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Original Research

Dilapan-S versus Phloroglucinol for Cervical Dilatation in Operative Hysteroscopy and Polyp Resection: A Prospective Cohort Study

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Abstract

Background: To compare the effects of Dilapan-S versus phloroglucinol on cervical dilation in hysteroscopic polyp resection. **Methods**: This prospective, observational study enrolled non-menopausal patients with endometrial polyps who underwent operative hysteroscopy for transcervical polyp resection between October 2021 and October 2022. The patients were given Dilapan-S or phloroglucinol for cervical dilation. The primary outcome was cervical dilation time; secondary outcomes included cervical softening and adverse events. Non-inferiority was prespecified with a margin of 6 seconds. **Results**: Among 105 included patients, 55 were given phloroglucinol and 50 Dilapan-S. There were no significant differences in age, body mass index (BMI), history of vaginal delivery, hysteroscopic electrotomy, and cervical conization between the two groups (all $p > 0.05$). The cervical dilation time in the Dilapan-S group was shorter than in the phloroglucinol group (41.74 ± 8.68 s *vs.* 62.04 ± 9.55 s, non-inferiority $p < 0.001$). Also, more patients achieved highly effective cervical softening in the Dilapan-S group compared to the phloroglucinol group (44/50 *vs.* 1/55, $p < 0.001$). There were 4 cases of diarrhea ($p = 0.103$), 12 cases of vaginal bleeding ($p < 0.001$), and 4 cases of abdominal pain in the Dilapan-S group ($p = 0.103$), and none in the phloroglucinol group. There were also 5 cases of intraoperative water leakage in the phloroglucinol group and 8 cases in the Dilapan-S group ($p = 0.283$). **Conclusions**: Dilapan-S is found to be equally effective for cervical dilation as phloroglucinol; however, it is associated with a higher incidence of diarrhea, vaginal bleeding, and abdominal pain complications.

Keywords: Dilapan; phloroglucinol; hysteroscopy; cervical dilatation; prospective study

1. Introduction

Hysteroscopic surgery is a common gynecological procedure for treating endometrial polyps (EP), which might result in uterine bleeding, infertility [1–3], and even malignant transformation [4]. Furthermore, about 50% of hysteroscopic surgery complications, such as cervical laceration, uterine bleeding, and perforation, occur during cervical penetration [5,6]. Therefore, preoperative cervix dilation is essential for an uneventful hysteroscopic surgery and fewer surgical complications.

Cervical pretreatment methods include mechanical and pharmaceutical approaches and clinical cervical softening through resorol injection and disposable cervical dilation rod insertion. Also, oral or cervical placement of prostaglandins is commonly used in clinical practice [7,8]. As a derivative of prostaglandin E1, misoprostol can degrade cervical collagen fibers, release collagenase and elastase, and soften the cervix through prostaglandin receptors [9]. However, previous studies have shown that misoprostol pretreatment can cause uterine bleeding, vomiting, lower abdominal swelling, abdominal pain, diarrhea, and other adverse events [10,11]. Due to the relatively widespread side effects, patients with liver or kidney diseases, hypertension, glaucoma, and asthma are not advised to use misoprostol [12].

