Heliyon 10 (2024) e27215

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

The efficacy of topical *sodium pentaborate* formulation on hemorrhoid disease: A randomized, double-blind, placebo-controlled trial

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ARTICLE INFO

Keywords:
Sodium pentaborate pentahydrate
Hemorrhoid disease
Randomized controlled trial

ABSTRACT

Background: The topical application of boron has been significantly associated with intensifying wound healing. Using 3% boric acid in deep wounds significantly contributes to wound healing and reduces the duration of hospitalization in the intensive care. The objective of this study was to assess the therapeutic impact of a topical gel containing *sodium pentaborate pentahydrate* on the management of wounds resulting from grade 1 to 3 hemorrhoids.

Methods: In this randomized double-blind placebo-controlled trial, we applied a topical gel consisting of *sodium pentaborate pentahydrate* 3% on 206 eligible patients with the diagnosis of grade 1, 2, and 3 hemorrhoid diseases. Then patients were randomly allocated to two groups of *sodium pentaborate pentahydrate* or placebo gel with a ratio of 1:1 and received the allocated gel for four weeks. Patient hemorrhoid symptoms severity, hemorrhoid degree, and anoscopy findings were compared before and after the trial.

Results: Before the intervention, symptom severity ($p > 0.05$) and anoscopy findings ($p = 0.815$) were similar between the two groups. Subsequent to the intervention, a majority of patients in the

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https://doi.org/10.1016/j.heliyon.2024.e27215
Received 15 December 2023; Received in revised form 23 February 2024; Accepted 26 February 2024
Available online 29 February 2024

intervention group experienced a reduction in anal itching compared to the placebo group [adjusted mean difference (aMD) 95% CI: -1.98 (−2.2 to −1.8), p = 0.007]. Moreover, resting pain [aMD (95% CI): -1.37 (−1.6 to −1.1), p = 0.015], pain during defecation [aMD (95% CI): -2.19 (−2.4 to −2.0), p = 0.005], feeling a lump in the anus (aMD (95% CI): -0.71 (−1.2 to −0.2), p = 0.011), bleeding during defecation (41.7% vs. 66.9%, p = 0.027), and hemorrhoid degree (p < 0.001) in the intervention group was less than the placebo group.
Conclusion: Our findings indicate the effectiveness of the study gel on hemorrhoid symptoms and anoscopy findings in patients.

1. Introduction

Hemorrhoid disease is a common disorder that significantly changes the quality of life [1]. Up to one-third of the general population suffer from hemorrhoids. It is defined as symptomatic enlargement and distal displacement of normal anal cushions [2,3]. The disease is usually characterized by anal bleeding during defecation with or without anal tissue prolapse [4,5]. This disease is classified as benign, but due to its high social impact, it is of great importance in terms of diagnosis and treatment [6]. Numerous risk factors have been cited for the exacerbations of the disease, including aging, obesity, depressed mood, and pregnancy [7]. In addition, some conditions associated with increased intra-abdominal pressure, such as constipation and prolonged contraction, progressively cause hemorrhoids by reducing venous drainage of the hemorrhoid network [8].

External hemorrhoids usually do not require special treatment unless they suddenly become thrombotic. Lower-grade internal hemorrhoids can be effectively treated with medication and non-invasive methods such as rubber band ligation and sclerotherapy injections. Surgery is used for high-grade internal hemorrhoids or when non-invasive methods have failed [9]. Classic treatments for grades I and II include increased water intake, a high-fiber diet, and the use of topical ointments such as steroids and anesthetics which might reduce the symptoms. Treatment for grades III and IV may include non-surgical or surgical interventions [10]. Different gels and ointments, creams, oral venoactive medicines, homeopathy, phytotherapy, and food supplements were encompassed within medicinal products and drugs [11]. Topical treatment may be helpful in selected groups of hemorrhoid patients, but many patients do not get enough symptom relief with these methods and may need more intervention [4]. The development of treatment strategies that can reduce the symptoms and control the underlying pathology in this disease, could be promising for disease management.

