Original Article

Comparison of therapeutic efficacy of three methods to prevent re-adhesion after hysteroscopic intrauterine adhesion separation: a parallel, randomized and single-center trial

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Background: This research aims to study the efficacy of an integrated approach to prevent and treat the recurrence of intrauterine adhesions (IUA) after hysteroscopic adhesiolysis.

Methods: A total of 96 patients diagnosed with moderate-to-severe intrauterine adhesions (IUA) in Nantong Maternal and Child Health Hospital from January 2016 to December 2019 were included in this parallel, randomized and single-center trial. Moderate (48 cases) and severe (48 cases) patients were randomly divided into three groups by a computer random generator: Group A (IUD, n=16), Group B, (Foley1w+IUD, n=16) and Group C (Foley1m+IUD, n=16). All patients received sequential treatment of estrogen and progesterone on the day of operation. Follow-up was performed at 1 and 3 months after treatment of uterine cavity, endometrial thickness, menstruation and pregnancy. Surgeons who performed the second-look and third-look hysteroscopy and postsurgical assessors were blinded to the randomization.

Results: In total, 96 patients (48 cases in each degree) were included in the final analysis, with 16 cases in each group. No cases were lost to follow up. The primary outcome measure was AFS score, which was significantly lower in Group C than that of women in group A and Group B at 1 month ($P<0.05$). Similar results were observed at 3-month follow up. In patients with moderate adhesions, the pregnancy rate in Group C (Foley1m+IUD) was higher than that in Group A and Group B ($P<0.05$). However, in patients with severe adhesions, there was no significant difference in the pregnancy rate among the three groups ($P>0.05$). There was no statistical significance in infection indicators among the three groups of moderate and severe patients ($P>0.05$). Postoperative complications such as uterine perforation, severe bleeding, water poisoning and intrauterine infection were not observed.

Conclusions: The effect of a Foley intrauterine balloon combined with IUD in preventing re-adhesion was better than that of an IUD alone. For patients with moderate adhesion, the prolongation of placement time could prevent intrauterine re-adhesion and significantly improve the pregnancy rate with strong safety. However, for patients with severe adhesions, the prolongation of intrauterine Foley balloon placement did not better prevent intrauterine re-adhesions, improve menstruation, or improve pregnancy rates.

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Introduction

Background

Intrauterine adhesions (IUA) are also known as Asherman syndrome, stemming from Asherman's systematic description of a series of symptoms of in 1948. IUA usually begins with endometrial damage which may be caused by various factors, and may result in fibrosis, leading to IUA occlusion and clinical symptoms, in which menstrual reduction and secondary infertility are the most common symptoms. Other symptoms include amenorrhea, periodical lower abdominal pain in women of childbearing age, and postmenopausal lower abdominal pain (1,2). Factors that induce IUA include uterine procedures (such as uterine curettage, cesarean section, and myomectomy), genital tract infections (such as bacterial vaginitis and mycoplasma infection), and genital tract malformations (including uterine mediastinum) (3). Sanders (4) studies on patients with IUA showed that intrauterine manipulation is a major factor in their pathogenesis, and the increased numbers of induced abortions in recent times has contributed to a rise in IUA cases. In a word, intrauterine adhesions are mostly caused by the fibrotic regeneration of the endometrium after severe damage.

The focus of current research is on determining measures to restore the structure and volume of the uterine cavity, prevent uterine wall adhesions, and relieve the clinical symptoms of patients, as measures to improve the reproductive function of women of childbearing age. With the development of minimally invasive technology, hysteroscopy has become the latest instrument for the accurate diagnosis of IUA, although other auxiliary examination methods, such as B-ultrasound and MRI, can improve the detection rate of IUA bands (5). However, the lack of clear vision of hysteroscopy contributes little to the comprehensive AFS score and further treatment after the detection of IUA. According to Dean *et al.*, research on current therapies for IUA focuses on five areas: (I) surgical treatments, such as TCRA under hysteroscopy; (II) prevention of re-adhesion, involving physical interventions such as intrauterine balloon, intrauterine device (IUD), and biological interventions including sodium hyaluronate and amniotic membrane; (III) promotion of endometrial regeneration, including estrogen and progesterone therapy, stem cells and Chinese traditional medicine to induce endometrial regeneration; (IV) anti-inflammatory treatment; (V) postoperative reassessment of TCRA, including non-invasive methods such as MRI and B-ultrasound examination and intrusive methods such as hysteroscopy.

The current preferred treatment for IUA in China is TCRA, which has revolutionized the field. The separation of adhesions can be realized by electrotomy separation and scissors separation (6), and to prevent uterine perforation and improve the chance of successful surgery, B-ultrasound or laparoscopy can be used for monitoring (7). The specific surgical method involves intraoperative layer by layer separation, which begins with the separation of loose tissue, the uterine cavity is then enlarged, and dense tissue such as scars are removed. This provides the opportunity to repair the region from the fundus to the midline of the uterus and then to the lateral wall of the adhered uterine cavity. TCRA has the contradictory characteristics of a high success rate and high recurrence rate. It has even been reported that the recurrence rate of severe adhesions can be as high as 48–62.5%, while the pregnancy rate is as low as 22.5–33.3% (8). Therefore, it is crucial to prevent re-adhesion and increase the chance of pregnancy after surgery. Chinese government has promoted the use of IUDs since 1959. According to the statistics in 2002, almost 50% married women of childbearing age in China choose IUD to prevent pregnancy. The use rate of IUD has been declining in the past decade, but it is still widely used (9). We conducted a systematic review of the available literature, found no current accurate use rate of IUD. While at present, IUDs and intrauterine balloons are

widely used, these come in many forms, and their use is still controversial, with no clear consensus on which is best (10,11). General opinion supports a balloon indwelling time of 5–7 days, while endometrial recovery after TCRA takes at least one month (12), and the mean time to fertilization after TCRA is 9.7±3.7 months. Further, as the severity of IUA increases, the fertilization rate decreases (13).

Foreign research on IUA has largely focused on the following aspects: (I) searching for a new classification system for IUA (14,15); (II) stem cell transplantation, where scholars expect to isolate endometrial stem cells to promote endometrial regeneration by extracting menstrual blood and umbilical cord blood stem cells (16); (III) new adjuvant methods combined with balloon therapy. Cai *et al.* investigated the effectiveness of an oxidative regenerative cellulose adhesion barrier plus an IUD (17); (IV) new intrauterine stents. Huang *et al.* established a new type of intrauterine stent with the expectation of finding a replacement for previous versions (18); (V) studies on the mechanism of IUA. Wu studied the signaling pathway of related factors in IUA (19).

Clinically, IUA is the type of disease which has great influence on the quality of life and reproduction of patients. The recurrence rate after surgery was as high as 62.5% (20), and while there are many factors affecting re-adhesion, the mechanism is still unclear. Present, research on the prevention of IUA is mainly retrospective, there are relatively few experimental studies, and due to the lack of an effective classification system for the evaluation of IUA, the evaluation of its efficacy is inconsistent. As new effective measures to prevent re-adhesion are mainly studied in animal experiments for ethical reasons (21), the prevention and treatment of IUA and re-adhesions is still a problem that scientists need to solve together.

Objectives

In attempt to evaluate the efficacy of an integrated approach to prevent and treat the recurrence of intrauterine adhesions (IUA) after hysteroscopic adhesiolysis, we conducted a parallel, randomized and single-center clinical trial. It was also expected to investigate the infection status and pregnancy rate of infertile women with intrauterine adhesions.

In the present study, 96 patients with moderate and severe IUA were evaluated in the Nantong Maternal and Child Health Hospital. Patients with different degrees of adhesion were divided into 3 groups, and the efficacy and safety of three different methods to prevent re-adhesion were discussed, focusing on the following: (I) Evaluation of the effect of intrauterine balloons combined with IUD and IUD alone in preventing re-adhesion. (II) Whether prolongation of intrauterine Foley balloon placement could improve postoperative intrauterine re-adhesion in patients with moderate and severe IUA, and its effect on menstruation and pregnancy rates. Our hypothesis is that intrauterine balloon plus IUD may be better in preventing IUA recurrence, and that the prolongation of balloon may achieve better therapeutic effect.

