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Original Article

Efficacy of hysteroscopic cold knife separation on intrauterine adhesions

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Abstract: Objective: This research aimed to explore the efficacy of hysteroscopic cold knife separation in the treatment of intrauterine adhesions (IUA). Methods: Altogether 110 patients with IUA who were treated in our hospital were randomized into the observation group (n=55, hysteroscopic cold knife) and the control group (n=55, hysteroscopic electroacupuncture and collecting ring). This research compared the operation-related indexes (operation time, intraoperative blood loss, amount of distending media), IUA and menstrual flow, endometrial epithelization of the uterine wound, endometrial thickness one month after operation, recurrence and pregnancy rates one year after operation. Results: The operation time and intraoperative blood loss in the observation group were less than those in the control group (all $P<0.05$). After treatment, the total effective rate of IUA, menstrual flow and satisfaction rate of endometrial epithelization of the uterine wound in the observation group were higher than those in the control group, and the recurrence rate of the former one year after operation was lower (all $P<0.05$). One month after operation, the thickness of the endometrium in the observation group was clearly larger than that in the control group on the 11th and 13th day of menstruation (all $P<0.05$). Conclusion: Hysteroscopic cold knife separation can improve the efficacy of IUA and protect the endometrium.

Keywords: Hysteroscopy, cold knife separation, intrauterine adhesions, endometrium

Introduction

Intrauterine adhesion (IUA) is a common complication after abortion. It occurs after intrauterine operations such as placing an intrauterine device. It can reduce menstrual flow, and will even lead to infertility in severe cases [1, 2]. With the development of hysteroscopy technology, hysteroscopic separation and resection of adhesion has become the main treatment. However, there are many kinds of separation and resection instruments, such as monopolar electrotomy, bipolar electrotomy, plasma electrotomy, and micro scissors (1.6-2 mm), etc. These can separate and remove the IUA tissue and improve the pregnancy rate of patients [3, 4]. However, there are some limitations. On the one hand, the operation has a great influence on the endometrium, and it takes a long time to recover after operation. On the other, the miniature scissors are too slender to cut off the thick septum.

With the development of medical technology and people's understanding of uterine mediastinum, an increasing number of women who want to have a baby choose the resection method with little influence on endometrium and high postoperative pregnancy rate. Medical workers are required to study the influence of different surgical instruments on postoperative uterine environment, in order to minimize postoperative recurrence and improve postoperative pregnancy rates. However, the efficacy of different separation techniques on IUA is a debatable point. Some scholars believe that hysteroscopic cold knife separation has a better effect on the separation and resection of adherent tissues. Others argue that cold knife separation is harmful to the endometrium, and is not conducive to its recovery after operation [5, 6]. The purpose of this research is to compare the therapeutic effects of hysteroscopic cold knife separation and electroacupuncture collecting ring separation in IUA patients, and to

analyze the effects on the endometrium after operation.

Materials and methods

General data

Altogether 110 patients with IUA who were treated in our hospital from February 2018 to March 2020 were randomized into the observation group (n=55, hysteroscopic cold knife) and the control group (n=55, hysteroscopic electroacupuncture and collecting ring). All of them understood the experiment purpose and signed an informed consent form. This research was approved by the Ethics Committee of our hospital. Inclusion criteria are as follows: 20-35 years old, those who are confirmed as having IUA by three-dimensional B ultrasound and hysteroscopy before operation; those with IUA caused by abortion, intrauterine device placement, myomectomy and other intrauterine operations; all patients are in accordance with the indications of hysteroscopic separation, resection and adhesion. Exclusion criteria are as follows: those who are complicated with other gynecological diseases, such as pelvic infection and severe cervical erosion; patients with coagulation dysfunction; those who participated in other research projects at the same time; those with malignancy, epilepsy, and mental illness, etc.

Methods

Patients in both groups were operated on at Day 5 to 7 after menstruation. Misoprostol tablets (Zhejiang Xianju Pharmaceutical Co., Ltd., H20084598, batch number: 190725, specification: 0.2 mg) were inserted into vagina to soften cervix 2 h before operation. Under general anesthesia, they were placed into the hysteroscope under the guidance of ultrasound, and the operation was performed under direct vision.