Recently, antispasmodics, such as phloroglucinol, drotaverine hydrochloride, and rociverine, have been extensively studied in labor induction. Phloroglucinol injection can directly act on the muscle and connective tissue of the cervical tube, thus relaxing and softening the cervix without affecting the uterine physiological contraction, which is partly due to its inhibition of catechol-O-methyltransferase [13]. Moreover, no obvious contraindications have been reported using phloroglucinol as a pretreatment for hysteroscopic surgery. Notable adverse reactions include nausea and dizziness, which were reported to disappear soon after dose reduction or drug withdrawal [14]. Dilapan-S (Minkai Medical Technology Company), a hygroscopic cervical expansion rod specially developed for obstetrics and gynecology, was introduced in China in 2017 [15]. It is made of polymer biomaterials (polypropylene transparent hydrolysis products), with wet volume gradually expanding 3–4 times, whose effect on dilation is achieved by mechanical irritation of the cervix, without any active ingredients [16]. As recent comparative data on mechanical and medical approaches for cervical dilation are inconclusive, more studies are needed to further improve the safety of hysteroscopy for endometrial polyps.
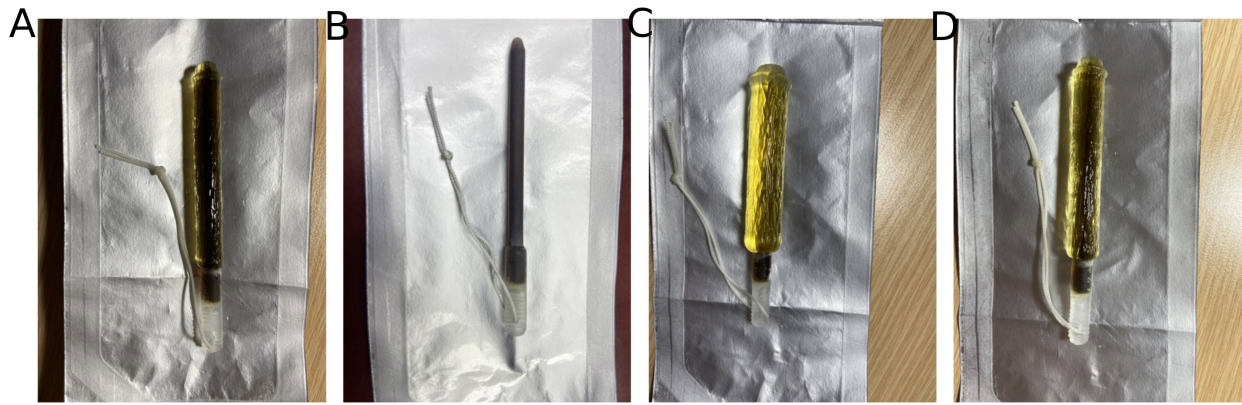
Fig. 1. Changes of Dilapan-S before and after water absorption. (A) No water absorption. (B–D) Water absorption for 1 h (B), 2 h (C), and 4 h (D).

Therefore, this study aimed to compare the effects of Dilapan-S versus phloroglucinol on cervical dilation before the operative hysteroscopy for endometrial polyps. In addition, non-inferiority design was applied to verify whether the clinical application effect on cervical dilation before hysteroscopy was comparable between the two methods.

2. Methods

2.1 Study Design and Participants

This prospective, observational study enrolled patients with endometrial polyps who underwent hysteroscopic electrosurgery at the Department of Gynecology, Huazhong University of Science and Technology Union Shenzhen Hospital, between October 2021 and October 2022.

Inclusion criteria were the following: (1) non-menopausal women aged 18–50 years old; (2) patients who underwent hysteroscopic electrosurgery under general anesthesia; (3) patients who received Dilapan-S or phloroglucinol for cervical dilation.

Exclusion criteria were the following: (1) poor compliance; (2) intrauterine adhesion; (3) acute or subacute pelvic infection; (4) active uterine bleeding; (5) recent history of uterine perforation or hysteroplasty; (6) reproductive tract tuberculosis without appropriate anti-tuberculosis treatment; (7) severe heart, lung, liver, kidney, and other organs deficiency; (8) invasive cervical cancer, endometrial cancer and other tumors of the reproductive tract.

The study was approved by the ethics committee of the Huazhong University of Science and Technology Union Shenzhen Hospital (NO. 072652). Written informed consent was obtained from all participants. All authors supported the accuracy and completeness of the data and adherence to the protocol.

2.2 Procedures

A routine preoperative examination was performed, including a routine blood test, leucorrhea routine screening, liver and kidney function, and electrocardiogram. Patients in the phloroglucinol group received an intravenous injection of 80 mg phloroglucinol (Nanjing Hang Seng Pharmaceutical Co., Ltd., 40 mL/bottle, Nanjing, Jiangsu, China) 15–30 min prior to the surgery. Disposable cervical dilator rod Dilapan-S (Kaim Medical Technology, 4×55 mm, Beijing, China) was used for cervical pretreatment of patients in the Dilapan-S group 2–4 h before the surgery. According to the manufacturer's instructions, the Dilapan-S was slowly inserted along the cervical canal, slightly exceeding the endocervix depth. Dry gauze was placed to block the orifice of the uterus. The vagina was disinfected again before the surgery, and Dilapan-S was withdrawn (Fig. 1).

The atropine and mechanical expansion were used if dilation failed. After successful dilation, the same experienced surgeons performed hysteroscopic endometrial polyp electrosurgery under general anesthesia.

2.3 Outcomes and Measurement

The primary outcome was the time of cervical dilation, which was defined as the time between the start of cervical dilation and the point at which the dilating rod of size 10 could be smoothly inserted into the endocervix.