We present the following article in accordance with the CONSORT reporting checklist (available at https://dx.doi.org/10.21037/apm-21-1296).

Methods

Experimental design and ethics

This is a parallel, randomized and single-center clinical trial with 1:1:1 allocation ratio of three therapies (trial protocol at https://dx.doi.org/10.21037/apm-21-1296). From January 2016 to December 2019, IUA patients in the Nantong Maternal and Child Health Hospital were evaluated. Patients with moderate and severe IUA (48 cases in each degree) were selected and admitted for TCRA treatment, then randomly divided into three groups, respectively (*Figure 1*). The sequence of simple randomization was generated through a computer random number generation and maintained by a doctor who was not involved in patient registry. No investigator had access to the sequence. Opaque sealed envelopes were used to store the documents and were opened before the surgery by gynecologists. Group A (IUD, n=16) received IUD implantation immediately post TCRA and the IUD was removed 3 months after operation. In Group B, (Foley1w+IUD, n=16) a Foley intrauterine balloon was placed immediately after TCRA and removed after 1 week when it was replaced with an IUD. After 3 months, the IUD was removed. In Group C, (Foley1M+IUD, n=16), a Foley intrauterine balloon was placed immediately after TCRA. After 1 month, this was removed and replaced by an IUD, which was removed after 3 months. All patients received sequential treatment of estrogen and progesterone on the day of operation, and the range and degree of adhesion were observed by hysteroscopy at 1 and 3 months after operation. Doctors who performed the second-look and third-look

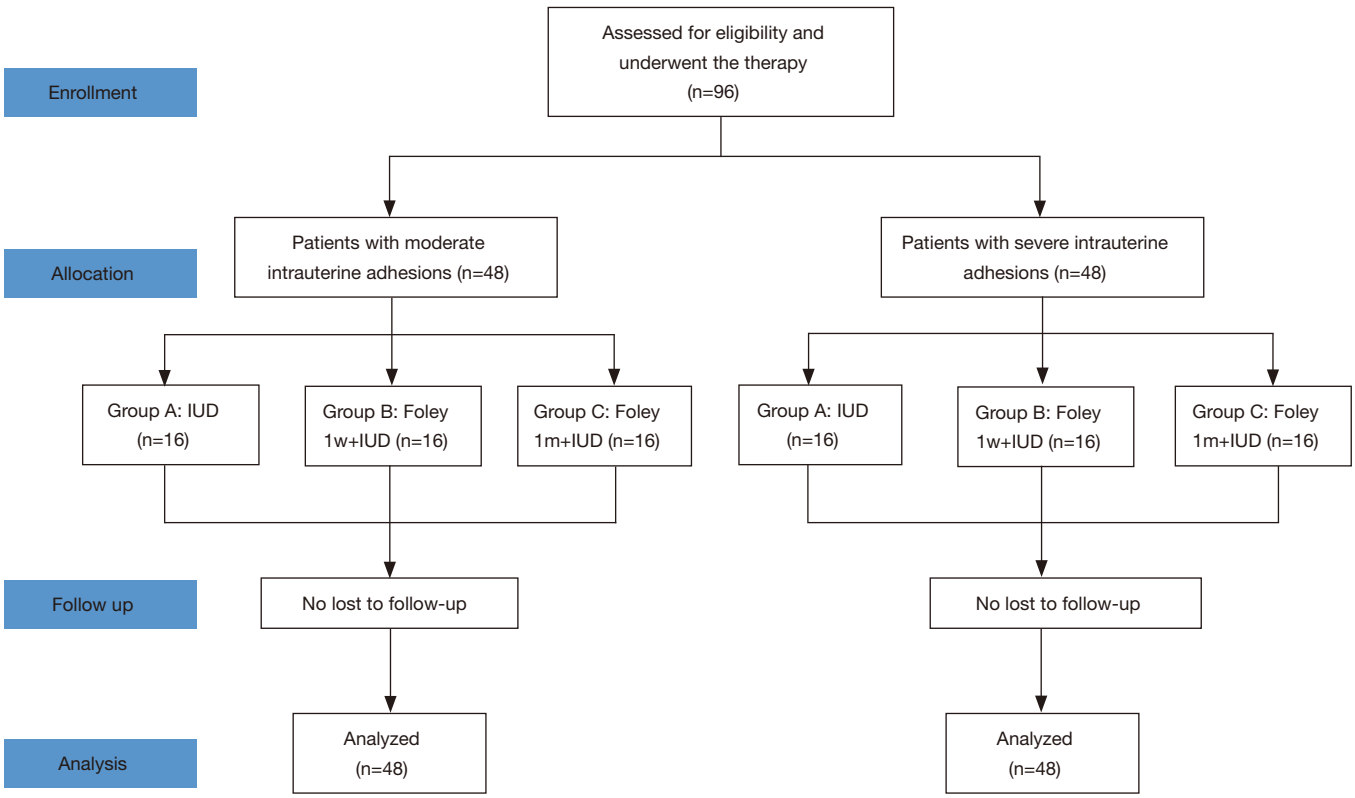

Figure 1 Flow diagram.

Box 1 AFS scale

Variable	Description (score)		
	<1/3: 1	1/3–2/3: 2	>2/3: 4
Adhesion type	Thin adhesion: 1	Between thin and dense adhesion: 2	Dense adhesion: 4
Menstruation situation	Normal: 0	Slight menstruation: 2	Amenorrhea: 4

AFS score = scope of uterine adhesion score + adhesion type score + menstruation situation score. AFS grades: grade I (mild): 1–4: grade II (moderate): 5–8; grade III (severe): 9–12.

hysteroscopy were blinded to the allocation. B-ultrasound examination was performed to detect endometrial thickness, telephone follow-up was performed to record menstruation and pregnancy. The severity of IUA was rated according to the American Fertility Society (AFS), as shown in the table below (Box 1).

The project was approved by the ethical committee of the Nantong Maternal and Child Health Hospital (No. Y2015095) and was in accordance with the Declaration of Helsinki (as revised in 2013). The trial protocol was explained to the patients with detail and informed consent were obtained from all the patients.

Participating women

The inclusion criteria were as follows: healthy women aged 20 to 35 years, with reduced menstrual volume or amenorrhea symptoms, diagnosed with moderate to severe adhesions, according to the AFS score, infertile women with a future fertility desire and IUA were the only infertile factor, without contraindications for the use of hormone drugs or antibiotics; with great treatment compliance. Patients were excluded if they (I) were diagnosed with serious medical or surgical disease which may impact analysis results; (II) had decreased ovarian

function according to sex hormone levels; (III) genital tract inflammation, tuberculosis, tumor, or malformation.

Sample size

Based on our preliminary experiment, a sample size of 75 participants (25 per group) was calculated to achieve 90% power. To allow for a 20% lost rate of follow-up, we planned to enroll 96 participants.

Interventions

Preoperative preparation

Patients with clinical symptoms and IUA confirmed by hysteroscopy were selected by outpatient doctors. IUA patients meeting the inclusion criteria were recruited by investigators and divided into moderate IUA and severe IUA groups according to AFS score. Patients in the two groups were numbered according to the order of admission [1–48], and a computer random generator was used to divide the patients into three groups, with 16 in each group. We use Yuan Gong medicated Cu-IUDs which were provided by Yantai Family Planning Medical Device Company Limited. Foley balloon catheters with external drainage bag were provided by Malaysia Youle Technology Company Limited (Model No. 2111430).

All participants were informed of the operation and the need for follow up, and were admitted to the day care ward. Non-amenorrhea patients were considered suitable for surgery 3–7 days after menstruation and amenorrhea patients at any time. After admission, a detailed medical history was recorded, and examinations were completed including blood leukocyte determination, leucorrhea analysis, and B-ultrasound (measurement of endometrial thickness). Preoperative vaginal cleaning was performed, and after screening for drug contraindications, a 0.5 mg carboprost methylate suppository (Kayunshuan, specification: 0.5 mg, Manufacturer: Northeast pharmaceutical group Shenyang No. 1 Pharmaceutical Co. LTD.) was placed in the posterior vaginal fornix to promote cervical softening. Perioperative antibiotics (Cefazolin sodium pentahydrate, 1.0 g) were used to prevent infection.

