Polidocanol versus phenol in oil injection sclerotherapy in treatment of internal hemorrhoids: A randomized controlled trial

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ABSTRACT

Background/Aims: *Management of Haemorrhoids is suboptimal and is largely based on traditional practices in the Indian population. Though injection sclerotherapy is a well-accepted treatment modality in early grade haemorrhoids, there is no consensus on the effectiveness of the drugs used for sclerotherapy. The study was done to compare the safety and efficacy of a standard sclerosant (polidocanol) and the conventionally used phenol in oil in bleeding grade-1 and 2 internal haemorrhoids.*

Materials and Methods: *All patients with grade-1 and 2 hemorrhoids, were selected and randomised into two groups, 3% polidocanol and 5% phenol group. All patients were followed-up for three months and observed for "free of bleeding" or "persistent bleeding." Pain, pruritus and patient satisfaction following the procedure was also assessed.*

Results: *A total of 150 patients were enrolled, 75 in each group. At the end of the first sclerotherapy session with polidocanol, 60.6% of patients versus 38.1% in phenol group had stopped per rectal bleeding (p=0.009). After the second sclerotherapy session, 94.7% of patients in the polidocanol group and 84% of patients in the phenol group were treated successfully. Polidocanol group required significantly fewer treatment sessions than the phenol group (1.39±0.49 vs. 1.62±0.49; p=0.035), and the total volume of injected sclerosant was also less (3.30±0.96 mL vs. 4.86±1.46 mL; p=0.001). The patient satisfaction was 87% in polidocanol group versus 73% in phenol group (p=0.040).*

Conclusion: *3% polidocanol is safe and more effective than 5% phenol in oil when used as injection sclerotherapy in the treatment of first and second-degree internal hemorrhoids.*

Keywords: *Hemorrhoids, sclerotherapy, polidocanol, phenol*

INTRODUCTION

Hemorrhoids are abnormally enlarged anal cushions that protrude into the anal canal (1). It is one of the most common causes of painless, per rectal bleeding during bowel movement bleeding in adults (2). Multiple etiological factors such as constipation and prolonged straining are associated with hemorrhoids. Hemorrhoids are broadly classified into internal and external depending on their location above or below the dentate line, respectively (3). Internal hemorrhoids are further divided into different grades. Treatment of internal hemorrhoids depends on the grade of the disease. Majority of hemorrhoids are usually managed with lifestyle modifications, high dietary fibers, sitz bath, and medications. Nonoperative treatment modalities available for internal hemorrhoids are sclerotherapy, rubber band ligation, infrared coagulation, cryosurgery, radiofrequency coagulation, direct current coagulation, and laser surgery (4). Operative measures are sought if the nonoperative measures fail or complications occur.

The management of grades 1 and 2 hemorrhoids is essentially suboptimal and largely based on traditional practices. Injection sclerotherapy and rubber band ligation are the commonly used treatment methods in lower grade hemorrhoids. The varieties of sclerosants are available without much standardization. Injection phenol in almond oil has been widely used conventionally in many Indian hospitals. Polidocanol is one of the standard sclerosants used in varicose veins and varices. Hence, this study was conducted to compare the safety and efficacy of a standard sclerosant (polidocanol) and the conventionally used phenol in oil in bleeding grades 1 and 2 internal hemorrhoids.

MATERIALS AND METHODS

The study was conducted in the department of general surgery at a tertiary care hospital in South India from February 2016 to April 2017. The study was approved by the Ethics Committee of the Institute and has been

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performed in accordance with the ethical standards laid down in an appropriate version of the Declaration of Helsinki (as revised in Brazil 2013).

All consecutive patients in the age group from 18 years to 75 years presenting with history of per rectal bleeding and grade 1 or 2 internal hemorrhoids on proctoscopic examination were included in the study. Patients with coexisting anal fissure, proctitis, perianal abscess, perianal hematoma, rectal prolapse, rectal varices, bleeding disorders, previous sclerotherapy during the last 12 months, and previous anal surgery as well as pregnant patients were excluded from the study. The study was designed as a prospective, single-blind, open-labeled, parallel arm, superiority randomized controlled trial. Block randomization was carried out using a computer program with randomly selected block sizes of four and six. Allocation concealment was ensured by a serially numbered opaque sealed envelope (SNOSE) technique. All patients who fulfilled inclusion criteria were randomized into two groups: Group A received 2 mL of 3% injection polidocanol sclerotherapy and Group B received 3 mL of 5% phenol in oil injection sclerotherapy. Sclerosant was injected submucosally at the base of each hemorrhoid at 3, 7, and 11 o'clock positions with the patient in a lithotomy position in the both groups. No patients received any concomitant medical treatment after injection sclerotherapy.