Secondary outcomes included cervical softening and adverse events. "Highly effective" cervical softening was considered when a dilating rod ≤ 7 could smoothly pass through the endocervix; "effective" cervical softening was considered when a dilating rod of size 7 could pass through the endocervix with resistance; and "ineffective" cervical softening was considered when a dilating rod of size 7 could not pass through the endocervix, and the procedure was delayed. The cervical dilatation and softening time were measured for all patients before the surgery.

Adverse events included intraoperative leakage during hysteroscopic surgery caused by excessive cervical dilation and nausea, vomiting, abdominal pain, diarrhea, chills, fever, or vaginal bleeding after phloroglucinol injection or placement of Dilapan-S until the patient entered the oper-

Table 1. Baseline characteristics of participants.

Group	Phloroglucinol (n = 55)	Dilapan-S (n = 50)	p value
Age (mean ± SD, year)	38.20 ± 7.83	38.96 ± 7.11	0.605
BMI (mean ± SD, kg/m^2)	21.85 ± 3.17	22.60 ± 3.50	0.253
History of Vaginal delivery			0.080
No (n)	22	12	
Yes (n)	23	38	
Hysteroscopic electrotomy			0.430
Yes (n)	5	7	
No (n)	50	43	
Cervical operation			0.496
Yes (n)	2	0	
No (n)	53	50	

BMI, body mass index.

Table 2. Comparison of Dilapan-S versus phloroglucinol.

Group	Phloroglucinol (n = 55)	Dilapan-S (n = 50)	p value
Dilatation time (seconds)	62.04 ± 9.55	41.74 ± 8.68	<0.001
Cervical softening (n)			<0.001
Highly effective	1	44	
Effective	42	6	
Ineffective	12	0	
Diarrhea (n)			0.103
No	55	46	
Yes	0	4	
Vaginal bleeding (n)			<0.001
No	55	38	
Yes	0	12	
Abdominal pain (n)			0.283
No	55	46	
Yes	0	4	
Leakage (n)			0.283
No	50	42	
Yes	5	8	

ating room for hysteroscopic surgery. A visual analogue scale (VAS) score was used to evaluate the pain.

2.4 Sample Size Calculation

GPower software (3.1, Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany) was used to estimate the sample size. Non-inferiority trial design [17] was used to compare the time of cervical dilation and the effect of cervical softening. Assuming a non-inferiority margin of 6 seconds, one-tailed alpha of 0.025, and a power of 0.90, the required sample size per group was 50.

2.5 Statistical Analysis

SPSS 26.0 (IBM Corp., Armonk, NY, USA) was used to perform statistical analysis. The normally distributed continuous variables were presented as mean ± standard deviation (SD) and analyzed using an independent-sample t-test, while variables with skewed distribution were presented as medians and tested by rank-sum test. Categorical variables were presented as n (%) and tested by Chi-square test. $p < 0.05$ indicated statistical significance.

3. Results

Among a total of 105 patients enrolled in this study, 55 received phloroglucinol, and 50 received Dilapan-S for cervical dilatation (Table 1). The participants in the phloroglucinol group were 38.20 ± 7.83 years old with a body mass index (BMI) of 21.85 ± 3.17 kg/m^2 *vs.* 38.96 ± 7.11 years and 22.60 ± 3.50 kg/m^2 in phloroglucinol group. There were no significant differences in age, BMI, history of vaginal delivery, hysteroscopic electrotomy, and cervical conization between the two groups (all $p > 0.05$) (Table 1).

The cervical dilation time was shorter in the Dilapan-S group than in the phloroglucinol group (41.74 ± 8.68 s *vs.* 62.04 ± 9.55 s, difference 20.35 s, 95% confidence interval [CI]: 16.84–23.86 s, non-inferiority; $p < 0.001$). Also, more patients achieved highly effective cervical softening in the Dilapan-S group than in the phloroglucinol group (44/50 *vs.* 1/55, $p < 0.001$) (Table 2).

All the Dilapan-S rods were removed intact. There

were 4 cases of diarrhea ($p = 0.103$), 12 cases of vaginal bleeding ($p < 0.001$), and 4 cases of abdominal pain in the Dilapan-S group ($p = 0.283$), all of which resolved spontaneously within 24 hours. No adverse reactions were observed in the phloroglucinol group. There were 5 cases of intraoperative water leakage in the phloroglucinol group and 8 in the Dilapan-S group ($p = 0.283$). No patients reported nausea, vomiting, or fever in any of the groups (Table 2).