Surgical procedures

All surgeries were performed by experienced gynecologists with titles of deputy senior, or above and qualifications in hysteroscopy. The surgical area was again disinfected before surgery to prevent infection, the position and depth of the uterus were probed, and the cervix was dilated with a dilatation stick to size 9. Using turgor medium normal saline, the normal shape of the patient's uterine cavity was restored after operation of the plasma electric cutting needle under B-ultrasound monitoring. The blockage of the bilateral oviduct openings were removed. Normal endometrial tissue should be protected as much as possible throughout the entire surgical procedure. After confirming no active bleeding, a sodium hyaluronate (Xinkeling, Specification: 3 mL, Manufacturer: Hangzhou Singclean Medical Products Co., Ltd.) was used, and after surgery, either IUD or Foley intrauterine balloon was placed according to the groups. Different doses of normal saline were injected into the balloon according to the volume of the uterine cavity, with the routine dose being 3–5 mL. However, during the actual operation, the fluid volume of the syringe was reduced by 0.5 mL after resistance was felt in the process of injecting water. After the operation was complete, an external drainage bag was used to fully drain the blood in the uterine cavity. During the postoperative hysteroscopy review, patients of three groups could not be blinded. Postsurgical assessors who were blinded to the randomization performed the second and the third hysteroscopy and evaluated the adhesion score. IUDs were removed at the second hysteroscopy.

Intravenous antibiotics were used to prevent infection during the perioperative period (1 day total), except those with allergies. Estrogen and progesterone were administered from the day of surgery and estrogen was administered orally from the day of surgery for 21 days. Dydrogesterone tablets (Dafutong, Specification: 10 mg, Manufacturer: Abbott Biologicals B.V.) were taken orally from the 12th day of operation for 10 days. The estrogen (Bujiale, Specification: 2 mg), Manufacturer: Abbott Biologicals B.V.) dose was 4–6 mg daily and the progesterone dose was 20 mg daily.

Main outcomes and measures

Hysteroscopy was performed in all three groups at 1 month and 3 months after operation. The primary outcome was AFS score, which contains the adhesion type, adhesion range and menstrual volume. The secondary outcomes included leucorrhea, white blood cell count, pregnancy and endometrial thickness. Type and range of intrauterine adhesion were recorded by surgeons immediately after hysteroscopy. Transvaginal ultrasound (TVU) was performed to measure endometrial thickness before

Table 1 Comparison of general data of three groups of patients with severe adhesions

Variable	Group A (IUD) (n=16)	Group B (Foley1w+IUD) (n=16)	Group C (Foley1m+IUD) (n=16)	F/χ^2	P
Age ($\bar{x}$±s)	29.8±4.18	30.00±2.61	28.25±2.82	1.422	0.252
BMI ($\bar{x}$±s)	21.25±3.24	22.00±2.16	21.75±2.49	0.328	0.722
Delivery time, n (%)	0: 10 (62.5)	9 (56.25)	7 (43.75)	0.075	0.963
	1: 2 (12.5)	4 (25.00)	6 (37.50)		
	≥2: 4 (25.0)	3 (18.75)	3 (18.75)		
Intrauterine operation number, n (%)	1: 4 (25.0)	5 (31.25)	5 (31.25)	0.24	0.888
	2: 6 (37.5)	6 (37.50)	4 (25.00)		
	≥3: 6 (37.5)	5 (31.25)	7 (43.75)		
Treatment causes, n (%)	Abnormal menstruation 13 (81.25)	12 (75)	13 (81.25)	1.50	0.96
	Infertility 1 (6.25)	2 (12.50)	2 (12.50)		
	Recurrent abortion 1 (6.25)	1 (6.25)	0 (0)		
	Hypogastralgia 1 (6.25)	1 (6.25)	1 (6.25)		

Notes: age (years), BMI (kg/m^2): F; number of labors, intrauterine operation number, treatment causes: χ^2.

menstruation preoperatively and postoperatively.

Statistical methods

All data were collected in Nantong Maternal and Child Health Hospital from January 2016 to December 2019 and were statistically processed by SPSS 23.0 software. Measurement data were expressed as mean ± standard deviation, and the three groups were compared by ANOVA. LSD analysis was used when variances were homogeneous, and Welch test was used when variances were not homogeneous. If P<0.05, it was considered statistically significant and post hoc test multiple comparisons were conducted. The *t*-test was used to compare the two groups, and P<0.05 was considered statistically significant. Enumeration data was expressed by rate (%), and the Chi-square test or Fisher's precision probability test were used for comparison. P<0.05 was considered statistically significant.

Results

Comparison of preoperative clinical data

A total of 96 patients were included in the final analysis. In this study, there were no cases of shedding during the follow-up. In each group of moderate and severe IUA patients, there were 16 cases included in the final analysis. Results were analyzed by original assigned groups.

Comparison of general data of three groups of patients with severe adhesions

The mean age of patients in group A (IUD) was 29.8±4.18 years, the mean BMI was 21.25±3.24 kg/m^2, and the mean delivery time was 0.68±1.01. The mean age of patients in group B (Foley1w+IUD) was 30.00±2.61 years old, the mean BMI was 22.00±2.16 kg/m^2, and the mean delivery time was 0.75±0.93; and the mean age of patients in group C (Foley1m+IUD) was 28.25±2.82 years old, the mean BMI was 21.75±2.49 kg/m^2, and the mean delivery time was 0.81±0.91. The common causes in the three groups were abnormal menstruation, infertility, recurrent abortion, and hypogastralgia, among which menstrual abnormality was the most common cause. The patients with abnormal menstruation in group A (IUD) accounted for 81.25%, while in group B (Foley1w+IUD) this was 75%, and in group C (Foley1m+IUD) 81.25%. There were no statistically significant differences in age, BMI, times of delivery, intrauterine operation number, and treatment causes among the three groups (P>0.05) (*Table 1*).

Table 2 Comparison of general data of three groups of patients with moderate adhesions

Variable	Group A (IUD) (n=16)	Group B (Foley1w+IUD) (n=16)	Group C (Foley1m+IUD) (n=16)	F/χ^2	P
Age ($\bar{x}$±s)	27.93±2.93	28.25±2.38	28.87±2.33	0.555	0.587
BMI ($\bar{x}$±s)	22.06±2.67	20.81±2.19	21.06±2.17	1.258	0.294
Delivery time, n (%)	0: 9 (56.25)	8 (50.0)	7 (43.75)	0.585	0.964
	1: 4 (25.0)	4 (25.0)	5 (31.25)		
	≥2: 3 (18.75)	4 (25.0)	4 (25.0)		
Intrauterine operation number, n (%)	1: 7 (43.45)	7 (43.75)	6 (37.5)	1.40	0.851
	2: 6 (37.50)	7 (43.75)	8 (50.0)		
	≥3: 3 (18.75)	2 (12.50)	2 (12.5)		
Treatment causes, n (%)	Abnormal menstruation 12 (75.00)	12 (75.00)	13 (81.25)	1.054	0.983
	Infertility 1 (6.25)	2 (12.50)	1 (6.25)		
	Recurrent abortion 2 (12.50)	1 (6.25)	1 (6.25)		
	Hypogastralgia 1 (6.25)	1 (6.25)	1 (6.25)		

Notes: age (years), BMI (kg/m2): F; number of labors, intrauterine operation number, treatment causes: χ^2.

Comparison of general data of three groups of patients with moderate adhesions

The mean age of patients in group A (IUD) was 27.93±2.93 years, the mean BMI was 22.06±2.67 kg/m^2, and the mean delivery time was 0.68±0.94. The mean age of patients in group B (Foley1w+IUD) was 28.25±2.38 years old, the mean BMI was 20.81±2.19 kg/m^2, and the mean delivery time was 0.75±0.85; and the mean age of patients in group C (Foley1m+IUD) was 28.87±2.33 years old, the mean BMI was 21.06±2.17 kg/m^2, and the mean delivery time was 0.85±0.95. The common causes of moderate adhesions in the three groups were abnormal menstruation, infertility, recurrent abortion and hypogastralgia, among which abnormal menstruation was the most common cause. The patients with abnormal menstruation in group A (IUD) accounted for 75%, group B (Foley1w+IUD) 75%, and group C (Foley1m+IUD) 81.25%. There were no statistically significant differences in age, BMI, times of delivery, intrauterine operation number, and treatment causes among the three groups (P>0.05) (*Table 2*).