Boron is known as an essential element for plants which is required to determine the structure and function of the cell wall. It is important in the nutrition and metabolism of the human body [12]. Boron properties include regulatory functions in the cell membrane and different enzymatic systems, exhibiting epithelializing, angiogenesis-enhancing, anti-inflammatory, antioxidant, and antimicrobial impacts [13,14]. Boron, an element not inherently toxic, holds potential for utilization in therapeutics, as recognized by medicinal chemists [15]. The topical application of boron has been significantly associated with improving wound healing [16]. Using boric acid in deep wounds as well as in chronic wounds significantly contributed to wound healing and reduced hospitalization time compared to silver nitrate or other widely used products [17,18]. The findings of previous studies revealed that the application of gel or solution containing *sodium pentaborate pentahydrate* versus Kloroben spray, placebo gel, topical conventional remedy, and chlorhexidine gel had a significant preventive effect on several categories of radiation dermatitis and therapeutic effects on diabetic wounds, diabetic foot ulcer, recurrent aphthous stomatitis, and postpartum episiotomy site, respectively [19–22].

Nevertheless, the influence of this element on the healing process of hemorrhoid wounds has not yet been investigated. The objective of the study was to determine the regenerative impact of a *sodium pentaborate*-based topical gel on the management of hemorrhoids (primary outcome); moreover, the possible side effects of the drug were assessed as a secondary outcome through this study.

2. Material and methods

2.1. Study design and participants

This study was designed as a randomized, double-blind, placebo-controlled, parallel-armed trial with registration number IRCT20190701044062N1 on 13/07/2019, which was approved by the Regional Research Ethics Committee of Tabriz University of Medical Sciences (IR.TBZMED.REC.1398.235). This research was implemented in accordance with the principles of the Declaration of Helsinki. All patients were verbally informed about the study protocol and written informed consent was obtained. The study was performed in the gastroenterology outpatient clinics of Tabriz Nejat Hospital, Tabriz Imam Reza Hospital, Tabriz Salamat Polyclinic, and Tabriz Valiasr Hospital through purposive sampling. We entered 206 patients with a ratio of 1:1 with the diagnosis of grade 1, 2, and 3 hemorrhoid diseases based on the Goligher classification [23]. The clinical diagnosis was established through physical examination, specifically through the utilization of digital rectal examination and colonoscopy, in patients presenting compatible complaints. The inclusion criteria included age between 18 and 65 years, and being diagnosed with grade I, II, or III internal hemorrhoids without the need for emergency interventions based on physical examination. We excluded patients with anal disorders including inflammatory bowel disease, fissure, fistula, perianal rash, rectal prolapse, anal tumors, and rectum and perianal infections; pregnancy or breastfeeding women; a history of serious heart, neurologic, liver, and kidney disease as well as taking any local analgesic/treatment or medical treatment for the past seven days, prohibition of topical use of vaseline or *sodium pentaburate*.

All information obtained from patients, including personal information, general health, questionnaires, and forms for assessing the clinical status of patients was considered confidential and archived using random codes assigned to each patient. Eligible patients were admitted to the study only by obtaining informed consent and explaining the study process to them.

2.2. Randomization and intervention

Patients were randomly assigned to receive either the formulation gel (containing 3% sodium pentaborate pentahydrate) [19] or the placebo gel in a double-blind trial. Randomization was conducted in the hospital pharmacy using a computer-generated method, ranging from one to the final participant. All gels were put in indistinguishable tubes and labeled as A and B by personnel who had no other involvement in the trial. The label code was kept undefined and remained with the biologist who prepared the drug during the trial and was not available to the investigators until the end of the trial, data collection, and analysis. The tubes containing placebo or active formulation were randomly labeled as A/B and distributed to the patients according to the generated sequence from one to the last participant by the physician after confirmation of inclusion criteria. Participants, care providers, and researchers were blinded after the assignment to interventions.

