAS index (19). Also they had to record presence or absence and frequency of bleeding and presence or absence of itching every day. Patients were followed for 30 days, during this period, they were visited twice within 15 days, and symptoms of bleeding, pain and itching were assessed. If the patient did not consent to continue treatment, they were not completed the forms and also if the patient needed another treatment during the study, they would be excluded.

Data analysis
After data collection, the database was prepared by PASW software (Version 18, © IBM SPSS Inc.) and the information entered. Descriptive results were extracted in the form of tables and diagrams. T-test was used to compare the response of treatment for quantitative variables; the comparison was calculated based on the mean of symptom reduction after intervention. In all cases were considered $\alpha = 0.05$.

Result
108 patients were studied in two groups which 53 (49.1%) were in the case group (receiving dioxide ointment) and 55 (50.9%) were in the control group (receiving placebo). Among them, 74.1% (n = 80) were diagnosed with chronic fissure and 25.9% (n = 28) with hemorrhoids. All patients with hemorrhoids in this study had grade 2 hemorrhoids. 78.3% of patients (85 patients) were female and 21.3% (23 patients) were male. The mean age of the patients was 12.13 ± 30.13 years.

Response to treatment was estimated for each patient by decreasing the mean pain score, decreasing the mean bleeding times per day, and decreasing the mean severity of itching from the beginning to the end of the study. As illustrated in the diagram 1, the mean pain score in all patients at the end of the study was significantly reduced compared to baseline, and this decrease was statistically significant. In addition, the mean bleeding times per day and mean severity of itching decreased significantly in all patients (Table 1).

Table 1: Response to treatment with (zinc oxide or placebo and other medical treatments) in patients with fissure or hemorrhoids in all patients (108 patients)

<table>
<thead>
<tr>
<th>Significance level</th>
<th>After treatment</th>
<th>Before treatment</th>
<th>The mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.001</td>
<td>1.28 ± 1.49</td>
<td>3.87 ± 2.90</td>
<td>Pain score</td>
</tr>
<tr>
<td>&lt;0.001</td>
<td>0.16 ± 0.17</td>
<td>0.38 ± 0.56</td>
<td>bleeding times per day</td>
</tr>
<tr>
<td>&lt;0.001</td>
<td>0.12 ± 0.33</td>
<td>0.44 ± 0.79</td>
<td>Itching severity</td>
</tr>
</tbody>
</table>

But there was no statistically significant difference between the two groups, case (zinc oxide) and control (placebo), in the mean pain score, mean bleeding times per day and mean itch severity from baseline to end of study (Table 2). In other words, the treatment in both groups had the same effect on the patients’ symptoms, and in this sense, the zinc oxide ointment had no superiority over vaseline (used as a placebo in this study).

Table 2: Comparison of treatment response in patients with fissure or hemorrhoids in the study groups

<table>
<thead>
<tr>
<th>Significance level</th>
<th>After treatment</th>
<th>Before treatment</th>
<th>The mean reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;0.05</td>
<td>2.52 ± 2.21</td>
<td>2.64 ± 2.63</td>
<td>Pain score</td>
</tr>
<tr>
<td>&gt;0.05</td>
<td>0.19 ± 0.51</td>
<td>0.25 ± 0.62</td>
<td>bleeding times per day</td>
</tr>
<tr>
<td>&gt;0.05</td>
<td>0.32 ± 0.51</td>
<td>0.31 ± 0.67</td>
<td>Itching severity</td>
</tr>
</tbody>
</table>

Diagram 1: Response to treatment (reduction of pain score) in patients with fissure or hemorrhoids in all patients (n = 108) and study groups of (zinc oxide, n = 53) and control (placebo, n = 55)
Study the effect of zinc oxide ointment on symptoms arising from hemorrhoids and anal fissure

According to diagram 2 and table 3, no statistically significant difference was observed between fissure and hemorrhoid patients in the case and control groups, in mean pain score, mean bleeding times per day and mean itch severity from baseline to end of the study. In fact, the zinc oxide ointment and vaseline ointment had the same effect on the reduction of fissure symptoms and also on the reduction of hemorrhoid symptoms. No complication was observed in either case or control group.

