MOTHERISK ROUNDS

The Effectiveness of Proctofoam-HC for Treatment of Hemorrhoids in Late Pregnancy

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Abstract

Objective: Currently no topical anti-hemorrhoidal agents have been studied for effectiveness in pregnancy. This study evaluated the effectiveness of Proctofoam-HC used during the last trimester of pregnancy.

Methods: In this prospective, open-label, observational study, pregnant women prescribed Proctofoam-HC were asked to complete two telephone interview questionnaires.

Results: A total of 88 women completed the study. All hemorrhoidal symptoms, including pain, pruritus, swelling, itching, decreased significantly ($P < 0.001$) and overall well-being improved. The improvement was clinically very significant after correction for potential placebo effect.

Conclusions: Proctofoam-HC appears to provide effective treatment of hemorrhoids in late pregnancy.

Résumé

Objectif : À l'heure actuelle, aucun agent anti-hémorroïdal topique n'a fait l'objet d'études quant à l'efficacité pendant la grossesse. Cette étude a évalué l'efficacité de *Proctofoam-HC* utilisé au cours du dernier trimestre de la grossesse.

Méthodes : Dans le cadre de cette étude observationnelle, ouverte et prospective, on a demandé à des femmes enceintes auxquelles l'on avait prescrit du *Proctofoam-HC* de participer à deux entrevues téléphoniques.

Résultats : Au total, 88 femmes ont participé à l'étude. Tous les symptômes hémorroïdaux (y compris la douleur, le prurit, l'enflure et la démangeaison) ont connu une baisse significative ($P < 0,001$); de plus, le bien-être global a connu une amélioration. L'amélioration s'est avérée très significative sur le plan clinique à la suite de la neutralisation d'un possible effet placebo.

Conclusions : *Proctofoam-HC* semble constituer un traitement efficace contre les hémorroïdes au cours des derniers stades de la grossesse.

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Key Words: Hemorrhoids, pregnancy, treatment

INTRODUCTION

Hemorrhoids affect up to 38% of women in the third trimester of pregnancy.[1] A combination of several factors makes hemorrhoids a common occurrence in pregnancy. Firstly, the enlarging uterus increases intra-abdominal pressure on pelvic veins and the inferior vena cava.[2,3] Secondly, there is an increase in circulating blood volume of 25% to 40% during pregnancy.[4] Thirdly, high circulating levels of progesterone lead to relaxation of venous walls and reduce venous tone.[5] A pregnancy-induced decrease in gut motility leads to constipation, which makes pregnant women more prone to hemorrhoids. High doses of iron supplementation in prenatal vitamins also increase constipation.[6]

The estimated overall prevalence of hemorrhoids in women is approximately 25%, and this is thought to increase during the childbearing years.[7] A few studies have examined the incidence of symptomatic hemorrhoids in pregnancy, with the reported incidences differing significantly. Abramowitz et al.[8] observed a risk of 7.9%, whereas Pradel et al.[9] estimated a 24% risk, and Simmons found a 38% risk.[1]

Very little data exist on the safety of anti-hemorrhoidal treatment in pregnancy. While hemorrhoids usually have a self-limiting course in non-pregnant adults, the course during pregnancy tends to be more prolonged, and hemorrhoids usually resolve completely only in the postpartum period.[10]

An increase in fibre and water intake is typically recommended for pregnant women to prevent straining due to constipation.[11,12] If these measures alone do not suffice, osmotic laxatives are recommended.[13] Stimulant laxatives are typically avoided because of the potential risk of uterine stimulation.[14]

To date, there have been no studies on the effectiveness of topical agents in the treatment of hemorrhoids in pregnancy. Proctofoam-HC is a mucoadhesive foam consisting of a combination of pramoxine hydrochloride 1% and hydrocortisone acetate 1% and is intended for both internal and external anorectal use. Some studies have shown the usefulness of pramoxine to treat itching associated with psoriasis and pruritus ani in non-pregnant patients.[15–17] A double-blind placebo-controlled study showed a significant decrease in duration and magnitude of experimental histamine-induced pruritus.[17]

