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REVIEW

Using phenol for treating pilonidal sinus: a systematic review and meta-analysis

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Abstract

Pilonidal sinus is an acquired disease that affects the natal cleft. Phenolization is a common conservative treatment approach due to its robust antiseptic effects. The aim of this study is to systematically review and evaluate the quality of the controlled clinical trials that investigated the effectiveness of phenol, as a standalone or an adjunct treatment, compared to surgical intervention in reducing sinus recurrence rate and hospitalization period**.** Four electronic databases were searched (MEDLINE (PubMed), Scopus, Web of Science, Cochrane) from inception to October 2018. The retrieved studies were screened by two independent reviewers. The risk of bias was assessed using the Jadad tool. Meta-analysis was conducted to examine recurrence rate and hospital stay using random effect model while I2 test was used to assess heterogeneity. Five studies were eligible for qualitative and quantitative assessment; 228 patients were treated with phenolization (45.6%) and 272 patients were treated with surgery (54.4%). Phenolization reduces the Likelihood of hospital stay after the procedure by 96–100% compared to surgery. For recurrence rate, the pooled analysis showed no significant difference between phenol and surgery treatment. However, 33.33% of cases did not recur after multi applications of crystallized phenol. Phenolization of patients with pilonidal sinuses is significantly associated with less hospitalization compared to surgical intervention. However, both approaches have a comparable recurrence rate and complications.

Keywords Phenolization · Pilonidal sinus · Surgery · Recurrence rate · Hospitalization

Introduction

Pilonidal sinus is an acquired disease that affects the natal cleft. It occurs due to the formation of a cavity that is lined with squamous epithelium containing granulation tissue and hair shaft [1]. These sinuses are discharging, which affect the subcutaneous tissues and they are usually continuous with the epidermis [2]. The patient typically complains of pain that is referred to the sacral region and apparent discharge [3]. Upon examination, pilonidal sinus is evident by the presence of tenderness and redness at the sacrococcygeal region. There is often a purulent discharge due to infection [3]. Effective clinical management is challenged by the high recurrence rate despite the availability of many conservative and surgical treatment options [4].

Phenolization is a common conservative treatment approach due to its robust antiseptic effects [5]. Scientific evidence supports a high success rate when phenol is applied to 2–3 sinuses within the first 3 weeks postoperatively [5]. On the other hand, phenol applied for 1–6 weeks was found ineffective in patients with prolonged purulent discharge [6]. However, the latter evidence was drawn from non-controlled clinical trials, which makes it hard to conclude the effectiveness compared to other available treatment options. Thus, the aim of this study is to systematically review and evaluate the quality and strength of evidence drawn from controlled clinical trials that investigated the effectiveness of phenol, as a standalone or an adjunct treatment, compared to surgical intervention in reducing sinus recurrence rate and hospitalization period.

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Methods

The protocol for this systematic review has been registered in the PROSPERO database (CRD42018092692). The PICO (P—patient, I—intervention, C—comparison, O—outcome) question format for this study was created as follows: (a) patient—primary or recurrent pilonidal sinus, (b) intervention—phenolization as a standalone treatment or an adjunct treatment, (c) comparison—control groups include individuals who undergo other surgical procedures or receive non-surgical treatment, and (d) outcome—recurrence rate and hospital stay.

Search strategy

Three electronic databases searched (MEDLINE (PubMed), Scopus, Web of Science, Cochrane) from inception to October 2018 using the following keywords and Boolean operators: ("pilonidal sinus*" OR "pilonidal cyst*") AND (phenol* OR "carbolic acid" OR Hydroxybenzene OR carbol). Also, manual searching of the bibliography was done.

Selection and eligibility

Two independent reviewers screened retrieved studies, first by title, then by abstract, and finally by reading the full text. Articles were eligible for this study based on the following inclusion and exclusion criteria.

Inclusion criteria:

1. Controlled clinical trials, cohort, and case-control studies that compared the effectiveness of phenol application in pilonidal treatment to other treatments
2. Articles published in the English language

Exclusion criteria:

1. Non-controlled trials
2. Case reports and case series studies
3. Insufficient details on measured outcomes (hospital stay and recurrence rate)
4. Insufficient details on patient characteristics
5. Conference proceedings

Each article had to fully satisfy the eligibility criteria to be included. None of the articles were excluded due to poor methodological quality. If disagreement existed, a consensus was reached through discussion.