The intervention and control groups received *sodium pentaborate pentahydrate* and placebo gel twice a day for one month. Patients were provided with instructions to cleanse the designated area using a mild cleansing agent and water, ensuring thorough rinsing, and subsequently gently drying the area prior to utilization. The application of the product was to be administered to the affected external area adjacent to the anus twice daily, once in the morning and once before retiring to bed. Additionally, participants were duly informed that in the event of any occurrence of adverse effects, immediate cessation of medication use was imperative, followed by prompt reporting. Subsequently, regular telephone communication was established on a weekly basis in order to facilitate necessary follow-up procedures and to reinforce appropriate usage. Following a duration of one month, patients from both groups were subjected to an evaluation in order to assess alterations in the severity of the ailment, potential complications, discontinuation of treatment, and adherence to the prescribed medication regimen. This evaluation was accomplished through the administration of questionnaires and re-evaluation conducted by the attending physician. In addition, at the beginning of the study, the participants were provided with one routine topical anti-hemorrhoid medicine to use only on necessary occasions and report to the researcher. Upon the identification of any cessation of treatment, a comprehensive investigation was conducted to determine the underlying cause.

At the end of the intervention, all participants were visited by a gastroenterologist, and if necessary, anti-hemorrhoid ointment and routine treatments were prescribed and necessary recommendations were given.

2.3. Data collection

After the careful selection of eligible patients, the participants subsequently proceeded to fulfill the demographic information form as well as a questionnaire specifically designed for patients.

The severity of hemorrhoid symptoms in patients before and after the administration of *sodium pentaborate* gel was determined using the Sodergren's scale of symptoms evaluated itching or irritation, instances of pain or discomfort experienced during periods of rest, as well as pain or discomfort encountered while defecating through scores ranging from 0 (no symptoms) to 5 (severe) and the frequency of feeling a lump in the anus (prolapse) ranging from 0 to 4 [24].

The grade and number of hemorrhoid cushions in patients before and after the administration of *sodium pentaborate* gel were evaluated using the Goligher prolapse score [25], physical examination, and rigid anoscopy.

During the first visit, both groups of patients were examined by a physician, and a rigid anoscopy was done on them. A second questionnaire, known as the physician's questionnaire, was filled by the examining physician to determine the extent and quantity of hemorrhoid cushions, and was subsequently archived for the purpose of assessing the findings subsequent to intervention.

At the end of the intervention, side effects and drug adherence were also assessed by the related questionnaires.

2.4. The preparation of the medicines

The sodium pentaborate pentahydrate 3% gel and placebo gel (without boron) were provided by Mofid Darou Pharmacy Company in a completely similar appearance (the shape and size of the container, and the odor and color of the gels). The gel *sodium pentaborate pentahydrate* 3% was prepared according to the previously described protocol [26]. Both topical gels were prescribed twice a day for one month.

2.5. The sample size estimation

The basic information needed to calculate the sample size was extracted from Doğan et al., in 2014 [27]. Using the G-Power software, with a 95% confidence interval, a test power of 80%, and a 20% probable drop, the sample size was calculated to be 206 for two groups.

2.6. Statistical analysis

Firstly, the normality of the distribution of continuous data was examined by utilizing Skewness and Kurtosis statistics. Data were described as number (%) for categorical variables and median (range) for continuous variables according to the groups. Two-tailed

hypothesis tests were set to test the equality of the two groups at a significance level of 5%. Independent *t*-test, Fisher's exact test, and Mann-Whitney test were performed for between and within group comparison of categorical variables. Furthermore, Independent *t*-test and ANCOVA adjusted for age, BMI, and patients' baseline status as confounders were used for between-group comparisons of continuous variables. SPSS version 26 was used for Data analysis. All analyses were based on intention-to-treat.

3. Results

This study was performed on 206 patients with symptomatic internal hemorrhoids (who underwent a colonoscopy to rule out any other disease) from August 2019 to April 2020. After selecting eligible patients who consented to participate, they were randomly divided into two groups of 103 people for each intervention group control group (Fig. 1). Among the 206 participants following the one-month intervention, 165 (80.1%) individuals reported adhering to the prescribed regimen on a daily basis, while a total of 24 individuals (11.6%) reported adhering to it on most days, 6 (2.9%) participants reported being adherent sometimes, 11 (5.4%) people discontinued intervention. No adverse events were reported following intervention in this study.