No studies have evaluated the efficacy of hydrocortisone acetate to alleviate any hemorrhoidal symptoms in pregnancy. Hydrocortisone has been shown to relieve itching associated with pruritus ani in non-pregnant adults; one study showed a 68% decrease in anal itch with the use of topical 1% hydrocortisone compared with placebo.[18]

Hydrocortisone has also been shown to decrease other anorectal conditions in the general population, such as pain, bleeding, and pruritus associated with anal fissures.[19]

Given the protracted course of hemorrhoids during pregnancy because of the persistence of the physiological changes inducing the symptomatology, it is essential to evaluate whether agents such as Proctofoam-HC may be effective during pregnancy. The objective of the present study was to evaluate the effectiveness of Proctofoam-HC in relieving hemorrhoid symptoms during the third trimester of pregnancy.

MATERIALS AND METHODS

We conducted a single-arm, prospective, observational study in pregnant women receiving Proctofoam-HC for hemorrhoids from their physicians. Each Proctofoam-HC aerosol container provides approximately 36 metered doses of pramoxine hydrochloride 1% and hydrocortisone acetate 1% as a mucoadhesive foam.

There is currently no validated tool to measure effectiveness of any anti-hemorrhoidal treatment. To overcome this barrier, we developed an effectiveness of treatment measurement scale (Appendix). This scale is a short, six-item questionnaire covering the five major symptoms of hemorrhoids: pain, itching, bleeding, swelling, and discomfort, as well as the overall effect of hemorrhoids on well-being. Participants were asked to score each symptom on a scale from 0 to 10, where 0 indicates none and 10 indicates maximum. This questionnaire was completed twice, once prior to use of Proctofoam-HC and again after treatment of at least two weeks' duration. At the time of completion of the second questionnaire, the participants were asked an additional single question regarding their overall improvement on Proctofoam-HC treatment, with 0 indicating no improvement and 10 indicating maximum improvement.

If the subject delivered less than two weeks after the first questionnaire was completed, the second questionnaire was completed postpartum.

The primary outcome of the study was pain, as it is a fairly common complaint among patients with hemorrhoids.[10] Secondary outcomes included all other hemorrhoidal symptoms, such as pruritus ani, discomfort, and anal swelling, as well as improvement in well-being and global improvement scores.

Symptom severity before and after treatment was compared using Student t test if the data were normally distributed, or Wilcoxon signed rank test if the data were not normally distributed. SigmaStat version 3.11.0 (Systat Software Inc, Point Richmond, CA) was used for the statistical analysis.

The study protocol was approved by the research ethics boards at the Hospital for Sick Children, North York General Hospital and Sunnybrook Health Sciences Centre. Study subjects gave verbal consent to participate.

RESULTS

A total of 88 women completed the effectiveness study. Their mean age was 32.9 years (median 33), and median gravidity was 2 and median parity 1. At baseline, almost all of the participants complained of hemorrhoidal swelling (99%) and anal discomfort (98%). Anal or rectal pain was noted by 90% of the women, and rectal bleeding was present in one half of the participants (53%). Almost all of the women (97%) reported that the hemorrhoids negatively affected their well-being.

Following the use of Proctofoam-HC, subjects reported a mean 73% decrease in pain (4.3 points, $P < 0.001$). A similar, significant decrease was seen in all secondary outcomes: itching (73%, $P < 0.001$), swelling (60%, $P < 0.001$), bleeding (74%, $P < 0.001$), and discomfort (77%, $P < 0.001$) (Table). Participants also reported significant improvement in their overall well-being (74%, $P < 0.001$) (Table). The above results are presented graphically in Figure 1. The mean score for global improvement with treatment was 7.6 ± 2.3 (range 0–10). Only one participant reported no improvement with treatment (score of 0), and another two experienced minimal improvement (scores of 1 and 2). Almost two thirds of the participants (62%) rated improvement as 8 or greater, and 29% (n = 26) reported the maximum possible improvement (score of 10).