Data extraction and risk of bias assessment

The two reviewers independently extracted the following information from all eligible studies: title, author name, publication year, sample size, population characteristics, study design, intervention group, control group, follow-up duration, recurrence rate, and the length of hospital stay (Tables 1, 2, and 3).

Then, studies risk of bias were assessed using the Jadad tool [12] which assesses articles based on randomization, blinding, and patient withdrawal and dropouts [12]. However, as the comparator was surgery, blinding was not possible, and hence, was scored as not applicable (N/A). Descriptive synthesis was done based on the quality assessment of the included studies.

Quantitative assessment (meta-analysis)

Meta-analysis was conducted to examine recurrence rate and hospital stay when the studies were thought to be homogenous and comparable in intervention and control groups. The studies were analyzed using Review Manager (RevMan) software. For dichotomous outcome variables, risk ratio (RR) and 95% confidence interval (95% CI) were used when the same outcome measures were used in studies. A random effects model was used to pool the treatment effects across the studies. A P value of ≤ 0.05 was considered statistically significant. Heterogeneity between studies was assessed using I^2 test. The degree of heterogeneity was categorized as low ($I^2 <$ 25%), moderate ($I^2 = 25$–75%), and high ($I^2 > 75\%$). A P value of ≤ 0.05 indicated studies heterogeneity.

Results

Search results

Initial database search identified 138 records. This number was reduced to 76 after duplicate removal. After screening by title and abstract, two articles were excluded due to being written in a language that was not English; one of these articles was a letter to the editor—resulting in only 7 articles which were found eligible. After reading the full text, this resulted in 5 eligible studies for qualitative and quantitative assessment (Fig. 1).

Study description

The study designs of the included studies were retrospective comparative studies [7–9] and prospective randomized trial [10, 11].

Population

The eligible studies had a sample size that ranged from 40 [11] to 140 [10]. One study enrolled pediatric patients with an age ranging from 13 to 17 years [8]. All other studies recruited adults aged from 19.4 [9] to 37.5 years [10]. All studies included more male than female patients. Only two studies [7,

Table 1 Study and population characteristics

Study	Age (mean) (± SD)		Sex (M/F)		Study design	Inclusion criteria	Exclusion criteria
	Phenol	Control	Phenol	Control			
Akan, K., et al. (2013) [7]	24.72 ± 5	26.84 ± 6.41	42/8	46/4	Retrospective comparative	–	Factors that disturb wound healing (recurrence, infection, and complicated pilonidal sinus)
Ates, U., et al. (2017) [8]	15.7 (± 1.41)	15.4 (± 2.30)	20/20	45/32	Retrospective comparative	–	–
Bayhan, Z., et al. (2016) [9]	26 ± 6.6	25.4 ± 5.9	29/8	38/6	Retrospective comparative	Adults up to 65 years old new cases only	- Steroid treatment - Recurrence disease - DM - Abscess formation following diagnosis of pilonidal disease - Concomitant pilonidal disease with malignant
Calikoglu, I., et al. (2016) [10]	30.1 ± 7.4	28.9 ± 7.8	54/16	55/15	Prospective RCT	More than or = 18 primary or recurrent chronic pilonidal sinus	- Acute pilonidal sinus or indurations - Abscess drainage within 2 months - Immunosuppressive and/or coagulation disorder - Pregnancy or lactating - Other acute surgical diseases
Topuz, O., et al. (2014) [11]	25.6 (± 6.1)	27.4 (± 7.8)	17/3	17/3	Prospective RCT	–	Acute pilonidal sinus

M male, *F* female, *SD* standard deviation

10] reported the preoperative symptom duration, which ranged in the phenol group from 4.05 months [7] to 54.1 months [10] and in the surgery group from 2.2 [10] to 33.2 months [10].

Out of the total of 500 participants included in the reviewed studies, 228 patients were treated with phenolization (45.6%) and 272 patients were treated with surgery (54.4%) (Tables 2 and 3).