Those in the control group were treated with hysteroscopic electroacupuncture and collecting ring separation [7]. In the first step, a needle electrode was used to separate the adherent tissue in the uterine cavity. In the second step, a ring electrode was used to remove the raised scar tissue in the uterine cavity. While those in the observation group were treated by hysteroscopic cold knife separation, and 3 mm miniature surgical scissors were placed to cut the adherent tissues in the uterine cavity directly [8, 9]. It should be noted that both operations were separated as far as possible until the bilateral fallopian tube openings were completely exposed. Hypertonic saline was used as distending media in both groups, and its flow rate was maintained at 120-150 mL/min. Intrauterine devices were placed routinely after operation, and estradiol valerate (Jenapharm GmbH & Co. KG, J20171038, batch number: 191009, specification: 1 mg) was taken orally once a day, for 2 consecutive menstrual cycles.

Outcome measures

Main outcome measures: (1) The operation-related indexes between both groups were compared, and the operation time, intraoperative blood loss and the amount of distending media were recorded. (2) The improvement of IUA was compared [10]. Cure: The uterine cavity shape is completely restored to normal, the bilateral fallopian tube openings are clear, the endometrial surface is smooth, and the three-line pattern is obvious. Effective: The shape of the uterine cavity is obviously improved, but there is still a little adhesion, and the opening of one fallopian tube is clear. Ineffective: Results are not up to the above standard. Effective rate = (cured + effective) cases/total cases × 100%. (3) One month after operation, the endometrial epithelization of the uterine wound of both groups was compared: Satisfactory: the endometrium creeps smoothly and the epithelialization is smooth. Basically satisfied: there is no necrotic tissue in the uterine cavity wound, and there is a thin layer of endometrium covered by endometrial epithelialization of the uterine cavity wound; Otherwise, it is not graded satisfied; the calculation satisfaction rate = (satisfied + basically satisfied) cases/total cases × 100%.

Secondary outcome measures: (1) One month after operation, the endometrial thickness of the patients was measured by vaginal ultrasound on the 8th, 11th and 13th day of menstruation. (2) The improvement of menstrual flow after treatment was assessed [11]. Cure: The menstrual flow returns to normal. Improved: The amount of menstruation increases, but does not return to normal. Ineffective: There is no improvement in menstrual flow. Effective

Table 1. Baseline data of both groups of patients (n, $\bar{x} \pm sd$)

Index	Observation group (n=55)	Control group (n=55)	χ^2/t	P
Age (years)	27.6±3.9	26.8±2.7	1.251	0.214
BMI (kg/m^2)	22.20±2.28	22.53±2.40	0.739	0.461
Pregnancy times (times)	3.2±0.9	3.4±0.7	1.301	0.196
Parity (times)	1.3±0.3	1.4±0.3	1.748	0.083
Number of abortions (times)	1.9±0.8	2.0±0.7	0.698	0.487
History of IUD use (n)			1.345	0.246
Yes	20	26		
No	35	29		
Degree of intrauterine adhesions before surgery (n)			0.628	0.731
Mild	19	16		
Moderate	22	26		
Severe	14	13		
Menstrual duration (d)			3.036	0.219
<2	20	14		
3-4	22	20		
5-6	13	21		

Note: BMI: Body mass index.

rate = (cured + improved) cases/total cases × 100%. (3) The recurrence and pregnancy rates between both groups were evaluated one year after follow-up; recurrence rate = recurrence cases/total cases × 100%; pregnancy rate = clinical pregnancy cases/total cases × 100%.

Statistical analysis

Data were collected and processed by SPSS 20.0. The counting data were expressed as (n/%) and analyzed by χ^2 test. The measurement data were indicated by ($\bar{x} \pm sd$). The intra-group comparison before and after treatment was made by paired t-test, and the inter-group comparison was analyzed with an independent t-test. The difference was statistically remarkable at (P<0.05).

Results

Baseline data

There was no marked difference in general data between the two groups (all P>0.05), as such the groups were comparable (**Table 1**).

Comparison of operation-related indicators

The operation time and intraoperative blood loss in the observation group were shorter/smaller than those in the control group (all P<0.05), with no obvious difference between both groups (P>0.05; **Table 2**).