Patients included 40 (38.8%) women and 63 (61.2%) men in the boron group and included 51 (49.5%) females and 52 (50.5%) men in the control group ($p = 0.123$). The mean ± standard deviation (SD) age of participants in the intervention and placebo group was 54.43 years ± 14.7 and 57.16 years ±14.8, respectively ($p = 0.689$). The mean ± SD weight of patients was 78.77 kg ± 14.74 in the intervention group and 79.14 kg ± 48.44 in the placebo group ($p = 0.731$). The mean ± SD BMI in the intervention group was 27.37 $kg/m^2 \pm 5.7$ and 27.4 $kg/m^2 \pm 7.9$ in the control group ($p = 0.655$). There were no statistically significant differences between the two groups regarding diet ($p = 0.218$), walking ($p = 0.369$), cycling ($p = 0.774$), cycling time ($p = 0.860$), doing professional sports ($p = 0.065$), professional exercise time ($p = 0.228$), job status ($p = 0.743$), classroom attending ($p = 0.147$), watching TV time ($p = 0.179$),

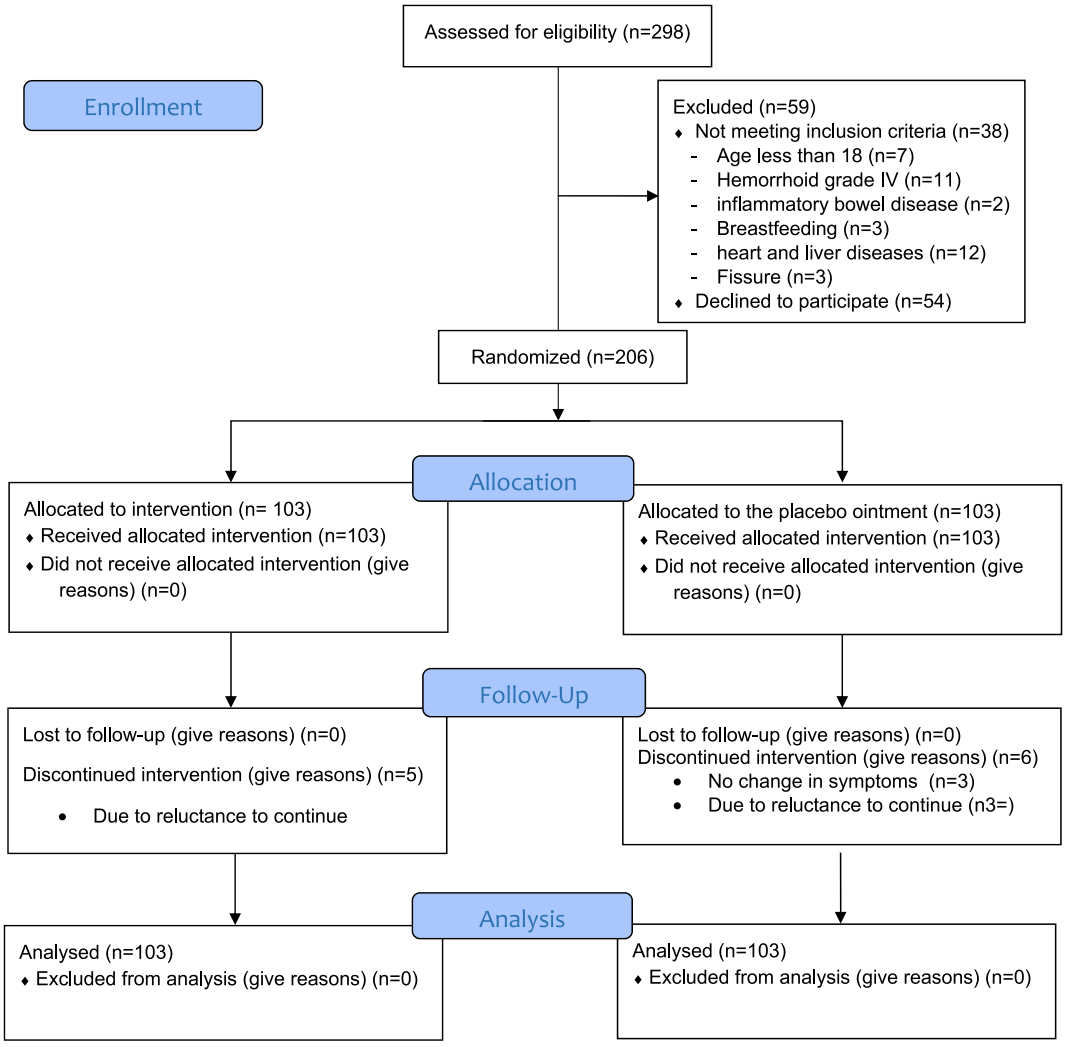

Fig. 1. The consort flowchart of the study.

average sleep in 24 h a day ($p = 0.352$), average daily sleep duration ($p = 0.727$), the average night sleep time ($p = 0.209$). However, walking time ($p = 0.018$), standing time ($p = 0.018$), and watching TV ($p = 0.024$) were different between groups (Table 1).

The results of Fisher's exact test indicated that the frequency of anal itching ($p = 0.470$) and itching intensity score ($p = 0.927$) was similar between groups at baseline. After one month of using *sodium pentaborate* and placebo gel, anal itching significantly decreased in the intervention compared to the placebo group (44 (42.7%) vs. 61 (59.2%) participants) ($p = 0.032$). ANCOVA adjusted for confounders showed a significant reduction was reported regarding the itching intensity score in the intervention compared to the placebo group (adjusted mean difference (aMD) (95% CI): -1.98 (−2.2 to −1.8); $p = 0.007$). In terms of pain at rest, according to Fisher's exact test, there was no significant inter-group difference at baseline ($P > 0.05$). Pain at rest significantly decreased in participants in the intervention group compared to the placebo group ((34 (33.0%) vs. 71 (68.9%)) ($p = 0.043$). A significant decrement was observed in the intensity score of pain in the boron in comparison with the