Comparison of preoperative AFS scores in patients with moderate and severe adhesions

To study preoperative AFS scores, ANOVA and chi-square test were used to compare patients with severe adhesions and moderate adhesions in the groups, and the differences were statistically significant (P<0.05) (*Table 3*). In severe and moderate patients, there was no statistical significance in adhesion type score, adhesion range score, menstrual status score, and AFS score among the three groups (P>0.05) (*Figures 2-5*).

Comparison of postoperative AFS scores in patients

Comparison of AFS scores in patients with moderate and severe adhesions 1 month after operation

We compared the scores of patients with severe and moderate adhesions in each group 1 month following surgery and found no significant difference in menstruation in group B (Foley1w+IUD) and group C (Foley1m+IUD) (P>0.05). However, there were significant differences in other data (P<0.05). Statistically significant differences were found in IUA range, adhesion type, menstrual status, and AFS score among the three groups of severe and moderate adhesion patients (P<0.05) (*Table 4*). Further, the results from ANOVA and post hoc test multiple comparisons showed the following: (I) Patients with severe adhesions: comparison in adhesions range and type: there were significant differences between Group C (Foley1m+IUD) and Group A (IUD), Group C (Foley1m+IUD) and Group B (Foley1w+IUD), respectively (P<0.05), but no significant difference between group A (IUD) and group

Table 3 Comparison of preoperative AFS scores in the three groups ($\bar{x}$±s)

Group	Subgroup	Group A (IUD) (n=16)	Group B (Foley1w+IUD) (n=16)	Group C (Foley1m+IUD) (n=16)	F	P
IUA range	Severe	3.13±1.03	3.25±1.00	3.19±1.11	0.057	0.944
	Moderate	1.93±0.25	2.06±0.57	2.00±0.63	0.237	0.79
	t	4.503	4.120	3.721		
	P	0.000*	0.000*	0.01*		
Adhesion type	Severe	3.38±0.96	3.50±0.89	3.31±1.08	0.095	0.91
	Moderate	2.50±0.89	2.43±0.96	2.62±0.95	0.165	0.848
	t	2.671	3.232	2.21		
	P	0.012*	0.003*	0.034*		
Menstruation status	Severe	3.63±0.81	3.50±0.89	3.75±0.68	0.391	0.678
	Moderate	2.75±1.00	2.87±1.02	2.62±0.95	0.253	0.778
	t	2.725	1.938	3.862		
	P	0.011*	0.049*	0.001*		
AFS score	Severe	10.13±0.50	10.25±0.68	10.31±0.87	0.296	0.745
	Moderate	7.18±0.98	7.37±0.88	7.25±0.93	0.167	0.846
	t	10.671	10.281	9.597		
	P	0.000*	0.000*	0.000*		

*, P<0.05. AFS, American Fertility Society; IUD, intrauterine device; IUA, intrauterine adhesion.

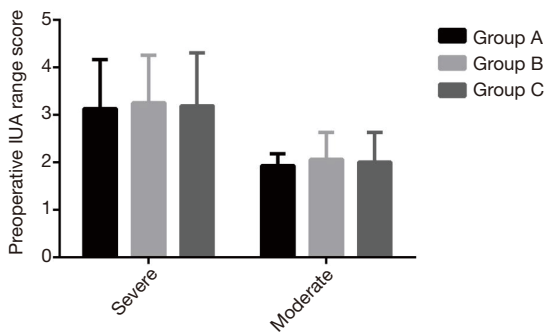

Figure 2 Preoperative IUA range score of patients in the three groups. Group A: IUD; Group B: Foley1w+IUD; Group C: Foley1m+IUD. IUA, intrauterine adhesion; IUD, intrauterine device.

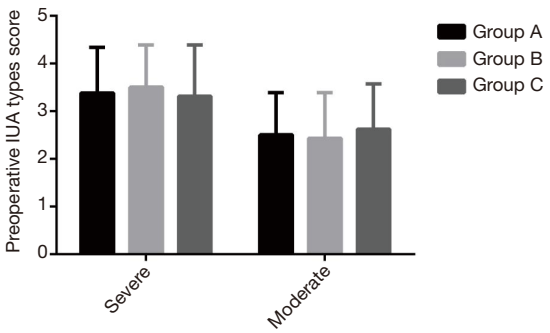

Figure 3 Preoperative IUA type scores of patients in the three groups. Group A: IUD; Group B: Foley1w+IUD; Group C: Foley1m+IUD. IUA, intrauterine adhesion; IUD, intrauterine device.

B (Foley1w+IUD) (P>0.05) (*Figures 6*,*7*). Comparison in menstrual improvement: There were significant differences between group A (IUD) and group B (Foley1w+IUD), group A (IUD) and group C (Foley1m+IUD), respectively (P<0.05). However, there was no statistically significant difference between Group B (Foley1w+IUD) and Group C (Foley1m+IUD) (*Figure 8*). Comparison in AFS score: Pairwise comparison among the three groups showed statistically significant differences (P<0.05) (*Table 5*) (*Figure 9*). Patients with moderate adhesions: There were statistically significant differences in IUA range,

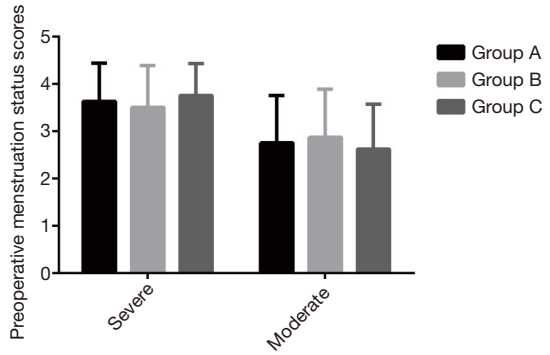

Figure 4 Preoperative menstruation status scores of the three groups. Group A: IUD; Group B: Foley1w+IUD; Group C: Foley1m+IUD. IUA, intrauterine adhesion; IUD, intrauterine device.

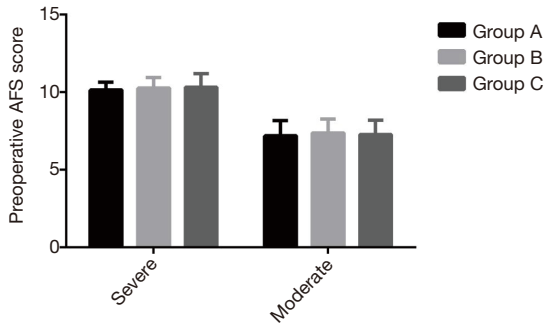

Figure 5 Preoperative AFS score of patients in the three groups. Group A: IUD; Group B: Foley1w+IUD; Group C: Foley1m+IUD. AFS, American Fertility Society; IUD, intrauterine device.

adhesion type, and AFS score (P<0.05). In terms of menstrual conditions, there were significant differences between the three groups, respectively but no significant difference between Group B (Foley1w+IUD) and Group C (Foley1m+IUD) (P>0.05) (*Table 6*).

Comparison of AFS scores in patients with moderate and severe adhesions 3 months after surgery

We compared the scores of patients with severe and moderate adhesions in groups A, B, and C 3 months after surgery and found significant differences in IUA range, adhesion type, menstrual status, and AFS score between the three groups, respectively (P<0.05) (*Table 7*). Further, the results from ANOVA and post hoc test multiple comparisons showed the following: (I) Patients with severe adhesions: Comparison in adhesion range, adhesion type, menstrual status, and AFS score: There were significant differences between group A (IUD) and group B (Foley1w+IUD), group A (IUD) and group C (Foley1m+IUD), respectively, and the differences were statistically significant (P<0.05) and no statistically significant difference between Group B (Foley1w+IUD) and Group C (Foley1m+IUD) (*Table 8*) (*Figures 10-13*). Patients with moderate adhesions: Comparison in adhesion range: There were significant differences between the three groups and no significant difference between group A (IUD) and group B (Foley1w+IUD) (P>0.05). Comparison in menstruation status: There were significant differences between group A (IUD) and group B (Foley1w+IUD) and group C (Foley1m+IUD), respectively, and the differences were statistically significant (P<0.05). There was no significant difference between Group B (Foley1w+IUD) and Group A (IUD) (P>0.05). Comparison in adhesion type and AFS score: Pairwise comparison among the three groups showed statistically significant differences (P<0.05) (*Table 9*) (*Figures 10-13*).