IUA and menstrual flow

Before operation, the mild, moderate and severe uterine adhesions in the control group were 16, 26 and 13 cases, respectively, while those in the observation group were 19, 22 and 14 cases, respectively. The mean duration of menstruation in the control group and observation group before operation was (3.57±1.10) d and (3.82±1.05) d. IUA and menstrual flow between both groups revealed no remarkable difference before operation (all P>0.05). The total effective rate in the observation group after treatment was higher than that in the control group (all P<0.05; **Tables 3**, **4**).

Endometrial epithelization of uterine cavity wounds

Hysteroscopic examination revealed that the uterine cavity was narrow, shallow, barrel-shaped or pinhole-shaped, with extensive scarring and muscle adhesion cord formation in the uterine cavity, with few and a discontinuous endometrium, and thick adhesions or an adhesion zone on the uterine wall, where most of the uterine cavity adhesion closed, with bilateral

Table 2. Comparison of surgical indicators between both groups ($\bar{x} \pm sd$)

Group	Operation time (min)	Intraoperative blood loss (mL)	Dilatation fluid dosage (mL)
Observation group (n=55)	23.85±4.55#	13.30±3.03#	2210.39±174.42
Control group (n=55)	27.89±5.40	18.27±3.64	2232.28±185.49

Note: Compared with the control group, #P<0.05.

Table 3. Improvement of intrauterine adhesions in both groups (n, %)

Group	Cure	Effective	Invalid	Total effective rate
Observation group (n=55)	28 (50.91)	24 (43.64)	3 (5.45)	52 (94.55)#
Control group (n=55)	20 (36.36)	25 (45.45)	10 (18.18)	45 (81.82)

Note: Compared with the control group, #P<0.05.

Table 4. Menstrual volume improvement in both groups (n, %)

Group	Cure	Get better	Invalid	Total effective rate
Observation group (n=55)	26 (47.27)	26 (47.27)	3 (5.45)	52 (94.55)#
Control group (n=55)	17 (30.91)	28 (50.91)	10 (18.18)	45 (81.82)

Note: Compared with the control group, #P<0.05.

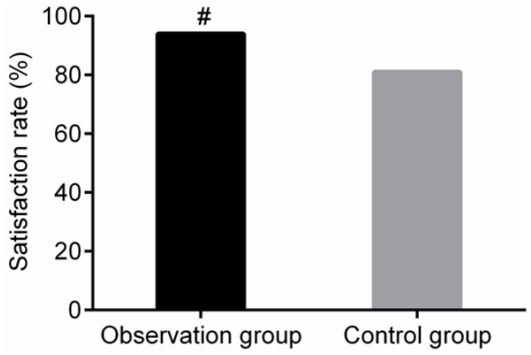

Figure 1. Comparison of satisfaction rate of endometrium epithelialization of uterine cavity wounds between both groups. Compared with the control group, #P<0.05.

fallopian tube openings that are not seen. Also the middle and upper end of the uterine cavity were basically closed. There was no marked difference between the two groups. One month after operation, the satisfaction rate of endometrial epithelization in the observation group was 94.55% (52/55), which was higher than that in the control group (81.82%, 45/55; P<0.05; **Figure 1**).

Endometrial thickness

Before operation, there was no obvious difference in endometrial thickness between the two groups on the 8th, 11th and 13th day of menstruation (all P>0.05). Compared with pre-operation, one month after operation, the endometrial thickness of patients in both groups increased on the 8th, 11th and 13th day of menstruation, and the observation group was thicker than the control group on the 11th and 13th day of menstruation (all P< 0.05; **Table 5**).

Recurrence and pregnancy rates

After one year of follow-up, the recurrence rate in the observation group was lower than that in the control group (P< 0.05), and there was no remarkable difference in pregnancy rate between both groups (P>0.05; **Table 6**).

Discussion

The amount of menstruation in IUA patients decreases obviously. In severe cases, amenorrhea may occur and even induce infertility [12]. Women who want to have a baby hope to reduce the influence on the endometrium as much as possible on the basis of releasing the IUA, so as to have a smooth pregnancy after operation. However, a large number of studies have confirmed that the disease recurrence after separation and resection of IUA is the main factor affecting the postoperative pregnancy [13-15]. So appropriate surgical methods need to be adopted to reduce the postoperative recurrence rate and improve the pregnancy outcome.