placebo group (aMD (95% CI): -1.37 (−1.6 to −1.1); $p = 0.015$) based on ANCOVA. The frequency and mean score of pain intensity during defecation were not different at baseline between groups ($P > 0.05$). Fisher's exact test illustrated that following the intervention, pain during defecation significantly decreased in the intervention group compared to the placebo group ((44 (42.7%) vs. 63 (61.2%) participants) ($p = 0.027$). According to ANCOVA, the pain intensity score during defecation in the intervention was significantly lower than in the placebo group (aMD (95% CI): -2.19 (−2.4 to −1.1); $p = 0.005$). In the study of feeling a lump in the anus and its intensity score, the two groups were not different before intervention ($P > 0.05$). After the intervention, feeling a lump in the anus significantly reduced in the intervention group compared to the placebo group (58 (56.3%) vs. 60 (58.2%) participants) ($p = 0.036$). ANCOVA adjusted for confounders indicated that the lump sensation score significantly dropped in the intervention compared to the placebo group (aMD (95% CI): -0.71 (−1.2 to −0.2); ($p = 0.011$). Fisher's exact test showed no significant inter-group difference in terms of bleeding during defecation at baseline ($p = 0.357$). Bleeding during defecation in the intervention (43 (41.7%)) was significantly more than in placebo (69 (66.9%)) ($p = 0.039$) following the intervention (Table 2).

Mann-Whitney test indicated that regarding the disease grade reported in colonoscopy, the two groups were similar at baseline ($p = 0.815$). After the intervention, significant improvement was observed in the intervention group compared to the placebo ($p < 0.001$) (Table 3).

The finding regarding the number of hemorrhoid cushions illustrated that the two groups were similar before intervention ($p = 0.911$). The number of hemorrhoid cushions significantly decreased in the intervention group [15 (14.56%) people had 1, 19 (18.44%) people 2, 24 (23.30%) people 3, 22 (21.35%) people 4, 17 (16.50%) patients 5 and 6 (5.82%) patients had 6 cushions] in comparison with the placebo group [7 (6.79%) patients 1, 5 (4.85%) patients 2, 22 (21.35%) patients 3, 33 (32.03%) patients 4, 26 (25.24%) patients 5, and 10 (9.70%) patients had 6 cushions] ($p = 0.023$) based on Mann-Whitney test (Table 4).