All patients were followed up for 3 months. They were advised to visit surgery outpatient department every 2 weeks. At the follow-up visit, the history of bleeding per rectum, pain, perianal pruritus, and patient satisfaction after sclerotherapy were documented. History of bleeding per rectum was categorized into "free of bleeding" or "persistent bleeding." Free of bleeding was taken as treatment success. Persistent bleeding at follow-up was defined as bleeding for at least 2 days following the second day of the procedure or bleeding for even 1 day within 3 days prior to the follow-up visit. In patients with "persistent bleeding," the sclerotherapy was repeated till they were "free of bleeding." The sclerotherapy session was repeated for a maximum of three times. Persistent bleeding following three times sclerotherapy was subsequently planned for band ligation. The pain was assessed by a three-point scale ("no pain," "pain during defecation," and "constant pain"). Pruritus was evaluated by a three-point scale ("no pruritus," "occasional pruritus," and "constant pruritus"). Patient satisfaction was recorded by a four-point scale ("very satisfied," "satisfied," "less satisfied," and "not satisfied").

Statistical analysis

The sample size was calculated using the OPENEPI[å] software. Considering the detection of eradication rate more than 20% between the two groups on two tail basis with 95% confidence interval and power of the study >80%, the sample size was calculated to be 75 in each group (5, 6). A sample size of 177 was defined in the study protocol to compensate for the potential dropouts (15%). Continuous variables such as number of patients with no per rectal bleeding for 12 weeks—treatment success—were summarized as means and tested using *t*-test. Dichotomous data such as stopping of bleeding after the first sclerotherapy (yes/no) summarized as proportions were tested using Fisher's test. Continuous variables such as the number of sclerotherapy sessions for treatment success and total amount (mg) of polidocanol and phenol injected for treatment success summarized as means and medians were tested using either Student's *t*-test or the Mann–Whitney test, depending on the distribution. Comparison of categorical variables such as pain, pruritus, and patient satisfaction summarized as proportions were tested by using a chi-square test.

MAIN POINTS

- *It can be concluded that 3% polidocanol is more effective than 5% phenol in oil when used as injection sclerotherapy in the treatment of first and second-degree internal hemorrhoids.*
- *Phenol in oil remains a reliable and time-tested treatment option for internal hemorrhoids with 84% success rate after the second session.*
- *This study demonstrated that polidocanol is a highly effective with 95% success rate after the second session in the treatment of first and second-grade internal hemorrhoids.*
- *As the side effects profile is similar to phenol in oil, it can be used as a treatment modality of choice to reduce the number of treatment sessions.*

RESULTS

Of the 177 patients with per rectal bleeding who were recruited and assessed for the eligibility, 150 patients gave consent to be included in the study (Figure 1). The mean age of patients in the polidocanol and phenol group was 44.45±14.4 and 46.9±16.3 years, respectively. There were 57 males (76%) and 18 females (24%) in the Polidocanol therapy arm, while the Phenol arm comprised 67 males (89.3%) and 8 females (10.7%).

The treatment success at the end of the first sclerotherapy session with polidocanol and phenol was 60.6% and 38.1%, respectively (p=0.009; Table 1). The overall differ-

ence in treatment success after the second sclerotherapy session was 94.7% and 84% in the polidocanol and phenol group, respectively (Figure 2). Of 75 patients in the polidocanol group, 5 (6.6%) patients needed a third sclerotherapy session; while 12 (16%) of 75 in the phenol group needed a third session. However, all the patients who needed the third session did not respond to the treatment. All of these patients were subjected to rubber band ligation as an alternative treatment method.