Comparison of endometrial thickness in patients with moderate and severe adhesions 3 months after surgery

We compared the endometrial thickness of patients with severe and moderate adhesions preoperatively and postoperatively in the three groups and the difference was statistically significant (P<0.05). While there was no significant difference in endometrial thickness 3 months after surgery (P>0.05) and no statistically significant difference in endometrial thickness before treatment (P>0.05), there was statistically significant difference in endometrial thickness after treatment (P<0.05) (*Table 10*) (*Figures 14,15*). Further, the results from ANOVA and post hoc test multiple comparisons showed the following: (I) In patients with severe adhesions, there were significant differences between Group A (IUD) and Group B (Foley1w+IUD) and Group C (Foley1m+IUD), respectively, and the differences were statistically significant (P<0.05). There was no statistically significant difference between Group B (Foley1w+IUD) and Group C (Foley1m+IUD) (P>0.05) (*Table 11*). (II) In patients with moderate adhesions, there were statistically significant differences among the

Table 4 Comparison of AFS scores in patients with intrauterine adhesions 1 month after operation ($\bar{x}$±s)

Group	Subgroup	Group A (IUD) (n=16)	Group B (Foley1w+IUD) (n=16)	Group C (Foley1m+IUD) (n=16)	F	P
IUA range	Severe	2.44±0.96	1.94±0.25	1.13±0.62	15.318	0.001*
	Moderate	1.62±0.61	1.06±0.77	0.50±0.51	12.191	0.000*
	t	2.837	4.314	3.101		
	P	0.008*	0.000*	0.004*		
Adhesion type	Severe	3.0±1.03	2.25±0.68	1.50±0.97	10.946	0.000*
	Moderate	1.81±0.83	1.25±0.85	0.50±0.51	11.335	0.000*
	t	3.587	3.651	3.651		
	P	0.001*	0.001*	0.001*		
Menstruation status	Severe	2.50±0.89	0.62±0.95	0.5±0.89	23.940	0.000*
	Moderate	1.50±0.89	0.62±0.95	0.50±0.89	6.667	0.006*
	t	3.162	0	0		
	P	0.004*	1.0	1.0		
AFS Score	Severe	7.93±1.48	4.81±1.32	3.12±2.06	34.865	0.000*
	Moderate	4.93±1.65	2.93±1.84	1.50±1.54	16.787	0.000*
	t	5.407	3.302	2.521		
	P	0.000*	0.002*	0.017*		

*, P<0.05. AFS, American Fertility Society; IUD, intrauterine device; IUA, intrauterine adhesion.

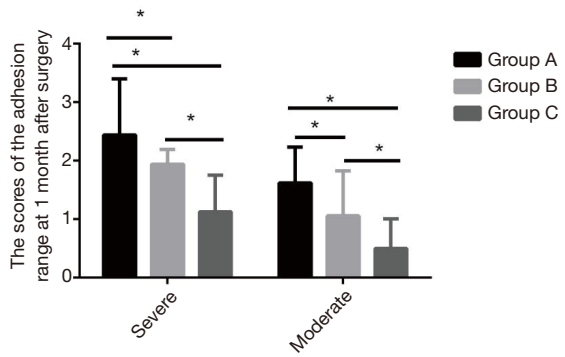

Figure 6 Scores of the adhesion range in the three groups 1 month after surgery (* represents statistical significance). Group A: IUD; Group B: Foley1w+IUD; Group C: Foley1m+IUD. IUD, intrauterine device.

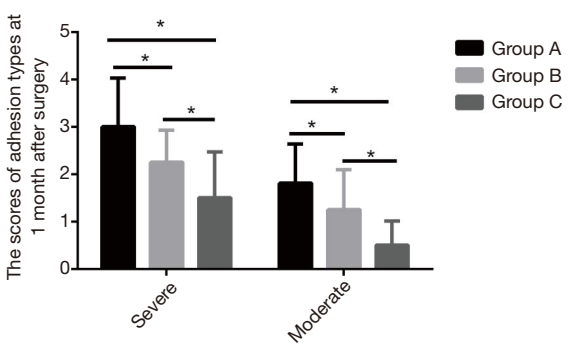

Figure 7 Scores of adhesion types in the three groups 1 month after surgery (* represents statistical significance). Group A: IUD; Group B: Foley1w+IUD; Group C: Foley1m+IUD. IUD, intrauterine device.

three groups (P<0.05) (*Table 12*).

Comparison of postoperative infection in the three groups

In patients with severe adhesions, the mean white blood cell count in Group A (IUD) was (5.26±0.81)×10^{12}/L, in Group B (Foley1w+IUD) was (5.24±0.87)×10^{12}/L, and in Group C (Foley1m+IUD) was (5.16±0.78)×10^{12}/L. In patients with moderate adhesions, the mean white blood cell count in Group A (IUD) was (5.13±0.69)×10^{12}/L, in

Group B (Foley1w+IUD) was (4.90±0.70)×10^{12}/L, and in Group C (Foley1m+IUD) was (4.98±0.49)×10^{12}/L. To study postoperative infection in the three groups, ANOVA was used to analyze the WBC count and leucorrhea routine differences of moderate and severe adhesions, and the results showed there was no statistical significance (P>0.05) (*Table 13*) (*Figure 16*).

Comparison of pregnancy and conception in moderate and severe adhesion patients

Comparison of pregnancy rate in patients with moderate adhesions

Among the patients with moderate adhesions, six (37.50%) were pregnant in Group A (IUD), seven (43.75%) in Group B (Foley1w+IUD), and 14 (87.50%) in Group C (Foley1m+IUD), and there was statistical significance in the pregnancy rate among the three groups (P<0.05) (*Table 14*). There were significant differences between Group C (Foley1m+IUD) and Group B (Foley1w+IUD) and Group A (IUD), respectively, and the differences were statistically significant (P<0.05) but no significant difference between Group A (IUD) and Group B (Foley1w+IUD) (P>0.05) (*Table 15*).

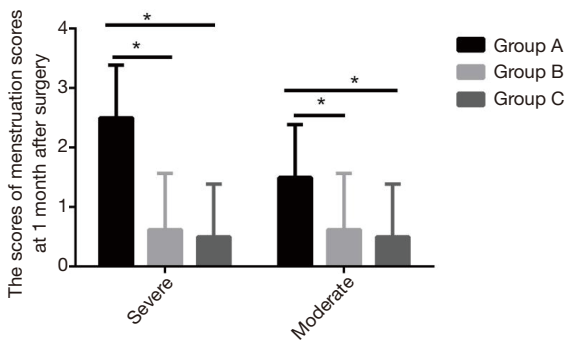

Figure 8 Scores of menstruation scores in the three groups 1 month after surgery (* represents statistical significance). Group A: IUD; Group B: Foley1w+IUD; Group C: Foley1m+IUD. IUD, intrauterine device.

Comparison of pregnancy rate in patients with severe adhesions

Among the patients with severe adhesions, four (25.0%) were pregnant in Group A (IUD), six (37.5%) in Group B (Foley1w+IUD), and eight (50%) in Group C (Foley1m+IUD). There was no statistical significance in the pregnancy rate among the three groups (P>0.05) (*Table 16*).

