Oxidized, Regenerated Cellulose Adhesion Barrier Plus Intrauterine Device Prevents Recurrence After Adhesiolysis for Moderate to Severe Intrauterine Adhesions

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ABSTRACT Study Objective: To compare the efficacy of an oxidized, regenerated cellulose adhesion barrier (Interceed; Ethicon, Somerville, NJ) combined with an intrauterine device (IUD) versus an IUD alone for preventing adhesion recurrence following hysteroscopic adhesiolysis for moderate to severe intrauterine adhesions (IUAs).

Design: Retrospective case series (Canadian Task Force classification III).

Setting: Tertiary care teaching hospital.

Patients: Patients undergoing treatment for moderate to severe IUAs. The severity of IUA was determined based on the American Fertility Society scoring system (mild, moderate, or severe).

Interventions: All cases of hysteroscopic adhesiolysis were reviewed.

Measurements and Results: Seventy-six women with moderate to severe IUAs treated between March 2009 and August 2015 were included. After hysteroscopic adhesiolysis, 35 patients were treated with an IUD alone (group 1), and 41 patients were treated with Interceed plus an IUD (group 2). A second hysteroscopy was performed in all cases three months after the initial hysteroscopy and both groups achieved significant reduction in adhesion scores and grade, especially in group 2 (scores, \( p < .001 \); grade, \( p = .039 \)). Compared with group 1, menstruation dysfunction, pregnancy rate, and live birth rate in group 2 improved with no statistical difference (menstruation improvement, \( p = .764 \); pregnancy rate, \( p = .310 \); live birth rate, \( p = .068 \)). However, an adhesion-free uterine cavity was regained significantly owing to the fewer operations in group 2 compared with group 1 (median, 3 vs 4; \( p = .001 \)). The interval from initial hysteroscopy to conception was significantly shorter in group 2 (median, 12 months vs 51 months; \( p < .001 \)).

Conclusions: For moderate to severe IUAs, Interceed combined with an IUD may be an alternative approach for reducing adhesion recurrence after hysteroscopic adhesiolysis. Journal of Minimally Invasive Gynecology (2016) - - - . © 2016 AAGL. All rights reserved.

Keywords: Adhesion recurrence; Adhesion reduction; Asherman’s syndrome; Hysteroscopy; Menstrual dysfunction; Pregnancy rate; Uterine synechiae
dysfunction, decrease the recurrence of IUAs, and improve infertility, especially in severe cases, the rate adhesion recurrence still remains as high as 14% to 48% [5–8]. Furthermore, a recent study [9] showed that the risk of IUA recurrence increases when successfully separated adhesions were originally found at the uterine cornua or cervicoisthmic region, or involved a large portion of the uterine cavity. Thus, more effective approaches to preventing IUA recurrence are needed.

Recently, an oxidized, regenerated cellulose adhesion barrier (Interceed; Ethicon, Somerville, NJ) has shown efficacy in preventing postoperative adhesions in various abdominal surgical procedures [10]. Interceed also has been shown to prevent postoperative adhesions in other surgical sites, including neovagina [11–13], breast [14,15], pleural cavity [16], and thyroid [17]. Few studies to date have demonstrated the use of Interceed in the uterine cavity, however. Paul et al [18] reported that Interceed plus preoperative gonadotropin-releasing hormone agonist (GnRHa) reduced IUAs in a rabbit model. In previous work, we found that Interceed reduces adhesions and improves endometrial receptivity in rabbits [19]. Owing to lack of effective treatment for IUAs and our previous findings [19], we have further explored the potential use of Interceed in clinical treatment, using a circular inert IUD as a mold for Interceed. This combination has shown promise as an alternative treatment for moderate to severe IUAs in our practice.

In the present retrospective study, we aimed to compare the efficacy of Interceed combined with an IUD versus an IUD alone for preventing adhesion recurrence following lysis for moderate to severe IUAs.

Methods

Patients

This study was approved by the Institutional Review Board of Zhujiang Hospital, Southern Medical University. Demographic and perioperative data for women who underwent initial hysteroscopic surgery at Zhujiang Hospital between March 2009 and August 2015 were collected retrospectively. Inclusion criteria were as follows: IUA confirmed by hysteroscopy; adhesion score ≥5 according to the American Fertility Society (AFS) scoring system [20]; a comprehensive infertility workup, involving a detailed history, clinical examination, and other specific investigations (e.g., transvaginal ultrasound, cervicovaginal discharge evaluation especially for mycoplasmas and chlamydia, serum basal hormone levels, hysterosalpingography, hysteroscopy combined with laparoscopy when necessary); age <40 years; and willingness to be followed up for at least 6 months. Exclusion criteria were indication of another primary cause of infertility and contraindication for hormone therapy. A flowchart depicting patient selection is shown in Figure 1.