The efficacy in terms of the number of sclerotherapy sessions for treatment success was on average 1.39±0.49 sessions in the polidocanol group, while it was 1.62±0.49 sessions in the phenol group (p=0.035). The difference in

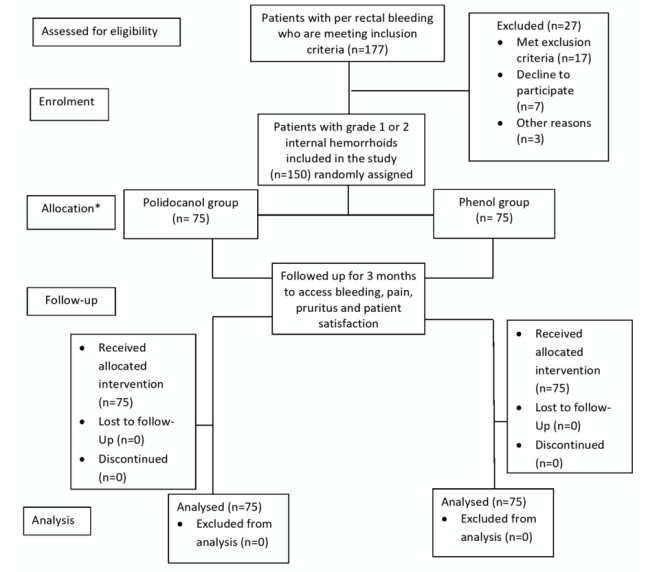

Figure 1. The overall scheme as per CONSORT flowchart.
*Allocation consealment was done by opaque sealed envelope method.

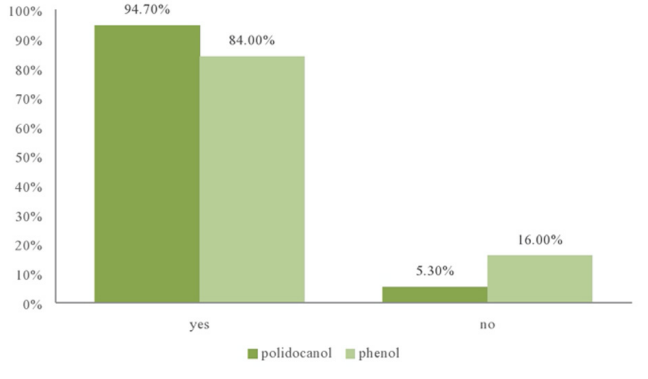

Figure 2. Overall treatment success between the patients in polidocanol and phenol group.

Table 1. Comparison of efficacy outcomes between the patients in the polidocanol and phenol groups.

Efficacy outcomes	Polidocanol	Phenol	p
Stopping of bleeding after the first sclerotherapy	43 (60.6%)	24 (38.1%)	0.009[a]
Number of required sclerotherapy sessions for treatment success (mean±SD)	1.39±0.49	1.62±0.49	0.035[b]
Total amount of injected sclerosant for treatment success (mean±SD, in mL)	3.30±0.96	4.86±1.46	0.001[c]

p<0.05 are considered significant and are set in bold.
[a]Fisher's exact test
[b]Mann–Whitney test
[c]Student's t-test

Table 2. Comparison of pain and pruritus as secondary outcomes between the patients in the polidocanol and phenol groups.

	Polidocanol, n (%)	Phenol, n (%)	p[a]
Pain during the first sclerotherapy			
No pain	51 (71.8)	42 (66.7)	0.702
Little pain	17 (23.9)	19 (30.2)	
Severe pain	3 (4.2)	2 (3.2)	
Pain in interval between visits 1 and 2			
No pain	63 (88.7)	52 (82.5)	0.587
During defecation	6 (8.5)	8 (12.7)	
Permanent pain	2 (2.8)	3 (4.8)	
Pruritus before sclerotherapy			
No pruritus	48 (67.6)	42 (66.7)	0.838
Occasional pruritus	21 (29.6)	18 (28.6)	
Permanent pruritus	2 (2.8)	3 (4.8)	
Pruritus between visits 1 and 2			
No pruritus	52 (73.2)	48 (76.2)	0.688
Occasional pruritus	17 (23.9)	12 (19)	
Permanent pruritus	2 (2.8)	3 (4.8)	

[a]chi-square test

Table 3. Comparison of patient satisfaction between the patients in the polidocanol and phenol groups after the data were pooled into satisfied and not satisfied groups.