### Table 3: Comparison of treatment response in study groups based on disease type (Fissure or Hemorrhoids)

<table>
<thead>
<tr>
<th>Significance level</th>
<th>Hemorrhoids</th>
<th>Fissure</th>
<th>The mean reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control group (14 people)</td>
<td>Case group (14 people)</td>
<td>Control group (41 people)</td>
</tr>
<tr>
<td>&gt; 0.05</td>
<td>0.25 ± 0.69</td>
<td>0.85 ± 1.23</td>
<td>3.30 ± 2.00</td>
</tr>
<tr>
<td>&gt; 0.05</td>
<td>0.43 ± 0.68</td>
<td>0.57 ± 0.89</td>
<td>0.10 ± 0.41</td>
</tr>
<tr>
<td>&gt; 0.05</td>
<td>0.29 ± 0.47</td>
<td>0.58 ± 0.82</td>
<td>0.33 ± 0.53</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Pain score bleeding times per day Itching severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>Pain score bleeding times per day Itching severity</td>
</tr>
</tbody>
</table>

Diagram 2: Comparison of treatment response in case (zinc oxide) and control (placebo) groups based on disease type (Fissure or Hemorrhoids)

### Discussion

- The present study showed that in all patients, both in the group receiving zinc oxide ointment and in the group receiving vaseline, symptoms were significantly reduced, in both groups. Similar studies have shown that many hemorrhoids patients benefit from the use of zinc oxide ointment twice a day in and out of the anus (1).
- Our study showed that there was no significant difference in effectiveness between patients with chronic fissure and patients with hemorrhoids. In fact, the study found that the zinc oxide ointment is not superior to vaseline in treating chronic fissure and hemorrhoids symptoms, and the both medications have the same effect in relieve the symptoms of these patients. This study have been reported that the zinc oxide ointment and vaseline medications caused reduction in injury and itching in patients with hemorrhoids. In the same study, both vaseline and oxide ointment used uniformly and gave similar effects to these two medications, that confirming our study findings and showed that these two medications are effective in reducing hemorrhoid symptoms and using either one or one of them can be helpful (6).
- Most of the studies related to the present study are not clinical trials and they comment with suspicious and doubt. As stated in a study, there are several topical medications and suppositories for the treatment of hemorrhoids. But there is little evidence to support the use of these drugs (21). Or another study in this regard has said that usage of non-prescription ointments containing steroids, analgesics, astringents (including zinc oxide) are often recommended. But no clinical trial study supports this use (22).
- About the Mechanism of the Effect of zinc oxide on fissure and Hemorrhoids, taking into account existing studies on the effect of topical zinc oxide on wound healing and accelerated wound epidermal layer (23), sun burn (20) improving biological metabolism performance (24) anti-inflammatory pathway and antibacterial effects (7), we expected that patients who receiving zinc oxide ointment would show a greater reduction in symptom severity than patients who receiving vaseline. But the two medications appear to have worked with a similar mechanism to hemorrhoids and fissure. Protective materials create a physical barrier on the skin that prevents stool from contacting the wound, reducing pain and itching. As regards that both vaseline and zinc oxide ointment are
both protective materials, it seems that the mechanism mentioned in the Gupta study has been effective in treating both hemorrhoids and fissure cases (4).

- Given that our findings indicate a positive effect of zinc oxide and Vaseline on hemorrhoids and fissure treatment, this result underscores the importance of fissure and hemorrhoids medical treatment with the use of high fiber diets and topical ointments and thereby reducing the need for surgery. This has also been mentioned in other studies (1-5). It is important to pay attention to non-aggressive treatment and prevention of hemorrhoids in reducing injury to patients, and there is an important list of medications and research related to this issue that emphasizes surgical reduction (25, 26). But the important point is that in many cases, non-surgical treatments, especially topical or medicinal methods, are not completely effective. Therefore, a progress in our understanding of the pathophysiology of these diseases is needed in order to develop new and innovative ways of treating them, is greatly felt.

Conclusion
Medical treatment including zinc oxide ointment helps to relieve symptoms in most fissure and hemorrhoids patients. In this treatment method, topical use of zinc oxide ointment is not superior to Vaseline and these two medications are both effective as part of medical treatment.

Conflict of Interest
The author has no conflicts of interest to declare.

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