IUA Procedure and Interceed Application

All patients were scheduled for hysteroscopy in their early proliferative phase, namely, on day 5 to 7 of their menstrual circle or any day of secondary amenorrhea. Three misoprostol tablets (600 mg) were administered orally for cervical dilation at 6 to 8 hours before the operation. All procedures were conducted by the same gynecologist (Y.-L.H.). Normal saline solution was used for distention. Adhesiolysis was initiated inferiorly and advanced cephalad until restoration of the uterine cavity was achieved.

Filmy adhesions were dissected first, followed by dense and extensive adhesions. The filmy adhesions were treated with only the tip of the 5-mm rigid hystroscope by blunt dissection. For dense and extensive adhesions, multiple hysteroscopic techniques using scissors and bipolar electrosurgical instruments were required to achieve satisfactory results. The scars were often too dense to be cut with scissors, and bipolar electrosurgical instruments were often required for precise cutting and good hemostasis.

The procedure was deemed complete when it was impossible to differentiate denuded myometrium from scar tissue, which increased the potential for uterine perforation, even when tubal ostias were not visible. Adhesiolysis was monitored by concurrent laparoscopy or abdominal ultrasonography when necessary.

At the end of the operation, meticulous verification of hemostasis was performed. For mild bleeding, a 5-mm Foley catheter filled with 2 mL of saline solution was inserted into the uterine cavity for 10 minutes to provide compression hemostasis. For substantial bleeding, the origin of bleeding was identified and controlled using a bipolar electrode needle under hysteroscopy. Cessation of bleeding was verified before placement of the IUD or Interceed under hysteroscopy.

In group 1, a circular inert IUD (Medical Suture Needle Factory Co., Ltd., Shanghai, China) was immediately inserted into the uterine cavity. In group 2, Interceed, which comes as a lightweight, tissue-like fabric sheet measuring 7.6 cm × 10.2 cm, was cut into 2 pieces and tailored to the size of the uterine cavity. One piece was wrapped around the circular inert IUD in a clockwise direction in vitro (Fig. 2A and B) and then introduced into the uterine cavity with the aid of a curved artery forceps (Fig. 2C). The other piece was placed in the central bare region of the uterine cavity by means of the artery forceps. Finally, hysteroscopy with less distension was used to verify Interceed and IUD placement. No active hemorrhage occurred to make Interceed become darkened (Fig. 2D).

Postoperative Procedures and Follow-Up

All patients received oral antibiotics (doxycycline; Yongxin Pharmaceutical Co., Ltd., Jiangsu, China), 400 mg/day for 7 days postoperatively. All patients also received oral estradiol valerate (Progynova; Schering, Berlin, Germany),...
5 mg twice daily for 28 days from day 5 postoperatively, and medroxyprogesterone acetate (Xianju Pharmaceutical Co., Ltd., Zhejiang, China), 10 mg once daily, during the last 10 days of estradiol therapy. The hormone therapy protocol was followed cyclically for 3 months.

The intrauterine presence of Interceed was identified via postoperative ultrasonography performed by the same ultrasound physician. Ultrasound scans were scheduled on days 2, 7, 14, and 21 after Interceed placement. Further follow-up was completed via outpatient visit and telephone contact every 3 months for at least 6 months. Information on menstruation and reproductive outcomes was recorded.

All second-look hysteroscopies were performed at 3 months after the initial hysteroscopy. The IUD was removed after initial inspection to evaluate the extent and severity of any recurrent IUAs. If significant adhesion recurrence was identified, reoperation was performed. Patients initially treated by IUD alone were then treated by estrogen (with alleviation of adhesions) or estrogen plus repeated IUD placement (without alleviation of adhesions). Patients initially treated by Interceed plus an IUD would be treated by estrogen with/without an IUD (with alleviation of adhesions) or the combination of estrogen, IUD, and Interceed (without alleviation of adhesions). Given the potential risks associated with long-term use of a relatively high dose of estradiol, if recurrent adhesions were identified as severe or moderate, then the estradiol dose was decreased to 5 mg/day for 28 days, cyclically for 3 months. If recurrent adhesions were identified as mild, then estradiol was decreased to 2 mg/day for 28 days, cyclically for 3 months.
Outcome Measures

The primary outcome was change in adhesions, including adhesion scores and grade between the initial hysteroscopy and second hysteroscopy. Adhesions were assessed according to the AFS scoring system (score 1–4, mild IUAs; 5–8, moderate IUAs; 9–12, severe IUAs) [20].