Patient satisfaction	Polidocanol, n (%)	Phenol, n (%)	p[a]
Satisfied	65 (86.7)	55 (73.3)	0.040
Not satisfied	10 (13.3)	20 (26.7)	

p<0.050 is considered significant and set in bold.
[a]chi-square test

amount of sclerosant needed for treatment success was 3.30±0.96 mL and 4.86±1.46 mL in the polidocanol and phenol group, respectively, which was statistically significant (p=0.001; Table 1).

Of 70 patients, 51 (71.8%) treated with polidocanol had no pain compared to 66.7% (42 of 63) in the phenol group (Table 2). In the polidocanol group, 88.7% of the patients were pain-free compared to 82.5% of the patients in the phenol group. There was no statistically significant difference in terms of pruritus following sclerotherapy between the two treatment groups (p=0.838). The percentage of patient satisfaction with their treatment was 86.7% and 73.3% in the polidocanol group and phenol group, respectively (p=0.040, Table 3). No severe or life-threatening adverse events occurred in either of the treatment group. Immediate complications of injection sclerotherapy such as bleeding and local pain were common in both the groups.

DISCUSSION

Internal hemorrhoids are the most common cause of painless rectal bleeding in adult population. They can also be seen in the extremes of age but are uncommon. The treatment of internal hemorrhoids varies according to the grade of hemorrhoids. Grade 1 and 2 hemorrhoids are treated with nonoperative methods. Injection sclerotherapy is a simple, safe, and feasible nonsurgical modality. Many studies have compared conventional injection sclerotherapy with other modalities of treatment of hemorrhoids, but there is a paucity of studies comparing polidocanol and phenol as injection sclerotherapy (7, 8). An injection with 5% phenol in almond oil has been conventionally used widely, but it has a list of complications that can be occasionally serious (9, 10). In contrast, polidocanol is a sclerosant and has a local anesthetic effect. This offers painless sclerotherapy that can be easily administered as an outpatient procedure. There are individual studies supporting the effectiveness of phenol in oil and polidocanol sclerotherapy in internal hemorrhoids (8, 11). However, similar reports comparing both of them are lacking.

The efficacy of phenol in oil as sclerotherapy has been demonstrated in several studies. Varma et al compared the coagulation current and 5% phenol in oil sclerotherapy for the treatment of internal hemorrhoids and established that 84% of the sclerotherapy patients were cured of bleeding compared to 64% of the coagulation patients. Bhuiya et al. (12) demonstrated the effect of injection phenol sclerotherapy on early hemorrhoids patients visiting surgical outpatient department and noticed that 60.41% (58 patients) had satisfactory result after the initial dose of sclerotherapy. Only six (15.78%) of the remaining 38 patients who underwent the second dose of sclerotherapy demonstrated satisfactory result. The third dose of sclerotherapy had satisfactory outcome only in one patient (3.12%) out of 32. Yuksel et al. (7) showed that 72% of patients were either free of symptoms or showed improvement after 3% polidocanol sclerotherapy. Madhumita et al. (8) reported that after three doses of injection polidocanol, 89.66% of the patients had satisfactory results. After the first dose of injection, 39 of 58 (67.24%) patients had satisfactory results. Remaining 19 patients were given the second dose of injection, of which 11 (57.89%) patients had satisfactory results. The third dose of injection given to the remaining eight patients proved satisfactory only in two (25%) cases. After three doses of injection, six (10.34%) cases failed to show any response. Kulshrestha showed that polidocanol sclerotherapy cured 78.86% (265/336) of the patients, improved 17.86% (60/336), and failed to cure 1.19% (4) of the patients. Of 336 patients, 15 (4.4%) patients had repeat session, and 17 (5.05%) had concomitant illness (11).

This study revealed that significantly more patients were successfully treated with 3% polidocanol injection sclerotherapy compared to 5% phenol in oil (95% vs 84%). At the end of the first sclerotherapy session in this study, 60.6% and 38.1% of patients in the polidocanol group and in phenol group, respectively, had been treated successfully. Aakerud et al. (8) in an RCT comparing the safety and efficacy of polidocanol with phenol, concluded that the success rate after the first sclerotherapy session was 91% and 88%, respectively, with phenol in oil treatment and with polidocanol treatment. After the second session, 97% of the patients were treated successfully in both the groups.