Discussion

Symptoms and risk factors of intrauterine adhesions

Mo *et al.* retrospectively analyzed factors influencing IUA and found age and BMI were not influencing factors, but female genital tract inflammation, an excessive number of pregnancies, history of intrauterine surgery [curettage, negative pressure suction, and cesarean section (22,23) were. Others have pointed out that more than two intrauterine operations, a curettage time of more than 15 minutes, and a history of myoma of uterus and polyps were also harmful factors (24,25). Chen *et al.* further conducted an in-depth study on patients with secondary infertility and found that the number of abortions and surgical methods were not risk factors for secondary infertility after induced abortion, but IUA, endometritis, chronic salpingitis, ovarian dysfunction, and endometriosis were (26). Based on the above results we believe to the most effective way of reducing IUA can be considered from four perspectives. The first of these concerns reducing the number of induced abortions through public health education on the range of contraceptive measures. Secondly, improving the skills of surgeons will reduce suction and scraping time, minimize endometrial damage, and potentially avoid the possibility of secondary or even multiple curettage caused by uterine residue; Thirdly, during uterine surgery, preoperative and postoperative

Table 5 Postoperative comparison of AFS scores at 1 month in the three groups of patients with severe adhesions (P value)

Group	IUA range	Adhesion type	Menstruation status	AFS score
Group A (IUD) and Group B (Foley1w+IUD)	0.171*	0.066*	0.000*	0.000*
Group A (IUD) and Group C (Foley1m+IUD)	0.000*	0.001*	0.000*	0.000*
Group B (Foley1w+IUD) and Group C (Foley1m+IUD)	0.000*	0.044*	1.000	0.018*

*, P<0.05. AFS, American Fertility Society; IUD, intrauterine device.

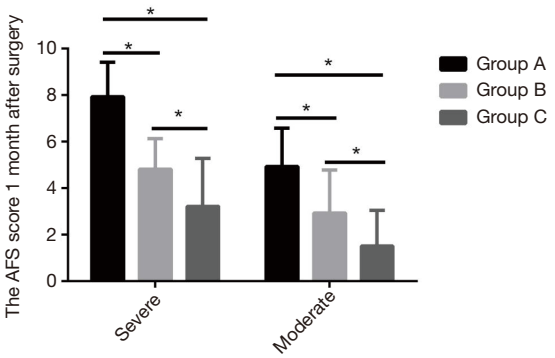

Figure 9 AFS score of the three groups 1 month after surgery (* represents statistical significance). Group A: IUD; Group B: Foley1w+IUD; Group C: Foley1m+IUD. AFS, American Fertility Society; IUD, intrauterine device.

infection prevention should be strengthened to reduce the occurrence of pelvic inflammation, and fourthly, regular physical examination should be carried out on patients after surgery, to monitor any changes and initiate timely treatment. There are seven evaluation criteria for the severity of IUA (27). In this study, the inclusion criteria of patients with moderate and severe adhesions were strictly controlled according to the AFS score, and there was no difference in the general data of patients in different groups, which improved the accuracy of the experimental results.

Analysis of the factors affecting the postoperative efficacy of intrauterine adhesions

Many researchers have analyzed the factors influencing

Table 6 Postoperative comparison of AFS scores at 1 month in the three groups of patients with moderate adhesions (P value)

Group	IUA range	Adhesion type	Menstruation status	AFS score
Group A (IUD) and Group B (Foley1w+IUD)	0.017*	0.040*	0.010*	0.002*
Group A (IUD) and Group C (Foley1m+IUD)	0.000*	0.000*	0.003*	0.000*
Group B (Foley1w+IUD) and Group C (Foley1m+IUD)	0.017*	0.007*	0.701	0.020*

*, P<0.05. AFS, American Fertility Society; IUD, intrauterine device.

Table 7 Comparison of AFS scores in patients with intrauterine adhesions 3 months after surgery ($\bar{x}$±s)

Group	Subgroup	Group A (IUD) (n=16)	Group B (Foley1w+IUD) (n=16)	Group C (Foley1m+IUD) (n=16)	F	P
IUA range	Severe	1.25±0.856	0.75±0.683	0.375±0.50	6.379	0.004*
	Moderate	1.062±0.853	0.56±0.51	0.00±0.00	13.676	0.000*
	t	0.784	0.878	3.000		
	P	0.540	0.387	0.005*		
Adhesion type	Severe	2.0±1.591	0.937±0.853	0.375±0.50	9.306	0.000*
	Moderate	0.937±0.771	0.625±0.619	0.00±0.00	11.170	0.000*
	t	2.403	1.185	3.000		
	P	0.023*	0.245	0.005*		
Menstruation status	Severe	1.625±1.5	0.625±0.957	0.5±0.894	4.601	0.015*
	Moderate	1.375±0.957	0.56±0.892	0.25±0.683	7.428	0.002*
	t	0.562	0.191	0.889		
	P	0.587	0.850	0.381		
AFS score	Severe	4.875±3.32	2.312±1.887	1.25±1.238	10.324	0.000*
	Moderate	3.375±1.707	1.75±1.807	0.25±0.683	17.632	0.000*
	t	1.448	0.861	2.828		
	P	0.158	0.396	0.008*		

*, P<0.05. AFS, American Fertility Society; IUD, intrauterine device.

Table 8 Postoperative comparison of AFS scores at 3 months in the three groups of patients with severe adhesions (P value)

Group (P value)	IUA range	Adhesion type	Menstruation status	AFS score
Group A (IUD) and Group B (Foley1w+IUD)	0.048*	0.050	0.018*	0.039*
Group A (IUD) and Group C (Foley1m+IUD)	0.003*	0.003*	0.025*	0.002*
Group B (Foley1w+IUD) and Group C (Foley1m+IUD)	0.402	0.093	1.000	0.198

*, P<0.05. AFS, American Fertility Society; IUD, intrauterine device.

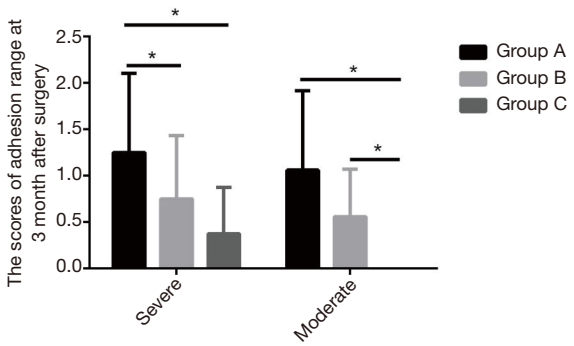

Figure 10 Scores of adhesion range in the three groups 3 months after surgery (* represents statistical significance). Group A: IUD; Group B: Foley1w+IUD; Group C: Foley1m+IUD. IUD, intrauterine device.

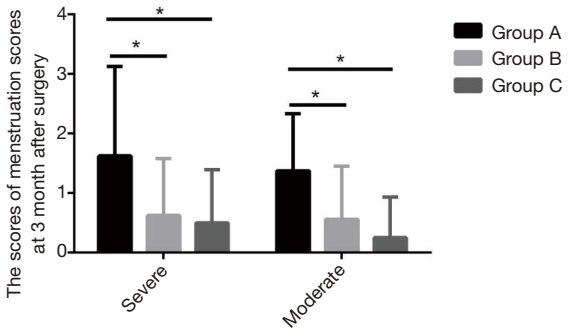

Figure 12 Scores of menstruation scores in the three groups 3 months after surgery (* represents statistical significance). Group A: IUD; Group B: Foley1w+IUD; Group C: Foley1m+IUD. IUD, intrauterine device.

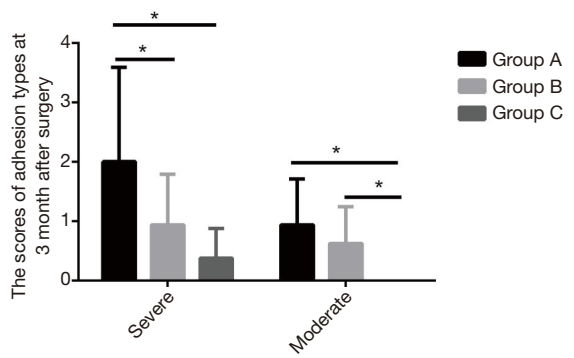

Figure 11 Scores of adhesion types in the three groups 3 months after surgery (* represents statistical significance). Group A: IUD; Group B: Foley1w+IUD; Group C: Foley1m+IUD. IUD, intrauterine device.