Secondary outcomes included (1) perioperative complications, including severe perioperative complications such as uterine perforation and operative hysteroscopy intravascular absorption syndrome, and postoperative complications such as spontaneous IUD expulsions, infection and hormone treatment-related complications; (2) change in menstrual pattern between hysteroscopies (identified as amenorrhea, hypomenorrhea, or eumenorrhea); (3) number of operations needed to achieve an adhesion-free uterine cavity; and (4) reproductive outcomes, including pregnancy rate and live birth rate. Each patient was required to use the same brand of feminine hygiene product during treatment and completed a semiquantitative menstrual pictogram [21] to estimate menstrual blood loss, with data provided to the study team at each follow-up visit. Accordingly, hypomenorrhea was defined as more than a 1/3 reduction in menstrual blood loss.

Statistical Analysis

All statistical analyses were performed using SPSS version 13.0 (SPSS, Chicago, IL). Data were verified for distributional assumptions using the Kolmogorov-Smirnov test. Quantitative data with normality were assessed by the independent-samples t test. Ranked data or quantitative data without normality were evaluated using the Mann-Whitney U test, and binomial distribution data were estimated using the χ² test. A 2-sided p value <.05 was considered to indicate statistical significance.

Results

Patient Characteristics

A total of 76 patients with moderate to severe IUAs were included in this study. Patient demographic data are presented in Table 1. Group 1 comprised 12 patients with moderate IUAs and 23 patients with severe IUAs. Group 2 comprised 17 patients with moderate IUAs and 24 with severe IUAs. There was no statistically significant difference in any baseline characteristics between the 2 groups.

Changes in Adhesion

At the second hysteroscopy, the median adhesion score was 7 in group 1 and 4 in group 2. All adhesions were

<table>
<thead>
<tr>
<th>Table 1</th>
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<tr>
<td>Demographic characteristics of the study population</td>
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<tr>
<td>Variable</td>
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<tr>
<td>Number</td>
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<tr>
<td>Age, yr, mean ± SD</td>
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<tr>
<td>Body mass index, kg/m², mean ± SD</td>
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<tr>
<td>Uterine size, cm³, mean ± SD</td>
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<td>Menstrual pattern, n (%)</td>
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<tr>
<td>Amenorrhea</td>
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<tr>
<td>Hypomenorrhea</td>
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<tr>
<td>Eumenorrhea</td>
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<tr>
<td>Etiologic factors, n (%)</td>
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<tr>
<td>DCEA</td>
</tr>
<tr>
<td>DCMIA</td>
</tr>
<tr>
<td>DCIDP</td>
</tr>
<tr>
<td>Cesarean delivery</td>
</tr>
<tr>
<td>Hysteroscopic surgery</td>
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<tr>
<td>Uterine artery embolization</td>
</tr>
<tr>
<td>Genital tuberculosis</td>
</tr>
<tr>
<td>Unknown</td>
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<tr>
<td>Adhesion grade, n (%)*</td>
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<tr>
<td>Moderate</td>
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<tr>
<td>Severe</td>
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</tbody>
</table>

DCEA = dilatation and curettage for elective abortion; DCIDP = dilatation and curettage for induction delivery or postpartum; DCMIA = dilatation and curettage for missed or incomplete abortion; IUD = intrauterine device.

* Referring to status at first hysteroscopy.
significantly reduced compared with those at the initial hysteroscopy (group 1, \( p < .001 \); group 2, \( p < .001 \)) (Fig. 3A and B). The median adhesion score was significantly lower in group 2 compared with group 1 (3 vs 5; \( p < .001 \)) (Fig. 3C).

At the second hysteroscopy, in group 1, 4 patients had no adhesions, 5 had mild IUAs, 9 had moderate IUAs, and 11 had severe IUAs. In group 2, 9 patients had no adhesions, 15 had mild IUAs, 10 had moderate IUAs, and 7 had severe IUAs. There was a significant reduction in adhesion grade in both groups (group 1, \( p = .001 \); group 2, \( p < .001 \)) (Fig. 3D and E), with a statistically significant difference between the 2 groups (\( p = .039 \)) (Fig. 3F).