Table 2 Phenol treatment for pilonidal sinus

Study	Number of participants	Recurrence	Recurrence after multiple application	Hospital stay (days)	Complications	Follow-up (mean)
Akan, K., et al. (2013) [7]	50	6	-	0	Infection, 4 Hematoma, 2	26 months
Ates, U., et al. (2017) [8]	40	1	-	0	Surgical site infection, 1	8.1 months
Bayhan, Z., et al. (2016) [9]	37	7	3 patients had recurrence after the second application. 1 was cured after the third application. 2 did not cure even after the 4th application	0	Surgical site infection, 4 Hematoma, 3	16.5 months
Calikoglu, I., et al. (2016) [10]	70	13	8 needed another application and 4 had recurrence	0	Abscesses, 4 Intergluteal maceration, 2	38.3 months
Topuz, O., et al. (2014) [11]	20	0	-	0	-	First follow-up is after 10 days

- no data, *LA* local anesthesia

Table 3 Surgical treatment in pilonidal sinus

Study	Number of participants	Procedure	Settings	Anesthesia	Recurrence	Hospital stay (mean)	Complications	Follow-up (mean)
Akan, K., et al. (2013) [7]	50	Limberg flap	Operating room	Spinal	4	1.46 days	Infection, 17 Hematoma, 23 Seroma, 3 Wound dehiscence, 4	26 months
Ates, U., et al. (2017) [8]	77	Excision and primary closure	Operating room	GA OR epidural	10	2.7 days	Wound infection, 6 Wound dehiscence, 1 Hematoma, 1	44.6 months
Bayhan, Z., et al. (2016) [9]	44	Modified Limberg flap	Operating room	-	7	1.25 days	Wound dehiscence, 7 Surgical site infection, 8 Hematoma, 8	17.9 months
Calikoglu, I., et al. (2016) [10]	70	Excision with open healing	Operating room	Spinal	9	1.10 days	Bleeding, 1	41.56 months
Topuz, O., et al. (2014) [11]	20	Excision and primary closure	Operating room	GA	0	1.5 days	Wound dehiscence, 2	Patients were seen postoperative days 7 and 14

- no data, *GA* general anesthesia

Clinical settings

Surgical treatment was done in operating rooms under spinal [7, 10], epidural [8], or general anesthesia [8, 11] (Table 2) whereas phenolization was done in an outpatient clinic [11] or local operating room [7] under local anesthesia except for one study that used sedation as participants were children [8] (Table 2 and 3).

Intervention

Phenolization

Phenol was applied under local anesthesia (LA) and supervised dilation of the pit with clamps was done to clean the sinus from hair and debris [7]. Phenolization was done once [7–11], twice [10], and up to four times [9] based on recurrence (Table 2).

Comparator

The control group underwent excision ([8, 10, 11]), Limberg flap [7] or modified Limberg flap [9] (Table 3).

Outcome measure

Recurrence rate

Recurrence was defined as detection of new orifices or discharge from the wound during the follow-up period after the procedure. The follow-up period was reasonable and ranged from 12.1 months[9] to 49.6 months [10] post operatively, except for Topuz and colleagues' study who followed patients up for only 10 days [11]. For phenol application, the recurrence rate ranged between 0% [11] and 18.9% [9]. Of the cases, 33.33% were cured after multi-applications of crystallized phenol (Table 2). For the surgical treatment, recurrence was recorded in 30 cases out of 261 (11.49%) (Table 3).

Length of hospitalization

After phenol application, all patients were discharged from the hospital immediately (the length of hospital stay was 0 (Table 2). On the other hand, after surgical intervention, the length of hospital stay ranged from 0.53 [8] to 4.87 days [8] (Table 3).