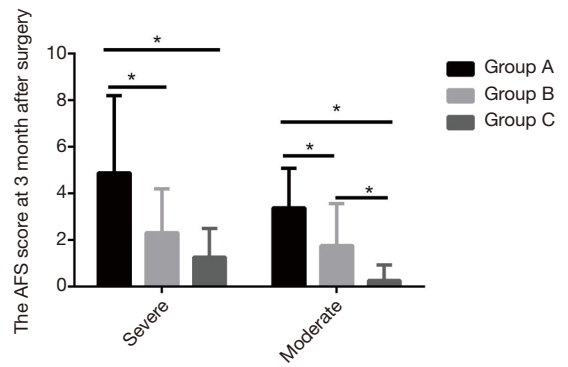

Figure 13 AFS score of the three groups 3 months after surgery (* represents statistical significance). Group A: IUD; Group B: Foley1w+IUD; Group C: Foley1m+IUD. AFS, American Fertility Society; IUD, intrauterine device.

the treatment effect of IUA using hysteroscopy. Yang *et al.* reported that a longer disease course caused IUAs to be become denser, and the larger the range of adhesions, the more likely they were to affect postoperative efficacy. In addition, the use of postoperative estrogen and progesterone was a protective factor (28). Therefore, the present study did not generally examine all types of patients with IUA, but separated patients with different severity and complexity. On this basis, differences in the efficacy of varying physical barriers to prevent re-adhesion after

Table 9 Postoperative comparison of AFS scores at 3 months in the three groups of patients with moderate adhesions (P value)

Group	IUA range	Adhesion type	Menstruation status	AFS score
Group A (IUD) and Group B (Foley1w+IUD)	0.131	0.427	0.048*	0.036*
Group A (IUD) and Group C (Foley1m+IUD)	0.000*	0.001*	0.002*	0.000*
Group B (Foley1w+IUD) and Group C(Foley1m+IUD)	0.001*	0.003*	0.514	0.015*

*, P<0.05. AFS, American Fertility Society; IUD, intrauterine device.

Table 10 Comparison of endometrial thickness pre-operation and post-operation in patients with intrauterine adhesions

Group	Subgroup	Group A (IUD) (n=16)	Group B (Foley1w+IUD) (n=16)	Group C (Foley1m+IUD) (n=16)	F	P
Pre-treatment (mm)	Severe	3.75±1.39	3.87±1.25	3.62±0.88	0.174	0.841
	Moderate	4.62±0.88	4.31±1.13	4.50±1.09	0.362	0.698
	t	–2.132	–2.031	–2.425		
	P	0.042*	0.049*	0.019*		
Post-treatment(mm)	Severe	4.81±1.37	6.37±0.71	6.25±0.57	13.179	0.000*
	Moderate	5.43±0.51	6.50±0.63	6.93±0.57	28..802	0.000*
	t	1.702	0.522	3.379		
	P	0.099	0.605	0.002*		

*, P<0.05. IUD, intrauterine device.

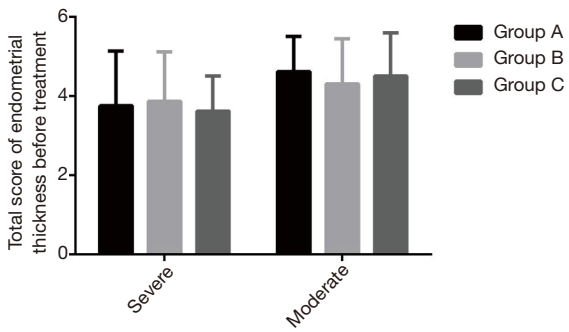

Figure 14 Total score of endometrial thickness before treatment in the three groups. Group A: IUD; Group B: Foley1w+IUD; Group C: Foley1m+IUD. IUD, intrauterine device.

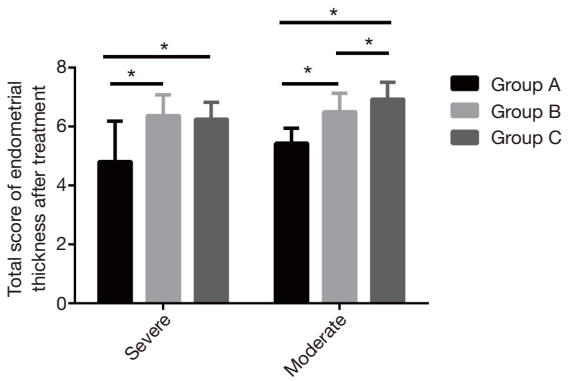

Figure 15 Total score of endometrial thickness after treatment in the three groups (* represents statistical significance). Group A: IUD; Group B: Foley1w+IUD; Group C: Foley1m+IUD. IUD, intrauterine device.

Table 11 Postoperative pairwise comparison of endometrial thickness among the three groups of patients with severe adhesions

	Group A (IUD) and Group B (Foley1w+IUD)	Group A (IUD) and Group C (Foley1m+IUD)	Group B (Foley1w+IUD) and Group C (Foley1m+IUD)
P	0.000*	0.002*	0.713

*, P<0.05. IUD, intrauterine device.

Table 12 Postoperative pairwise comparison of endometrial thickness among the three groups of patients with moderate adhesions

	Group A (IUD) and Group B (Foley1w+IUD)	Group A (IUD) and Group C (Foley1m+IUD)	Group B (Foley1w+IUD) and Group C (Foley1m+IUD)
P	0.001*	0.000*	0.037*

*, P<0.05. IUD, intrauterine device.

Table 13 Comparison of postoperative infection in patients with moderate and severe intrauterine adhesions

Variable	Subgroup	Group A (IUD) (n=16)	Group B (Foley1w+IUD) (n=16)	Group C (Foley1m+IUD) (n=16)	F/χ^2	P
WBC ($\bar{x}$±s)	Severe	5.26±0.81	5.24±0.87	5.16±0.78	0.075	0.926
	Moderate	5.13±0.69	4.90±0.70	4.98±0.49	0.540	0.586
	t	0.467	1.202	0.760		
	P	0.644	0.239	0.453		
Leucorrhea routine n (%)	Severe	Cleanliness Grade I 14 (87.5)	15 (93.7)	14 (87.5)	0.45	0.79
		Cleanliness Grade II 2 (12.5)	1 (6.2)	2 (12.5)		
	Severe	Cleanliness Grade I 15 (93.7)	15 (93.7)	14 (87.5)	0.540	0.772
		Cleanliness Grade II 1 (6.2)	1 (6.2)	2 (12.5)		
	χ^2	0.367	0.0	0.0		
	P	0.054	1.0	1.0		

WBC ($\times10^{12}$/L): F: leucorrhea routine: χ^2.

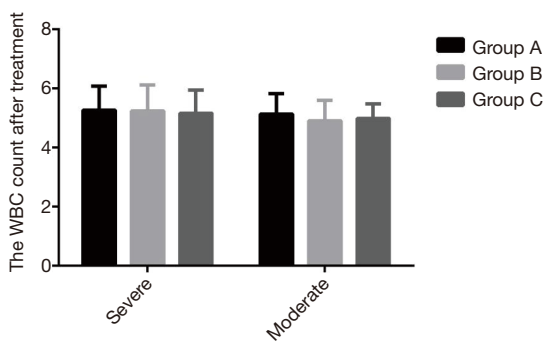

Figure 16 WBC count in the three groups after treatment. Group A: IUD; Group B: Foley1w+IUD; Group C: Foley1m+IUD. IUD, intrauterine device.

Table 14 Comparison of conception rate in patients with moderate adhesions

Group	Conception	No conception
Group A (IUD) (n=16)	6 (37.50%)	10 (62.5%)
Group B (Foley1w+IUD) (n=16)	7 (43.75%)	9 (56.25%)
Group C (Foley1m+IUD) (n=16)	14 (87.50%)	2 (12.50%)
χ^2	9.651	
P	0.008*	

*, P<0.05. IUD, intrauterine device.