### Perioperative Complications

There were no perioperative complications; no uterine perforation or operative hysteroscopy intravascular absorption syndrome was recorded. Postoperatively, 5 patients (6.6%) experienced complications, including 2 patients (5.7%) in group 1 and 3 patients (7.3%) in group 2. The difference between groups was not statistically significant (\( p = .803 \)) (Table 2). In group 1, 1 patient developed vulvovaginal candidiasis and 1 patient developed a urinary tract infection. In group 2, 2 patients had vulvovaginal candidiasis and 1 had a urinary tract infection. These complications were alleviated by meticulous management.

There were no spontaneous IUD expulsions during the study. Intrauterine retention of Interceed was observed via postoperative ultrasonography until day 21 for 10 patients in group 2. Typical ultrasonographic images of Interceed plus IUD in the uterine cavity are shown in Figure 4. The median duration of Interceed retention in the uterine cavity was 19 days (range 15–26 days) in group 2.

Although a relatively high dosage of estrogen was administered after the initial hysteroscopy, no complications were noted on hematologic and imaging examinations during the entire study and follow-up period. There were no statistical differences in activated partial thromboplastin time, thrombin time, or fibrinogen and liver enzyme levels between the initial hysteroscopy and second hysteroscopy. Although prothrombin time was statistically significantly shorter before the second hysteroscopy than before the initial hysteroscopy (12.4 ± 1.5 seconds vs 12.8 ± 0.8 seconds;
p = .047), in both cases the range was within the normal reference value range (11.0–15.0 seconds) (Table 3).

**Change in Menstrual Pattern**

In group 1, 15 patients had amenorrhea, 15 had hypomenorrhea, and 5 had eumenorrhea before the initial hysteroscopy, and 4 patients had amenorrhea, 13 had hypomenorrhea, and 18 had eumenorrhea after the initial hysteroscopy. In group 2, 9 patients had amenorrhea, 24 had hypomenorrhea, and 8 had eumenorrhea before the initial hysteroscopy, and 2 patients had amenorrhea, 19 had hypomenorrhea, and 20 had eumenorrhea after the initial hysteroscopy. Both groups exhibited significantly improved menstruation function after the initial hysteroscopy (group 1, p = .001; group 2, p = .006).

In group 1, 2 patients experienced reduced menstruation, 14 had no change in menstruation, and 19 had improved menstruation. In group 2, 1 patient had reduced menstruation, 17 had no change in menstruation, and 23 had improved menstruation. There was no statistical difference in menstruation improvement between group 1 and group 2 (54.3% vs 56.1%; p = .764) (Table 2).

**Number of Operations Needed to Achieve an Adhesion-Free Uterine Cavity**

At the second hysteroscopy, 13 of 76 patients (17.1%) were free of adhesion recurrence. The median number of operations needed to achieve an adhesion-free uterine cavity was 4 (range, 1–9) in group 1 and 3 (range, 1–5) in group 2, a statistically significant difference between the groups (p = .001) (Table 2). In group 2, 39 of 41 patients (95.1%) regained an adhesion-free uterine cavity after 4 repeat operations, and 2 (4.9%) patients did so after 5 repeat operations. In group 1, 29 of 35 patients (82.9%) regained an adhesion-free uterine cavity after 5 repeat operations.

**Reproductive Outcomes**

Among the 76 patients, 24 achieved pregnancy, 4 chose not to attempt pregnancy, and the remaining 48 planned to still attempt pregnancy. Among the 24 pregnancies, 4 were achieved via in vitro fertilization (2 in each group), and the remainder were spontaneous. The pregnancy rate was higher in group 2 than in group 1, but with no statistical difference (36.6% vs 25.7%; p = .310); however, the median interval from initial hysteroscopy to conception was

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**Table 3**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Initial hysteroscopy (n = 76), mean ± SD</th>
<th>Second hysteroscopy (n = 76), mean ± SD</th>
<th>Own reference range</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PT, s</td>
<td>12.8 ± 0.8</td>
<td>12.4 ± 1.5</td>
<td>11.0–15.0</td>
<td>.047</td>
</tr>
<tr>
<td>APTT, s</td>
<td>38.1 ± 3.6</td>
<td>36.8 ± 4.9</td>
<td>28.0–45.0</td>
<td>.060</td>
</tr>
<tr>
<td>TT, s</td>
<td>16.4 ± 2.4</td>
<td>17.0 ± 1.4</td>
<td>14.0–21.0</td>
<td>.075</td>
</tr>
<tr>
<td>Fibrinogen, g/L</td>
<td>2.7 ± 0.7</td>
<td>2.7 ± 0.5</td>
<td>2.0–4.0</td>
<td>.541</td>
</tr>
<tr>
<td>GPT, IU/L</td>
<td>17.3 ± 8.7</td>
<td>18.0 ± 14.4</td>
<td>5.0–40.0</td>
<td>.738</td>
</tr>
<tr>
<td>GOT, IU/L</td>
<td>17.5 ± 6.6</td>
<td>18.0 ± 10.4</td>
<td>4.0–40.0</td>
<td>.755</td>
</tr>
</tbody>
</table>