No adverse event was reported during this trial. Drug adherence was 86% and 89% among participants in the placebo and intervention group, respectively, according to the daily use checklist and consumed drug tubes.

4. Discussion

In this study, we evaluated the efficacy of *sodium pentaborate* gel in the treatment of hemorrhoid disease by investigating patients' symptoms and rigid anoscopy findings by physicians. In the study of gender, age, weight, height, BMI, marital status, level of education, diet, type of diet, walking, cycling status, cycling duration, professional exercise, professional exercise time, the status of employment, attending classes, and extracurricular activities, duration of watching TV, duration of sleep in 24 h a day, duration of

Table 1
Demographic data of the participants by study groups.

Variable	**Intervention**	**Placebo**	**P-value**
	n=103	**n=103**	
Age **(year)**	14.7 ± 54.43	14.8 ± 57.16	0.68[a]9[a]
Gender **(male/female)**	63/40	52/51	0.123[b]
Weight **(kg)**	14.74 ± 78.77	48.44 ± 79.14	0.731[a]
Height **(cm)**	88.66 ± 168.8	41.01 ± 169.7	0.632[a]
BMI **(kg/m^2)**	5.7 ± 27.37	7.9 ± 27.4	0.655[a]
Marital status (married/single)	93/10	95/8	0.669[b]
Diet (yes/no)	10/93	16/87	0.218[b]
Walking (yes/no)	99/4	102/1	0.369[b]
Cycling (yes/no)	7/96	6/97	0.774[b]
professional sport (yes/no)	7/96	1/102	0.065[b]
Employed/unemployed	67/36	63/40	0.743[b]
Classroom attending (yes/no)	9/94	4/99	0.147[b]
non-course class (yes/no)	3/100	3/100	1.00[b]
Watch TV (do/do not)	103/0	98/5	0.024[b]
Sleep duration 24 h a day	2.39 ± 8.52	2.8 ± 8.28	0.352[a]
Average daily sleep duration	0.87 ± 1.39	0.4 ± 1.47	0.727[a]
Average night sleep duration	1.95 ± 7.13	1.69 ± 6.81	0.209[a]

[a] Independent *t*-test.
[b] Fisher exact test.

Table 2
Pre and post-treatment symptoms presence and their intensity among participants by study groups.

Symptoms	Intervention n (%) n = 103	Placebo n (%) n = 103	p-value±	Intervention Mean ± SD	Placebo Mean ± SD	Adjusted MD 95% CI	p-value
Anal itching				**Intensity score** (1–5)			
Baseline	66 (64%)	61 (59.2%)	0.47	3.14 ± 0.36	3.17 ± 0.61	–	0.927[a]
End	44 (42.7%	61 (59.2%)	0.032	1.12 ± 0.09	3.10 ± 0.52	−1.98 (−2.2 to −1.8)	0.007[b]
Pain at rest				**Intensity score** (1–5)			
Baseline	44 (42.7%)	43 (41.7%)	0.112	2.72 ± 0.33	2.53 ± 0.46	–	0.871[a]
End	34 (33.0%)	71 (68.9%)	0.043	1.32 ± 0.09	2.69 ± 0.32	−1.37 (−1.6 to −1.1)	0.015[b]
Pain at defecating				**Intensity score** (1–5)			
Baseline	57 (55.4%)	56 (54.3%)	0.888	3.58 ± 0.52	3.16 ± 0.36	–	0.064[a]
End	44 (42.7%)	63 (61.1%)	0.027	1.23 ± 0.19	3.42 ± 0.51	−2.19 (−2.4 to −2.0)	0.005[b]
Feeling a lump in anus				**Intensity score** (1–4)			
Baseline	62 (60.2%)	59 (57.2%)	0.669	2.53 ± 0.34	2.55 ± 0.22	–	0.064[a]
End	58 (56.3%)	60 (58.2%)	0.036	1.72 ± 0.16	2.43 ± 0.29	−0.71 (−1.2 to −0.2)	0.011[b]
Bleeding in defecating							
Baseline	75 (72.8%)	69 (66.9%)	0.357	–	–	–	–
End	43 (41.7%)	69 (66.9%)	0.039	–	–	–	–

Sodergren Hemorrhoid symptom severity scoring system (1–5 or 1–4): from lowest to highest severity.
± Fisher's exact test.
[a] Independent *t*-test.
[b] ANCOVA adjusted for baseline status.