TCRA were obtained in patients with different degrees of disease severity. Cai *et al.* studied estrogen receptors after TCRA and found that estrogen can effectively improve menstrual and uterine morphology, and the expression of ER is closely related to the efficacy of estrogen (29). Haas (30) and Bu (31) confirmed through their respective studies that the combined use of estrogen and progesterone was significantly better than that of estrogen alone in maintaining endometrium stability and improving the pregnancy rate. However, the views of scholars differ on the dosage of estrogen. While Liu (32) believed that large doses of estrogen were effective, Zhou (33) held that physiological doses were safe and effective. In the present study, estrogen and progesterone were mainly used in combination. Estradiol valerate was selected for estrogen

Table 15 Results of pairwise comparison with Fisher's exact test

	Group A (IUD) and Group B (Foley1w+IUD)	Group A (IUD) and Group C (Foley1m+IUD)	Group B (Foley1w+IUD) and Group C (Foley1m+IUD)
P	1.000	0.009*	0.023*

*, P<0.05. IUD, intrauterine device.

Table 16 Comparison of pregnancy rate in patients with severe adhesions

(Severe adhesion) Group	Conception	No conception
Group A (IUD) (n=16)	4 (25%)	12 (75%)
Group B (Foley1w+IUD) (n=16)	6 (37.5%)	10 (62.5%)
Group C (Foley1m+IUD) (n=16)	8 (50%)	8 (50%)
χ^2	2.133	
P	0.344	

IUD, intrauterine device.

(4–6 mg/day), and dydrogesterone tablet was used for progesterone (20 mg/day). The three groups of patients received this hormone regimen simultaneously and at the same dose, facilitating the protective effect of estrogen in the prevention of adhesion.

Necessity of measuring endometrial thickness

Intrauterine adhesions are an important cause of infertility in women, and endometrial damage is by far the most important, though not the total, cause of IUA. When the morphology and function of the intima are normal, menstruation can be formed by periodic growth and shedding, which can also provide a good endometrial environment for embryo implantation. The amount of menstruation after surgery also reflects whether the function of the endometrium is intact.

Many scholars believe that the thickness of endometrium that can promote pregnancy should be at least 8 mm. In clinical practice, endometrium thickness is usually monitored *in vitro* by auxiliary means such as B-ultrasound to predict the chance of pregnancy. Endometrium thickness before and after hysteroscopic repair (5,34) is helpful in assessing the possibility of conception, as endometrium thinness can directly affect conception and even lead to adverse pregnancy outcomes. When the uterine cavity volume and endometrial thickness can be recovered in time after intrauterine surgery, it can effectively protect the uterus and prevent IUA, as shown by Evans-Hoeker *et al.* (5). Therefore, the present study compared the efficacy of three different methods by measuring endometrial thickness before and after surgery. We concluded that the postoperative intrauterine implantation of IUA patients with an IUD or Foley balloon, regardless of the severity of adhesion, could effectively improve endometrial thickness, as could the appropriate extension of intrauterine balloon implantation time in patients with moderate adhesions. Further, these findings may provide effective guidance for clinical practice.

Pregnancy rate post TCRA

Foreign studies (35) reported that the pregnancy rate after TCRA could reach 52%, but in the case of severe adhesion, this figure would significantly decrease. However, domestic data show a significantly lower value, with one study reporting a pregnancy rate of only 22.5–33.3% (8). While the direct effect of endometrial thickness on pregnancy was described above, Zhao *et al.* (36) listed other influencing factors, including age, endometrial area, preoperative adhesion degree, postoperative menstrual improvement, and adhesion recurrence. Many factors have been identified as inducing infertility, including immune system dysfunction and complications of internal medicine and surgery. However, most studies have examined these factors from the perspective of determining the chances of postoperative pregnancy, while few have directly followed postoperative pregnancy for extensive durations. The appropriate time for pregnancy after TCRA is within 1 year of surgery, and when there is no need for delayed fertility treatment after surgery (37). In the present study, we recommended patients receive fertility guidance in the reproductive assisted pregnancy clinic of our hospital immediately after the second hysteroscopy, and their pregnancy status under different treatment methods was followed up one year after surgery. Our results showed that the placement of an intrauterine balloon and IUD could improve postoperative pregnancy, but for patients with moderate adhesions,

the effect of prolonged implantation of an intrauterine balloon was better than that of IUD implantation and short time balloon placement. However, in patients with severe adhesions, the duration of balloon placement had no significant effect on postoperative pregnancy rate. This adds weight to the conjecture that even if the physiological structure is restored, it is difficult for patients with severe adhesions to return to normal reproductive function. Novel and effective treatments to deal with these circumstances remain to be developed.

Prevention and treatment of intrauterine re-adhesion: IUD and intrauterine balloon

Yu *et al.* (8) showed that the re-adhesion rate after TCRA can be as high as 62.5%, which seriously impacts postoperative menstrual improvement and fertility. At present, commonly used anti-adhesion methods include IUDs and intrauterine balloons and auxiliary measures including biological materials (hyaluronic acid and hydroxymethyl chitosan), and estrogen, while amniotic membrane (38), stem cells (39), and traditional Chinese medicine (40) have not been widely used in clinical practice. Some studies have investigated the use of a single method (41), while others have investigated a combination of multiple methods. Some researchers (42) have compared patients who used a balloon uterine stent alone with those who received an IUD combined with intrauterine balloon and found that the combined use of the stent prevents adhesion recurrence better than the use of the stent alone. Others (43) compared patients with 7, 14, and 28 days of balloon placement, and believed that the chance of re-adhesion could be reduced if the balloon placement was 28 days, but there was no further study on how this may influence pregnancy. In the present study, the IUD group [Group A (IUD)]and balloon group [Group B (Foley1w+IUD)] were set, with Group C (Foley1m+IUD, i.e., the extended balloon placement time group) added as a contrast, and differences were found among the three groups. Prolongation of balloon placement could improve adhesion type, adhesion range, AFS score, and endometrial thickness in patients with moderate adhesion, and in terms of menstrual improvement, the effect was the same as that of longer balloon placement versus shorter balloon placement. However, there was no improvement in the efficacy of prolonging balloon placement time in patients with severe adhesions. The results may be related to endometrial injury repair mechanism or intrauterine infection. Therefore, for patients with severe intrauterine adhesions, the optimal treatment is IUD combined with intrauterine balloon, and it's unnecessary to prolong the placement of balloon. Comprehensive consideration of the above conclusions can effectively guide clinical work, as different anti-adhesion methods should be chosen according to the different degree of IUA.

Deficiency and prospect

Although prolonged balloon placement has been proven effective in moderate IUA, there is a risk of balloon shedding during clinical procedures, and some patients have reported lower abdominal pain. How much water can be injected into the balloon to achieve an anti-adhesion effect without affecting the blood supply of the endometrium and without causing lower abdominal pain remains is subject to further study.

As this study involved a small sample size and was conducted in a single center, studies with larger sample sizes and conducted across multiple centers are required to confirm the results.

The follow-up time of pregnancy in this study was short, and there was a lack of further tracking of long-term pregnancy, pregnancy outcomes, and fetal conditions.

Use of the term "infertility" as a chief complaint and as an indication for hysteroscopy is still controversial. Determining the specific plan for repeated hysteroscopy after TCRA, especially for patients with fertility requirements, is still to be resolved.

At present, there are not enough effective anti-adhesion materials used in the clinical setting, and the efficacy of various methods is not uniform. We expect the emergence of new materials may go towards resolving this.

Conclusions

In this study, 96 patients with moderate and severe intrauterine adhesions were studied and the prevention of intrauterine re-adhesion and improvement of pregnancy rate were analyzed in depth. The main conclusions were as follows:

(I) The effect of an intrauterine balloon combined with IUD in preventing re-adhesion was better than that of IUD alone. In clinical practice, combined treatment can have a better therapeutic effect.

(II) Appropriate prolongation of intrauterine Foley

balloon placement has no significant advantage for patients with severe adhesions, but for patients with moderate adhesions, it can safely significantly improve adhesion prevention and the pregnancy rate.

(III) Patients with severe adhesions need further exploration to find appropriate treatment methods.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The project was approved by the ethical committee of the Nantong Maternal and Child Health Hospital (No. Y2015095) and was in accordance with the Declaration of Helsinki (as revised in 2013). All patients signed informed consent prior to participation.

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