APTT = activated partial thromboplastin time; GPT = glutamic oxalacetic transaminase; GPT = glutamic pyruvic transaminase; PT = prothrombin time; TT = thrombin time.
significantly shorter in group 2 than in group 1 (12 months vs 51 months; p < .001) (Table 2).

After pregnancy, 9 patients chose elective abortion (4 for blighted ovum and 5 for maternal factors). Live births occurred in 13 of 76 patients (17.1%), with a higher rate in group 2 compared with group 1, but without statistical significance (24.4% vs 8.6%; p = .068) (Table 2). Among the 13 cases with live births, 12 achieved a term or near-term delivery and 1 was still pregnant at the time of this report. There were no obstetric complications during any of the pregnancies.

Discussion

In this study, we preliminarily prove that for moderate to severe IUAs, compared with an IUD alone, the combination of Interceed and an IUD has greater efficacy in reducing adhesion recurrence and improving menstrual function and fertility, with no additional risk of perioperative complications.

In the off-label applications of Interceed in other surgical sites, reported advantages include preventing adhesions [11–17], accelerating reepithelialization of neovagina [11–13], making up for deficiencies after partial mastectomy [14,15], and improving neck discomfort after thyroidectomy [17], all without additional complications. Accordingly, because both the uterine cavity and abdominal cavity are hollow organs, we deemed the use of Interceed to be theoretically reasonable in this application. Given the lack of effective treatment for IUAs, the combination of Interceed and an IUD was considered a promising innovation that merited exploration. Furthermore, our previous study in rabbits showed that Interceed could potentially improve the morphology and receptivity of the endometrium in IUAs [19]. Paul et al [18] also reported the antiadhesive property of Interceed in a rabbit model. A major difference between these 2 studies is that the antiadhesive effect could be maximized by Interceed combined with estrogen or GnRHa. The exact mechanism for GnRHa-induced reduction of adhesions remains elusive [18], whereas estrogen is recognized as beneficial for IUA reduction by accelerating endometrial regeneration and covering the denuded endometrial layer [3]. Therefore, in the present study we used Interceed in combination with estrogen rather than with GnRHa.

Before Interceed is used in clinical applications, 4 key issues need to be addressed. First, Interceed is a lightweight, tissue-like fabric that is placed at the surgical site and transforms into a gel covering the surgical area. But unlike the plane area in abdominal surgery or the elongated uterus in rabbits, the uterine cavity in women is an inverted triangular shape, which might limit Interceed from spreading in situ to cover the denuded endometrial layer. Thus, a mold is necessary to support Interceed placement. Second, Interceed can be completely absorbed within 2 weeks when applied in a single layer in the abdomen [22]. In addition, several other commercially available mechanical barriers have been suggested for IUAs, such as Foley catheter and intrauterine balloon stent, both of which must be removed after just a few days. An IUD is the only barrier that can be placed in the uterine cavity for several months [3], making it an optimal mold for applying Interceed. Third, 2 types of IUD, T-shaped and circular-shaped, have been used for IUAs in our clinical practice. Only the circular-shaped IUD is feasible for wrapping Interceed in a clockwise direction in vitro. Furthermore, the T-shaped IUD is suboptimal in preventing adhesions because it contains copper and may induce an inflammatory reaction [23]. Fourth, in clinical treatment of IUAs by circular IUD alone, we found that recurrent IUAs were often localized in the IUD-free area, although the recurrent adhesions location also might be related to the original location and extent of IUAs [9]. Accordingly, the application of Interceed must prevent both central and peripheral recurrence, which can be achieved by placing Interceed in the central IUD-free region.