Complications

Complications associated with phenolization were reported in 9.21% of patients. For surgical treatment, complications were seen in 31.03% of patients. With phenolization, out of 20 complications, 13 were due to surgical infection [7–10], 5

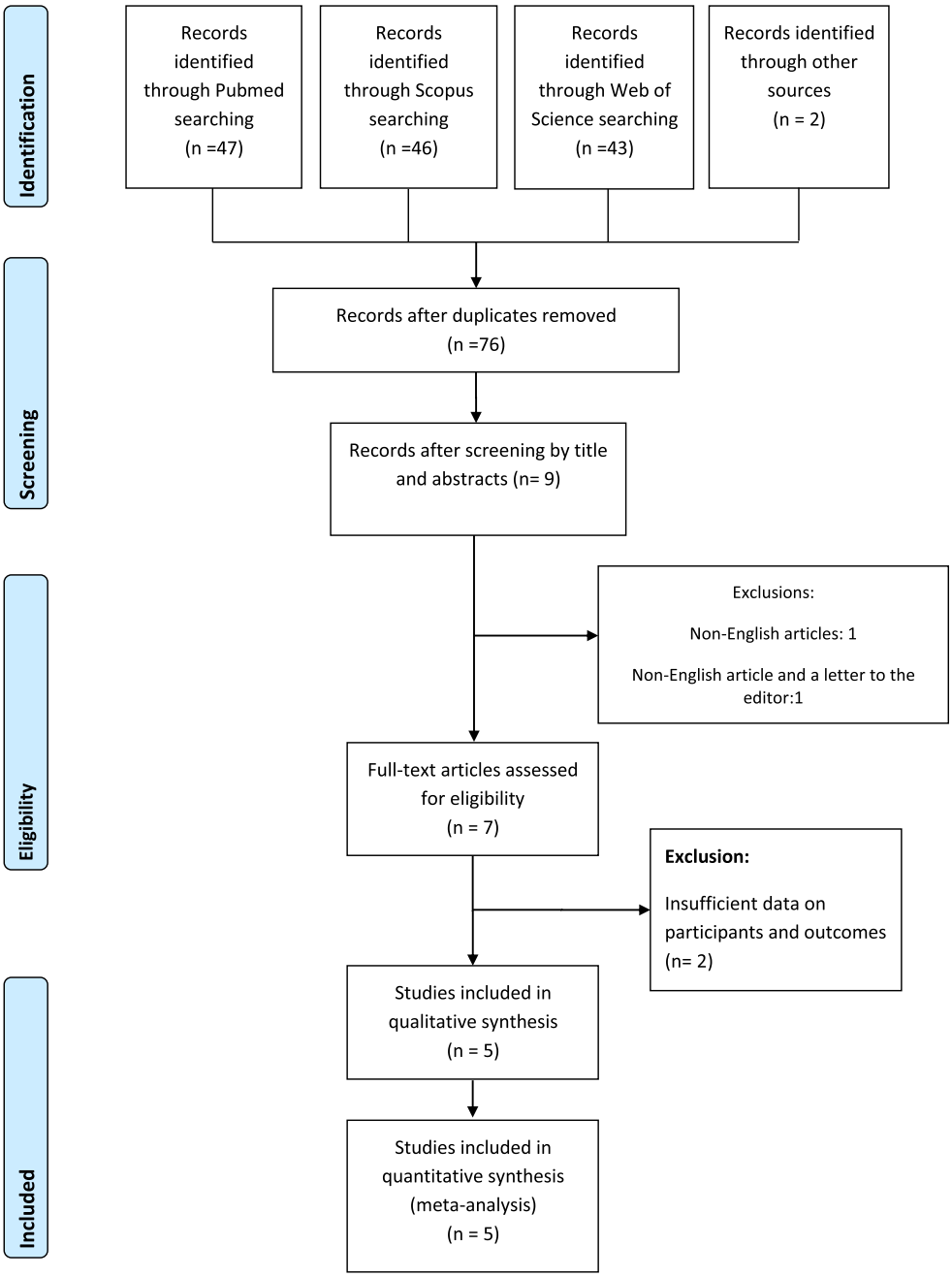

Fig. 1 PRISMA flowchart

had local hematoma [7, 9], and 2 patients showed maceration [10] (Table 2). For surgical excision patients, 31 cases (11.87%) developed surgical site infection [7–9], 32 cases developed hematoma [7–9], and 14 patients (5.36%) developed wound dehiscence [7–9, 11] (Table 3).