Details on the changes in anorectal scores following local treatment with Proctofoam-HC

Symptom	n	Before treatment (SD)	After treatment (SD)	Mean decrease in score (SD)	% decrease	*P**
Pain	79	6.4 (2.4)	1.7 (2.1)	4.3 (2.6)	73.4	< 0.001
Itching	66	4.9 (2.2)	1.3 (1.9)	3.3 (2.3)	73.5	< 0.001
Swelling	87	6.8 (2.4)	2.7 (2.7)	3.8 (2.9)	60.3	< 0.001
Bleeding	47	3.9 (3.0)	1.0 (1.4)	2.9 (2.7)	74.4	< 0.001
Discomfort	86	6.9 (2.6)	1.6 (2.2)	5.1 (3.0)	76.8	< 0.001
Well-being	85	6.5 (2.6)	1.7 (2.1)	4.5 (3.0)	73.8	< 0.001

Scores ranked on an 11-point numerical scale where 0 indicates no pain and 10 indicates maximum pain.

*Wilcoxon signed rank test

DISCUSSION

With the effect size shown, 23 patients were required to detect a clinically significant decrease in the primary outcome of pain.

Several efficacy studies on oral and local preparations for the treatment of symptomatic hemorrhoids used a four-point scoring scale,[20–23] while others used a Likert-type scale that included two or three options.[24–26] and a few studies used a combination of the two.[27,28] However, we felt that none of these scales was sufficiently detailed to measure the continuity of given symptoms quantitatively and qualitatively, and they tended not to include all major symptoms of hemorrhoidal disease. The effectiveness of treatment measurement scale used in the present study consisted of an 11-point range, which we felt was better able to detect smaller changes in symptoms. The scale included assessment of all of the major symptoms of hemorrhoids: pain, swelling, bleeding, itching, and discomfort. To help us better understand changes in the patient's quality of life, we also included questions about changes in well-being. Finally, global improvement scores were included in the scale questionnaire. Because of this greater detail, we concluded that our effectiveness of treatment measurement scale (Appendix) was more likely to detect effectiveness of treatment than previous scales; however, this scale has not been fully validated externally, although this process is under way.

In the present study, local treatment with Proctofoam-HC was found to be very effective in reducing all symptoms related to hemorrhoids. A significant decrease in the primary outcome (pain) was noted. In previous studies, a decrease of 2 points from baseline on the 11-point pain intensity numerical rating scale has been considered to be clinically significant.[29] In the present study, the decrease in pain reported was twice as large, with a decrease of 4.3 points from baseline. One study found that patients only considered a 50% improvement in pain as a treatment success.[30] The 73.4% decrease in pain observed in this study could therefore be interpreted as showing a high level of success in treating hemorrhoids during pregnancy.

A significant decrease of 73% to 77% in itching, swelling, discomfort, and bleeding was also noted post treatment. These results are corroborated by the reported 74% increase in overall well-being after treatment. The primary goal of effective antihemorrhoidal treatment in pregnancy is to improve well-being, and thus quality of life, which these results clearly demonstrate.

At the end of the second questionnaire, women were asked a single question regarding the overall magnitude of improvement with the treatment. The mean response by the participants was 7.6 ± 2.3 (range 0–10), with a median response of 8. Previous epidemiological studies have reported that 10% to 20% of patients have persistent symptomatic hemorrhoids requiring surgery.[31] Based on this statistic, we expected that between nine and 18 women in the study sample would have persistent hemorrhoids that would not heal. The numbers observed in the study were at the lower end of that range, which is reassuring.

A major limitation of the present study was the lack of a placebo group. Since hemorrhoids in pregnancy are chronic in nature, the chance of spontaneous improvement before delivery is believed to be small, suggesting that the size of the effect observed in this study was probably a true measure of effectiveness and devoid of a significant placebo effect. Nonetheless, it is important to estimate the outcome if there was indeed a placebo effect. To that end, we reviewed the literature on interventional anti-hemorrhoidal trials with a placebo group. A total of 11 studies were identified.[20–28,32,33] Of these, only two included pregnant women.[25,28] The duration of treatment in the nine studies of non-pregnant subjects ranged from seven days to two months. Symptoms of hemorrhoids in non-pregnant adults tend to be self-limiting and may subside without medication.[34] In one study, [22] the mean healing time without