The results of postoperative ultrasonography and hysteroscopy show that our design addresses the foregoing issues reasonably and effectively. Compared with an IUD alone, Interceed plus an IUD can better prevent adhesion recurrence. The application of Interceed did not increase the risk of perioperative complications, and controlled both the central and peripheral recurrence of IUAs. Group 2 had fewer repeat hysteroscopies, and thus a lower risk of IUAs that can result from surgical trauma. The interval between the initial hysteroscopy and conception was statistically shorter in group 2, which is associated with fewer repeat hysteroscopies. Fewer repeat hysteroscopies reduces the risk of IUUA recurrence from surgical trauma, and also is beneficial for endometrial repair and subsequent fertility.

In the present study, the adhesion recurrence rates were 78.0% (32 of 41) in group 1 and 88.6% (31 of 35) in group 2. These rates are inconsistent with those reported by Lin et al [24] and Amer et al [7]. The former reported reformation rates of 30.0% (25 of 82) in their balloon group and 35.0% (28 of 80) in their IUD group [24], and the latter reported a reformation rate of 48% (12 of 25) in their amnion grafting group [7]. Overall, the adhesion recurrence rate in our patients, especially in group 1, was clearly higher than the rates reported in those 2 previous studies. Nevertheless, this discrepancy might be related to the proportion of severe cases in these studies. The percentage of severe cases was 61.8% (47 of 76) in our study, compared with 40.7% (66 of 162) in the study of Lin et al [24] and 52.0% (13 of 25) in the study of Amer et al [7]. Moreover, adhesion scores were reduced by 3 in our group 2 and by 5 in our group 1, compared with 8 in the balloon group and 4.5 in the gel group from another previous study [25]. The antiadhesive effect of adjuvant therapies in our study appears to be smaller than that reported in that previous study. A possible explanation for this discrepancy could be the higher percentage of severe cases in our cohort compared with the previous study (61.8% vs 30% [6 of 20] in the balloon group and 33% [6 of 18] in the gel group [25]). Thus, although all of the patients in our present study and the previous studies were diagnosed
with moderate to severe IUAs according to the AFS classification system, the differing percentages of severe cases makes comparisons of our findings and results from the previous studies challenging. For specific patients included in our study, we can preliminarily conclude that compared with an IUD alone, the combination of Interceed and an IUD achieves better results.

Meticulous verification of hemostasis was performed via Foley catheter compression or bipolar electrode under hysteroscopy before the placement of Interceed. This prevented bleeding from significantly reducing the antiadhesive effect of Interceed.

A second benefit of Interceed placement was the prolonged process of absorption. Compared with Interceed in abdominal surgery, which is often absorbed within 2 weeks, postoperative ultrasonography indicated a longer persistence of Interceed in the uterine cavity. This meant that raw surfaces of uterine walls would be separated for longer than 2 weeks, which helped prevent adhesion recurrence and promote endometrial repair.

A third benefit of Interceed may involve its biological effect. Gago et al. [26] found increased expression of tissue plasminogen activator and a higher tissue plasminogen activator:plasminogen activation inhibitor 1 ratio in fibroblasts and mesothelial cells being incubated with Interceed. This fibrinolytic activity could promote dissolution of fibrin and prevent subsequent adhesion development. Thus, Interceed’s ability to prevent adhesion recurrence may be derived from both its barrier and biological effects.

This study has some limitations. First, as a nonrandomized retrospective study, there may be significant selection bias owing to the wishes of patients and the final consensus achieved by physicians and patients regarding which adjuvant therapy to use. Of note, however, the baseline characteristics of our groups, including the severity of IUAs, were not statistically significantly different. Moreover, the severity of IUA is a comprehensive measure of the difficulty of hysteroscopic surgery. Nonetheless, further prospective randomized studies are warranted. Second, only 76 of 311 patients with moderate to severe IUAs were evaluated with strict exclusion criteria, a small sample size that impacted data analysis. Other than menstrual function, pregnancy rate, and live birth rate, the differences between the 2 groups had no statistical significance, possibly related to the small sample size and limited follow-up time. Furthermore, Interceed ideally should be applied in a single layer, but clinical conditions made this application difficult, even in the abdominal surgeries. Although we proved that Interceed applied in multiple layers, either intentionally (such as with Interceed wrapped around an IUD) or involuntarily (owing to folding during and after surgery from compression by the uterine wall), limited efficacy, more precise manufacturing should be developed to facilitate the application of a single layer.

In summary, our findings suggest that compared with an IUD alone, Interceed combined with an IUD is more effective in preventing IUA recurrence, leading to subsequent pregnancies, with no additional risk of perioperative complications. Considering the limited efficacy of current preventive strategies, Interceed combined with an IUD following hysteroscopic lysis is promising in treating IUAs, with further large-scale prospective randomized blinded studies warranted.

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References