Risk of bias

The Jadad score was low and scored as 0 [8, 9] and 1 in four studies [7, 11]. Only one study had a high quality score of 3 [10]. Two out of the five studies did not mention or describe the randomization method [8, 9]. Four studies did not describe the withdrawal and dropouts of patients [7–9, 11]. Blinding was not applicable due to the nature of the interventions (Table 4).

Quantitative data synthesis and analysis

For recurrence rate, Topuz et al. study [11] was excluded as it reported a 0 recurrence rate in both phenol and surgery groups. The pooled analysis of the remaining 4 studies ($n = 438$) showed no significant difference between phenol and surgery treatment with a RR of 1.34 (P value = 0.46; 95% CI = 0.62–2.88) (Fig. 2). There were no heterogeneity in the hospital stay

Table 4 Jadad assessment scores for all included studies

Jadad item	Akan, K., et al. (2013) [7]	Ates, U., et al. (2017) [8]	Bayhan, Z., et al. (2016) [9]	Calikoglu, I., et al. (2016) [10]	Topuz, O., et al. (2014) [11]
Was the study described as randomized (this includes words such as randomly, random, and randomization)?	1	0	0	1	1
Was the method used to generate the sequence of randomization described and was it appropriate?	0	0	0	1	0
Was the study described as double blind?	N/A	N/A	N/A	N/A	N/A
Was the method of double blinding described and was it appropriate?	N/A	N/A	N/A	N/A	N/A
Was there a description of withdrawals and dropouts?	0	0	0	1	0
Total score	1	0	0	3	1
Quality grade	Low quality	Low quality	Low quality	High quality	Low quality

N/A not applicable

($I^2 = 0$, $P = 0.98$). Moreover, there is nonsignificant moderate heterogeneity in recurrence rate ($I^2 = 39\%$, $P = 0.19$).

For the length of hospital stay, the phenol group was zero in the nominator; thus, the rule of three was employed to calculate the RR [13]. This implies if none of the patients showed the event of interest; there is a 95% confidence that the chance of this event is at most three in number (i.e., 3/*n*). The pooled analysis of 5 studies ($n = 478$) showed a significantly less hospital stay for patients in the phenol treatment compared to those who received surgical intervention, with a RR of 0.01 (P value < 0.001; 95% CI = 0.00–0.04). This implies that phenolization reduces the risk of hospital stay after the procedure by 96–100% compared to surgery (Fig. 3).

Discussion

This review assessed the strength and quality of evidence in controlled trials that compared the conservative treatment of pilonidal sinuses using phenolization to surgical excision with or without flap. The primary outcome was recurrence rate and the length of hospitalization. The secondary outcome was the frequency of complications associated with each treatment. Although two previous systematic reviews were done to assess the effectiveness of phenolization, reviewed studies were not controlled [5, 6].

In this review, five studies were found eligible. All studies were included for qualitative analysis and quantitative analysis of the hospitalization length; yet only four studies were included in the quantitative analysis of recurrence rate. Four studies were of poor quality [7–9, 11] and one was of a high quality [10]. None of the studies reported blinding; however, masking patients and treatment providers were not applicable due to the nature of the interventions.

In all reviewed studies, sinus severity was not considered, and patients were randomly assigned to phenolization and surgery groups. Severity of sinuses may influence patient's response to various treatments [14]. Future studies should consider a stratified random sample based on disease severity.

Further, although the outcome measures of recurrence rate and length of hospitalization are quantitative and objective measures, one study reported the length of hospitalization based on patient reported self-outcome questionnaire, which may be subjected to recall bias [11].

Excluding articles based on language may result in a language bias. However, the excluded study based on language was in favor of phenol treatment over surgery in hospital stay and showed a comparable recurrence rate which is similar to the results of this review [15].

The major complication reported in these studies was wound dehiscence, which prolongs hospitalization as patient will need multiple dressings. Further, this impacts upon a patients' outcome due to increased work absenteeism and poor quality of life.