Table 3
Pre and post-treatment colonoscopy grade of participants by study.

Colonoscopy grade	Intervention group n (%)	Placebo group n (%)	P- value[a]
Baseline			
1	48 (46.60%)	50 (48.54%)	0.815
2	41 (39.80%)	38 (36.89%)	
3	14 (13.59%)	15 (14.56%)	
End of Intervention			
1	74 (71.84%)	48 (46.60%)	
2	26 (25.25%)	39 (37.86%)	<0.001
3	3 (2.91%)	16 (15.53%)	

Goligher Classification: 1) No prolapse 2) Prolapsed with defecation, but reduced spontaneously 3)Prolapse with defecation requiring manual reduction 4) prolapsed and non-reducible.
[a] Mann-Whitney.

Table 4
Pre and post-treatment number of hemorrhoid cushions of participants by study groups.

Number of hemorrhoid cushions	Intervention n (%)	Placebo n (%)	P-value
Baseline			
1	11 (10.67%)	7 (6.79%)	0.911
2	6 (5.82%)	5 (4.85%)	
3	23 (22.33%)	21 (20.38%)	
4	33 (32.03%)	34 (33%)	
5	21 (20.38%)	26 (25.24%)	
6	9 (8.73%)	10 (9.70%)	
End of intervention			
1	15 (14.56%)	7 (6.79%)	
2	19 (18.44%)	5 (4.85%)	
3	24 (23.30%)	22 (21.35%)	0.023
4	22 (21.35%)	33 (32.03%)	
5	17 (16.50%)	26 (25.24%)	
6	6 (5.82%)	10 (9.70%)	

¥ Mann-Whitney.

sleep during the day, and duration of sleep during the night between the two groups, there was no significant difference. However, more patients in the intervention group watched TV.

Prior to the implementation of the intervention, none of the variables exhibited any significant differences between the two groups. Nevertheless, following the implementation of the intervention, it was observed that a majority of patients in the boron group experienced a reduction in anal itching compared to those in the placebo group. Also, resting pain, pain intensity at rest, pain during defecation, pain intensity during defecation, feeling lump in the anus, the score of a feeling lump in the anus, and bleeding during defecation in the intervention group was less than the placebo group. The grade and number of hemorrhoid cushions were also significantly lower than the placebo group. These findings collectively demonstrate the efficacy of topical *sodium pentaborate* gel in alleviating hemorrhoid symptoms among patients.

Although almost nothing is known about the mechanism of boron in wound healing, limited studies have reported some molecular changes in cellular activity after treatment with boron in vitro. Sodium borate, the sodium salt of boric acid, has been shown to have inductive effects on human keratinocyte migration without causing cell proliferation [28]. The wound-healing activity of *sodium pentaborate* has been evaluated previously by in vitro wound healing studies and in vivo models of excisional, burn, and diabetic chronic ulcer wounds. Boron increased cell viability and migration of fibroblast cells and induced re-epithelization which facilitated the wound-healing process [27,29,30]. Kapukaya in a clinical trial on participants with chronic wounds of diverse etiological reasons (diabetic, decubitus ulcer, secondary to trauma, etc) indicated that the administration of sponges containing boric acid has the potential to positively affect the healing process of chronic wounds. This is achieved through the enhancement of cellular proliferation, cellular differentiation, cellular migration, and the provision of antimicrobial properties when used in conjunction with the negative pressure on the wound [18]. Another study conducted by Kanaza Gul et al. demonstrated that the use of a Boron-based gel on the postpartum episiotomy site in primiparous patients, twice daily for a duration of 10 days, resulted in expedited healing of the episiotomy wound and a reduction in pain experienced [21]. Furthermore, in another clinical trial, boric acid powder was employed in the treatment of two patients with diabetic wounds. It effectively eliminated necrosis and expedited the wound-healing process [22].