Hysteroscopy can effectively separate and remove the IUA and restore the normal shape of the uterine cavity. After operation, giving estrogen or placing and IUD can reduce the recurrence and improve the pregnancy rate [16]. Research has shown that different surgical methods of separating and excising cervical adhesion tissue under hysteroscope have different effects on the endometrium, and the

Table 5. Endometrial thickness of both groups at 1 month after surgery ($\bar{x} \pm sd$, mm)

Group	time	8th day of menstruation	11th day of menstruation	13th day of menstruation
Observation group (n=55)	Preoperative	3.57±0.44	4.34±0.20	5.54±0.64
	Postoperative	4.77±0.67*	6.27±0.93*,#	8.84±1.04*,#
Control group (n=55)	Preoperative	3.59±0.53	4.48±0.30	5.63±0.71
	Postoperative	4.56±0.83*	5.50±0.79*	7.34±0.93*

Note: Compared with preoperative, *P<0.05; compared with control group, #P<0.05.

Table 6. Recurrence and pregnancy in both groups within 1 year (n, %)

Group	Relapse	Pregnancy
Observation group (n=55)	3 (5.45)#	27 (49.09)
Control group (n=55)	10 (18.18)	24 (43.64)

Note: Compared with the control group, #P<0.05.

postoperative recurrence and pregnancy rates are also quite different [17]. In this research, the effects of hysteroscopic cold knife separation and electroacupuncture-collecting ring separation in treating IUA were compared and analyzed. The results revealed that the operation time and intraoperative blood loss in the observation group were less than those in the control group, while the total effective rate of IUA and menstrual flow of the former after treatment was higher. This suggested that compared with electroacupuncture-collecting ring separation, hysteroscopic cold knife separation was more effective. It can improve menstrual flow more effectively, with less intraoperative blood loss, which is more conducive to postoperative recovery. Sun et al. also found that hysteroscopic cold knife separation was more effective in the separation of uterine adhesion tissue [18]. It is believed that since the hysteroscopic cold knife separation can be inserted at 3 mm with miniature surgical scissors under direct vision, and cut off the adhesion tissue in uterine cavity, the adhesion tissue can be removed more thoroughly.

The endometrium is the main place for embryo implantation. Too thin of an endometrium or decreased endometrial receptivity can affect the implantation of fertilized eggs and reduce the clinical pregnancy rate. Normal uterine cavity shape, smooth crawling, normal floating and uniform distribution of the endometrium are the prerequisites for maintaining the normal function of the endometrium [19, 20]. In this research, one month after operation, the satisfaction rate of endometrial epithelization in the observation group was higher than that in the control group, and the endometrial thickness of patients on the 11th and 13th day of menstruation was larger than that in the control group. This revealed that hysteroscopic cold knife separation had less of an effect on the endometrium in patients after IUA separation, which can promote endometrial growth more effectively. Takahashi et al. also explained that the endometrial epithelization of patients with uterine wound after hysteroscopic cold knife separation was better [21].

Recurrence after separation and resection of IUA is the main factor affecting postoperative pregnancy [22]. One year after follow-up, the recurrence rate of the observation group was lower than that of the control group, which indicated that hysteroscopic cold knife separation can effectively reduce the recurrence of IUA compared with electroacupuncture and collecting ring separation. Nevertheless, there was no statistical difference in pregnancy rates between the two groups, which may be related to the limited number of subjects included. In the later stage, it's necessary to enlarge the sample size and analyze the efficacy of hysteroscopic cold knife separation on IUA.

This research only counted the endometrial development of patients one month after operation. To get more powerful conclusions, the effects of different surgical methods of hysteroscopic separation and resection of cervical adhesion tissue on patients' endometrium still needs to be continuously investigated for several menstrual cycles. In addition, the effects of different surgical methods of hysteroscopic separation and resection of cervical adhesion tissue on the live birth rate of pregnant patients after operation need to be further studied.

In general, hysteroscopic cold knife separation for IUA has less of an influence on patients' endometrium, which can effectively improve menstrual flow and efficacy. Hence, it's worthy of clinical promotion.

Disclosure of conflict of interest

None.

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