Nijhawan et al. (13) performed video-endoscopic injection sclerotherapy using 1.5% polidocanol and demonstrated that the average sessions for treatment success were 1.2. A German study demonstrated the number of sclerotherapy sessions needed for treatment success using polidocanol was 1.42±0.64 (7). The results of these studies are comparable to this study. In this study, the polidocanol injection sclerotherapy showed a reduced number of treatment sessions for treatment success (1.39 sessions). This finding can be considered important for the patients because it can be a one-stop therapy for them. This can as well increase the patient's and physician's faith in this treatment modality.

Nijhawan et al. (13) found that the total volume of 1.5% polidocanol required was 6.4±2.2 mL per patient. The amount of sclerosant per case needed for treatment success in this study was significantly less in the polidocanol group compared to the phenol group (3.30±0.96 mL vs 4.86±1.46 mL). The less volume of polidocanol required in this study could be attributed to the higher (3%) concentration of polidocanol. The volume needed in the polidocanol group was nearly 60% less than in the phenol group. This offers an advantage to the patients because the adverse events also reduce with the decrease in the volume of the sclerosant.

Moser et al. (5) demonstrated that during the first sclerotherapy session with 3% polidocanol, 64.1% of the patients had no pain, 32.8% had little pain, and 3.1% had severe pain. In the interval between the first and the second sclerotherapy session, 96.9% had no pain, and 3.1% had pain only during defecation, and no patient had permanent pain following 3% polidocanol sclerotherapy. In this study, following polidocanol injection sclerotherapy, 71.8% of the patients had no pain, 23.9% had mild pain, and 3% had severe pain. Their results (7, 8, 13) were comparable to this study. More pain during or immediately after the procedure was experienced in the phenol group. This can be attributed to the anesthetic effect of polidocanol and less volume of sclerosant injected in the polidocanol group.

There are few reports regarding the pruritus ani post injection sclerotherapy in internal hemorrhoids (7, 14). Akindiose et al. (14) found that 28% of the patients had pruritus ani before treatment and 1% had pruritus after treatment with 5% phenol in oil. Similarly, Moser et al. (5) reported that 45.3% of the patients had no pruritus, 48.4% had occasional pruritus, and 6.3% had permanent pruritus before treatment. However, 78.1% had no pruritus, 21.9% had occasional pruritus, and none had permanent pruritus after treatment with 3% polidocanol. The results of this study were similar to those of Moser et al. (5) In the polidocanol group and the phenol group 73% patients and 76%, respectively, suffered from pruritus. It can be attributed to the higher viscosity of the phenol compared to the polidocanol.

Regarding patient satisfaction, patients who received polidocanol were significantly more satisfied than those who received phenol (p=0.040). Similar results were obtained in other individual studies using phenol in oil and polidocanol. The higher patient satisfaction can be attributed to the relatively less volume of sclerosant needed for sclerotherapy in the polidocanol group. It can also be attributed to the lesser number of sclerotherapy sessions required to achieve the result.

There were no major side effects or life-threatening adverse events observed with both the study groups. The only adverse effects in both the study groups were local pain at the injection site and bleeding. Nijhawan et al. (13) demonstrated that no significant complications were noted except bloating (12.6%) and rectal pain (7.6%) using 1.5% polidocanol. Immediate complications were observed only in 2.08% patients, but there were no late complications. In the study conducted by Kulshrestha using polidocanol as sclerotherapy, 2.38% patients had local pain and 0.6% had a small local ulcer as complications. Polidocanol, however, was associated with fewer adverse drug reactions. Phenol frequently showed injection site pain and ulcers (11). The side-effect profile in this study was better with polidocanol because the total volume of sclerosant required for treatment success was reduced by 60% in the polidocanol group. Thus, there was high overall safety of sclerotherapy within both the treatment groups.

The only limitation of this study was that it was a single center study.

In conclusion, this study found that polidocanol was more effective than phenol when used as injection sclerotherapy for the treatment of first- and second-degree internal hemorrhoids. Polidocanol was highly effective after the second session in the treatment of the first- and second-grade internal hemorrhoids. The complications and patient satisfaction was comparable between the two groups.

Ethics Committee Approval: Ethics committee approval was received fort his study from the Institute Ethics Committee of Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER) (Decision date 15.05.2015. Decision number JIP/IEC/2015/29/785).

Informed Consent: All the participants included in the study were given written informed consent.

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