Nagoba and colleagues demonstrated that the establishment of an acidic milieu through boron administration effectively regulates wound healing processes. This is achieved by managing wound infections, augmenting antimicrobial efficacy, modulating protease activity, facilitating oxygen release, mitigating the cytotoxicity of bacterial byproducts, promoting epithelialization, and enhancing angiogenesis [31]. These findings bear similarity to the observations made in the present investigation. In a preceding investigation, Şafak and colleagues aimed to compare the efficacy of oxytetracycline and *sodium pentaborate pentahydrate* in the remedy of anterior epistaxis. The study included a total of 66 patients with recurrent anterior epistaxis, with 32 patients receiving topical *sodium pentaborate pentahydrate* gel and 34 patients receiving topical oxytetracycline treatment. The results indicated that the use of *sodium pentaborate pentahydrate* gel yielded similar treatment outcomes to oxytetracycline. However, there was a significant reduction in the frequency of epistaxis during the first week following treatment with *sodium pentaborate pentahydrate* gel [32]. This discovery is incongruous with our own in relation to diminishing the quantity of bleeding from the rectum.

Demirci et al. demonstrated that boron derivatives play a role in regulating the proliferation and movement of cells, expression of growth factors, and inflammation during the healing of wounds in a diabetic ulcer animal model induced by streptozotocin. In laboratory settings, boron derivatives, owing to their antimicrobial activity, incite proliferation and expression of growth factors, thereby augmenting the protective effects of dermal cells [17]. While all of the aforementioned studies have not been conducted on hemorrhoid disease, the outcomes of the present study align with previously reported findings.

The current treatment options are costly, and the limited accessibility for numerous patients necessitates a cost-effective and affordable approach. Boron derivatives and formulations based on boron may offer a promising solution as an available and affordable compound and could be properly used in clinics. Our research encompasses some limitations such as the absence of long-term follow-ups. Future studies with extended follow-up periods could provide more comprehensive insights to investigate the long-term effects of the boron-based topical gel. This study was conducted on people aged 18–65 years without gender limitation.

5. Conclusions

Our study indicated that the topical *sodium pentaborate* gel can help reduce hemorrhoid symptoms such as anal itching, resting pain, pain during defecation, the feeling of a lump in the anus, and bleeding during defecation. The entirety of these findings collectively substantiates the efficacy of topical *sodium pentaborate* gel in alleviating hemorrhoid symptoms among patients.

Funding

The present study was jointly supported by Tabriz University of Medical Sciences, Tabriz, Iran (No. 62036), and Yeditepe University, Istanbul, Turkey. The funding body had no role in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

Availability of data

The dataset supporting the findings of this study is available from the corresponding author upon reasonable and justified request.

CRediT authorship contribution statement

Fikrettin Şahin: Writing – review & editing, Project administration, Conceptualization. **Azizeh Farshbaf-Khalili:** Writing – original draft, Methodology, Conceptualization. **Samin Alihosseini:** Writing – original draft, Investigation, Data curation, Conceptualization. **Parvin Sarbakhsh:** Writing – review & editing, Formal analysis, Conceptualization. **Mohammad Sadegh Pirouzpanah:** Writing – review & editing, Visualization, Conceptualization. **Erhan Ayşan:** Writing – review & editing, Conceptualization. **Ayşegül Doğan:** Writing – review & editing, Conceptualization. **Afshin Gharekhani:** Writing – review & editing, Conceptualization. **Manouchehr Khoshbaten:** Writing – review & editing, Supervision, Project administration, Funding acquisition, Conceptualization. **Mohammad-Bagher Pirouzpanah:** Writing – original draft, Project administration, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

We would like to thank Tabriz University of Medical Sciences and Yeditepe University for their financial support as well as all the people who participated in this study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e27215.

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