It should be noted that surgical outcome is dependent on a surgeon's competencies. The surgery in Calikoglu et al. was

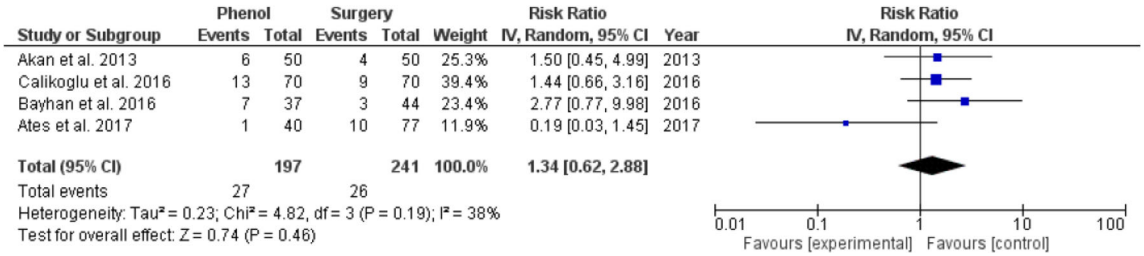

Fig. 2 A forest plot showing no significant difference in sinus recurrence rate in patients receiving phenol or surgical treatments

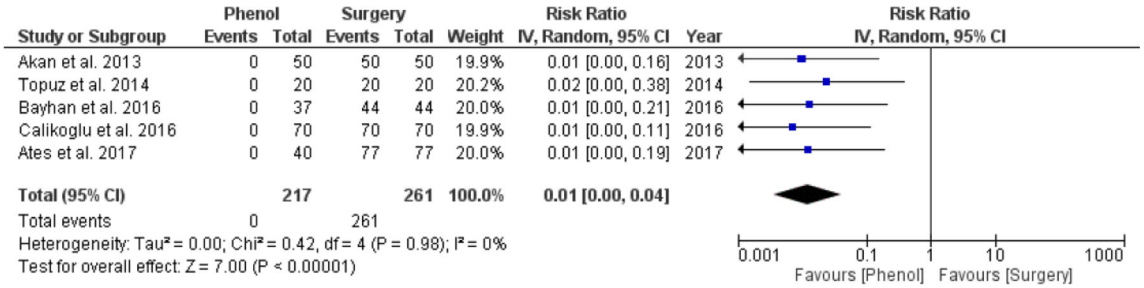

Fig. 3 A forest plot showing a significantly less hospital stay in in patients receiving phenolization compared to those who were treated surgically

performed by a surgery resident who was blinded to the research protocol. The remaining studies did not mention surgeons' experience level. Further, none of the studies described postoperative care.

Future studies are encouraged to consider measuring other important outcomes including healing time, longer follow-up, and the influence of the number of sinuses on the patients' response to treatment.

Limitations

A few limitations exist in this review. First, retrospective clinical trials were included; thus, some information was missing. Further, most of the included studies were non-randomized; thus, the qualitative and quantitative analyses were based on studies of lower scientific quality. Moreover, the meta-analysis was done on heterogeneous studies in terms of the follow-up period, which might bias the calculated recurrence rate. Finally, this review included only articles that were published in the English language.

Recommendation

Future studies are recommended to adapt a more rigorous methodology including achieving an adequate sample size (based on statistical calculation), and a more homogenous sample with regard to the recruited participants' age, sinus severity, and recurrence rate. Further, objective and valid measures and clearly described criteria of recurrence and hospital discharge should be employed. A longer follow-up should be considered to eliminate the potential of missing recurrent sinuses. Finally, future reviews should include higher quality studies and consider economic studies to provide a clear conclusion for clinicians and policy makers.

Conclusion

Based on the available evidence, phenolization of patients with pilonidal sinuses is significantly associated with less hospitalization compared to surgical intervention. However, both approaches have a comparable recurrence rate and complications. Thus, in indicated cases, phenolization could reduce the costs associated with hospitalization and expose patients to less surgery-related complications such as those associated with anesthesia.

Conflict of interest Ahmed Hagiga, Mohamed Aly, Mariia Gultiaeva, and Henry Murphy declare that they have no conflict of interest.

Informed consent Informed consent was not required because this was a review study.

Ethical approval For this type of study, formal consent from a local ethics committee is not required.

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