Figure 1. Change in hemorrhoidal symptoms with treatment

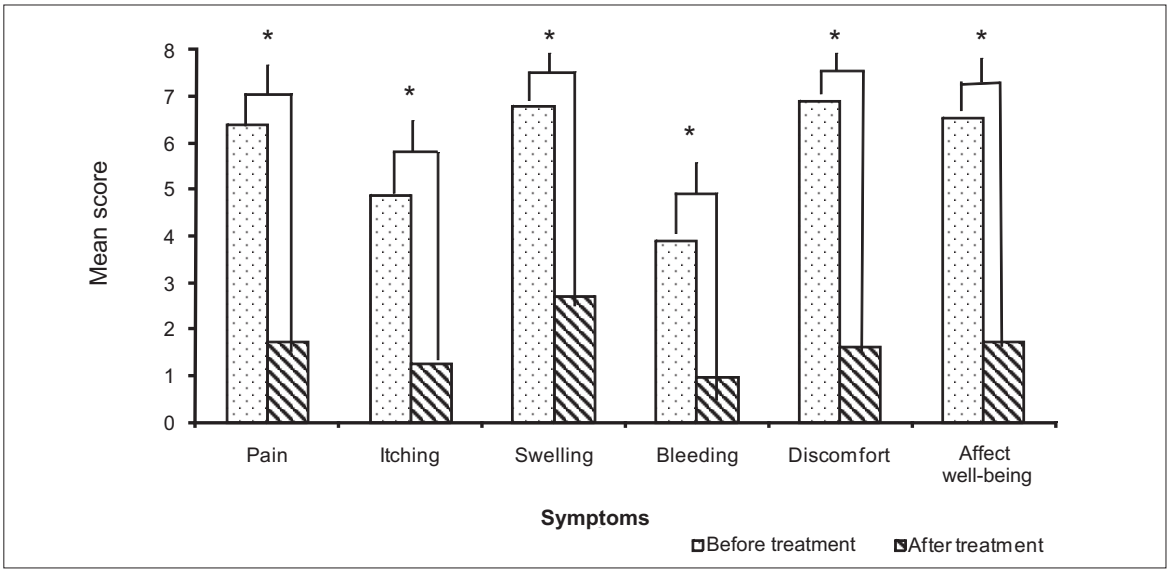
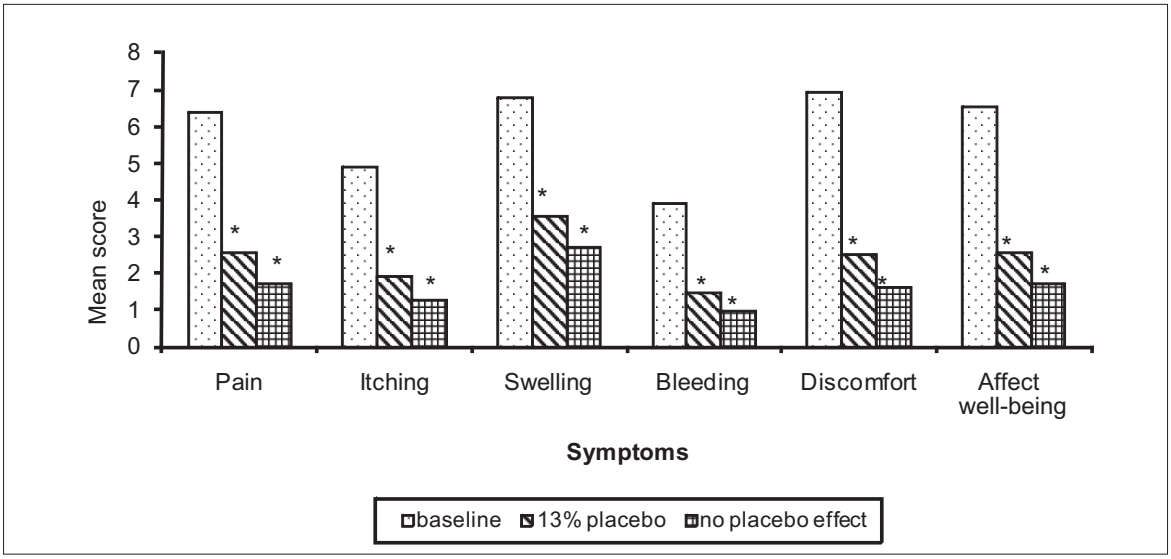


Figure 2. Change in symptoms after adjusting for placebo effect



treatment was 5.6 days for anal bleeding and 6.5 days for pain. Other studies have shown remission of severely thrombosed hemorrhoids within 7 to 24 days.[10,35] It is possible that the beneficial effects of treatment in these studies in non-pregnant patients reflected a strong placebo effect, which we would expect to be less prevalent in pregnant women.