4. Discussion

The results of the present study showed that Dilapan-S could achieve shorter cervical dilation time. Also, more patients presented with highly effective cervical softening in the Dilapan-S group than in the phloroglucinol group. To the best of our knowledge, this is the first study that compared the two cervical dilation methods. Therefore, our results may help to improve safety and shorten the operation time of hysteroscopy, thus achieving better treatment effects.

Recent studies have reported that among different surgical methods used to treat EP, hysteroscopy has the best performance in view of the operation time, success rate, and complications [17–19]. In addition, a recent review of more than 1000 cases showed that 32% of infertile women had endometrial polyps, where surgical removal of polyps could promote natural pregnancy and improve the success rate of assisted reproduction [20]. Therefore, this study focused on non-menopausal patients who underwent the hysteroscopic resection of endometrial polyps. These patients all needed cervical dilation before surgery. We did not prescribe antibiotic prophylaxis prior to operative hysteroscopy, which was consistent with existing literature [21].

After Dilapan-S was approved by the US Food and Drug Administration (FDA) in 2015, several studies have compared its effect with traditional labor induction methods [22,23]. It was found that the application of Dilapan-S could gradually dilate and soften the cervix and initiate endogenous prostaglandin release, causing collagen degradation [24,25]. In this study, the application of phloroglucinol and Dilapan-S led to successful dilation in all patients, indicating that these two methods could effectively dilate the cervix. The cervical dilation time in the Dilapan-S group was 41.74 ± 8.68 s. Also, more patients achieved highly effective cervical softening in the Dilapan-S group than in the phloroglucinol group. These results are consistent with previous studies by Crosby *et al*. [26] and Baev *et al*. [27], reporting that the dilation time achieved by Dilapan-S was shorter than misoprostol in the comparable population. Therefore, the application of Dilapan-S might have a more prominent effect on cervical dilation than phloroglucinol.

It is important to note that more patients presented with diarrhea, vaginal bleeding, and abdominal pain in Dilapan-S than in the phloroglucinol group. Diarrhea is related to Dilapan-S stimulation of the rectum and anus.

Vaginal bleeding may be related to Dilapan-S direct stimulation of the vagina and cervix. Abdominal pain is related to Dilapan-S stimulation of the vaginal sphincter and rectal contraction.Previous studies also noted these adverse events, which appeared to be caused by uterine contraction [28]. Moreover, the efficacy of the medication-based methods is uncertain, as drug absorption is decisive in causing excessive cervical dilation, which affects the surgical field, or results in insufficient dilation that increases the operation time and may lead to cervical trauma bleeding [29,30]. Although misoprostol was found to have some efficacy in office hysteroscopy compared to placebo [31], it was contraindicated for people with cardiovascular disease, glaucoma, gastrointestinal disorders, asthma, and allergies [7,14]. No adverse events such as nausea, vomiting, or fever were reported in this study in the two groups. Since 10 mm of dilation is sufficient for hysteroscopic electrotonic surgery, the placement time could be shortened, which might reduce abdominal pain, vaginal bleeding, diarrhea, and other side effects. Moreover, Dilapan-S could be applied in patients with a scarred uterus, as 4 mm rods swell up to 15 mm in 12–24 hours [32].

The present study has some limitations. Due to a relatively small sample size, observing all adverse effects was impossible. The present study was conducted in a single center, which may have led to the low variability in management and may therefore be less applicable to other centers. No uterine and cervical length and width were measured before dilation or surgery. Future multicenter studies with expanded sample sizes are needed to further investigate safety concerns.

5. Conclusions

Dilapan-S is found to be equally effective for cervical dilation as phloroglucinol; however, it is associated with a higher incidence of vaginal bleeding, diarrhea and abdominal pain complications. We advocate other large-scale studies here.

Availability of Data and Materials

The data that support the findings of this study are available on request from the corresponding author.

Author Contributions

ZL and YX carried out the studies, participated in collecting data, and drafted the manuscript. AL and ZL performed the statistical analysis and participated in its design. AL drafted the manuscript and revised it critically for important intellectual content. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

This work has been carried out in accordance with the Declaration of Helsinki (2000) of the World Medical As-

sociation. The study protocol was approved by the Ethics Committee of Department of Huazhong University of Science and Technology Union Shenzhen Hospital (NO. KY-2021-042-01). All patients signed informed consent forms before they were performed surgery.

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Conflict of Interest

The authors declare no conflict of interest.

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