In the studies involving pregnant women, subjects were randomized to receive oral rutosides or placebo, and the results of treatment were recorded after two weeks and again after four weeks. The first study[28] only included patients with grade 1 and grade 2 hemorrhoids. Grade 1 and 2 hemorrhoids are typically associated with very mild symptoms and are often not diagnosed unless they worsen and present with bleeding and prolapse. Most first degree hemorrhoids are easily managed by lifestyle changes and resolve faster than more severe hemorrhoids.[10,35] Since significant swelling and bleeding was observed in the sample population in the effectiveness study, it is likely that a significant proportion had some degree of prolapse, and thus grade 3 and possibly grade 4 hemorrhoids. Hence, this first placebo controlled study in pregnancy[28] did not estimate the placebo effect appropriately for comparison with our study. The second study, by Wijayanegara and colleagues,[25] observed a 12% and 14% improvement of their placebo-treated pregnant patients at week two and week four, respectively. Most of the women included in the study had grade 2 or 3 hemorrhoids. Extrapolating this observed placebo effect, we conducted a secondary analysis after taking into consideration a potential 12% to 14% placebo

effect. Since subjects in the Wijayanegara et al. study did not use a symptom scoring scale, the average of the total improvement (13%) was subtracted from every symptom in our effectiveness study. After analysis with the Wilcoxon signed rank test, a highly significant decrease in all hemorrhoidal symptoms ($P < 0.001$) was still observed (Figure 2).

These results further suggest that Proctofoam-HC enabled significant global improvement, and was highly effective in treating hemorrhoidal symptoms in the majority of the pregnant patients. Nevertheless, more studies of other anti-hemorrhoidal agents in pregnancy are needed, as the pathophysiology of hemorrhoids during pregnancy does not allow the direct extrapolation of results obtained in non-pregnant patients.

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Appendix

Hemorrhoid Survey Scale

Please answer the following survey to the best of your knowledge. The first set of questions asks you about your health **PRIOR** to using Proctofoam-HC® for the treatment of your hemorrhoids. The second set of questions asks you about your health **AFTER** the use of Proctofoam-HC®. We would like to assess whether Proctofoam-HC® provided any relief for your pregnancy related hemorrhoidal symptoms.

Please answer each question with 0 being 'none' and 10 being 'maximum'.

Prior to treatment with Proctofoam-HC®:

How do you rate the pain you experienced?

0 1 2 3 4 5 6 7 8 9 10

How much itching did you have?

0 1 2 3 4 5 6 7 8 9 10

How much swelling was present?

0 1 2 3 4 5 6 7 8 9 10

How much bleeding did you experience?

0 1 2 3 4 5 6 7 8 9 10

How much discomfort did you experience?

0 1 2 3 4 5 6 7 8 9 10

How much did your hemorrhoids affect your well-being?

0 1 2 3 4 5 6 7 8 9 10

Post Treatment (with Proctofoam-HC®):

How do you rate the pain you experienced?

0 1 2 3 4 5 6 7 8 9 10

How much itching did you have?

0 1 2 3 4 5 6 7 8 9 10

How much swelling was present?

0 1 2 3 4 5 6 7 8 9 10

How much bleeding did you experience?

0 1 2 3 4 5 6 7 8 9 10

How much discomfort did you experience?

0 1 2 3 4 5 6 7 8 9 10

How much did your hemorrhoids affect your well-being?

0 1 2 3 4 5 6 7 8 9 10

How would you rate the overall improvement? With 0 being 'no improvement' and 10 being 'maximum improvement'.

0 1 2 3 4 5 6 7 8 9 10