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Prevention of postoperative adhesion reformation by intermittent intrauterine balloon therapy: a randomised controlled trial

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Objective To compare the efficacy of intermittent intrauterine balloon dilatation versus standard care in the prevention of adhesion reformation.

Design Single-blind randomised controlled trial.

Setting Hysteroscopic Centre of a tertiary University Hospital.

Population Two hundred patients with moderate to severe (European Society for Gynaecological Endoscopy Grade ≥II) intrauterine adhesions who underwent hysteroscopic adhesiolysis.

Methods All participants were randomised to a balloon group or a control group postoperatively. The balloon group received intrauterine balloon dilatation therapy at 2 weeks and 6 weeks after surgery, whereas the control group did not. All patients underwent follow-up hysteroscopy at 4 and 8 weeks postoperatively.

Main outcome measures The adhesion reformation rate and the Pictorial Blood Loss Assessment Chart scores were analysed.

Results A total of 191 patients successfully completed the study protocol (94 cases for the balloon group and 97 cases for the control group). According to hysteroscopic evaluation at the 8th week, the overall adhesion reformation rate was significantly lower in patients in the balloon group than patients in the control group (20.2% versus 40.2%, respectively; $P < 0.05$). There was also a significant increase in menstruation flow, as assessed by the Pictorial Blood Loss Assessment Chart score (30 versus 9, respectively; $P < 0.001$).

Conclusions Postoperative intermittent intrauterine balloon dilatation therapy can significantly reduce postoperative adhesion reformation and significantly increase menstruation flow.

Keywords Asherman syndrome, balloon, hysteroscopic adhesiolysis, intrauterine adhesions, recurrence.

Tweetable abstract RCT: Postoperative intermittent intrauterine balloon therapy can prevent adhesion reformation after hysteroscopic adhesiolysis.

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Introduction

Intrauterine adhesions (IUA) can occur after trauma to the basalis layer of the endometrium with any surgery performed within the uterine cavity. The syndrome occurs most frequently after incomplete miscarriage (50%), postpartum haemorrhage (24%), and elective termination of pregnancy (17.5%).[1] Other aetiological factors include myomectomy, hysteroscopic resection, diagnostic curettage, caesarean section, tuberculosis, caustic abortifacients, and uterine artery embolization.[1–4]

Patients with IUA may present with amenorrhoea with or without severe dysmenorrhoea, oligomenorrhoea, infertility or recurrent miscarriages.[5] Patients with amenorrhoea and cyclic pain associated with haematometra are likely to have viable endometrium above the occlusive adhesions. Sequelae of pregnancy in the presence of adhesions include higher incidences of ectopic pregnancy, recurrent miscarriage, premature labour, and abnormal placentation.[5]

The high recurrence rate of adhesions following hysteroscopic adhesiolysis in IUA remains one of the most difficult

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URL of the registration site: https://clinicaltrials.gov/show/NCT03131596.

challenges in reproductive surgery.[6] It is reported that increasing severity of disease is associated with lower pregnancy rate[7–10] and a higher chance of requiring repeat surgery. Several studies have reported various methods to prevent adhesion reformation. A recent network meta-analysis identified six randomized controlled trials (RCTs)[11] that examined the use of solid barriers (intrauterine contraceptive device [IUD], stent or balloon catheter),[12] semisolid barriers (hyaluronic acid and auto-cross-linked hyaluronic acid gel)[13,14] and tissue barriers (fresh and freeze-dried amnion grafts).[15–17] It reported potential improvements with all methods, although it is clear that there are urgent calls for further well-designed trials. In 2017, the American Association of Gynecologic Laparoscopists (AAGL) in collaboration with the European Society of Gynaecological Endoscopy (ESGE) published a practice guideline on IUA,[18] including recommendations for the prevention of adhesion reformation. The only methods to receive a Level A grade were the solid barriers and semi-solid barriers described above.

Interestingly, despite adhesion reformation being recognised as a biological process that develops over a relatively prolonged period of time, to our knowledge, solid and semi-solid barriers have only been examined within the context of a single use at the end of the hysteroscopic adhesiolysis surgery. Recently, we reported preliminary observations from a simple outpatient technique in which a Foley-catheter was used under ultrasound guidance to dilate the intrauterine cavity in order to resolve early IUA or prevent the adhesions from recurring.[19,20] We conducted an RCT to test the hypothesis that intermittent use of intrauterine balloon dilatation in the postoperative period may reduce adhesion reformation rates.

Methods

Trial design

This was a prospective surgeon-blinded RCT, performed at the Hysteroscopic Centre of the Fuxing Hospital, Beijing, China, which is a tertiary University hospital referral centre with a particular clinical and research interest in the treatment of women with IUA.[4,6,21,22] Patients were not involved in the development of this research. Institutional review board approval was obtained (reference No. 2016FXHEC-KY, 20 October 2016), and the trial was prospectively registered at ClinicalTrials.gov (identifier NCT 03131596, 24 April 2017).

Patients suspected to be suffering from IUA were recruited following a systematic pre-operative assessment process. This included a detailed history of the menstrual pattern, previous intrauterine surgery, and reproductive history, as well as 2D/3D transvaginal ultrasound. The severity and extent of intrauterine adhesions were scored according to the European Society of Gynaecological Endoscopy (ESGE) classification system of 1995.[23] The inclusion criteria included the following: (1) women aged 18–40 years; (2) moderate to severe intrauterine adhesion (ESGE Grade ≥II)[6]; and (3) first episode of hysteroscopic adhesiolysis at Fuxing hospital. The exclusion criteria included the following: (1) minimal adhesions (ESGE Grade ≤I) and (2) a previous hysteroscopic adhesiolysis procedure at Fuxing hospital or other hospitals. All enrolled women provided written informed consent and agreed to the entire study protocol prior to surgery.

Sample size

To our knowledge there have been no previous RCTs to assess the effectiveness of this technique. However, based on the reported rates of adhesion reformation from previous retrospective cohort studies using intrauterine balloon catheters and hormone therapy, we estimated a clinically reasonable and meaningful reduction in the adhesion reformation rate from 45% in the control group to 20% in the balloon group.[12,24] Accepting a type 1 error of 0.05, and a type 2 error of 0.10, the number of subjects required in each arm to demonstrate significant differences would have to be 79. Assuming a dropout rate of 20%, the total number of subjects for recruitment was set as 100 in each arm.

Randomisation

Randomisation was performed electronically using SPSS statistical software version 21.0 (SPSS, Inc., Chicago, IL, USA). The randomised number was concealed in an opaque, sealed envelope for each enrolled patient and was opened consecutively by a study nurse in the ward before their hysteroscopic surgery after verbal and written consent. Recruited patients were randomised to one of two groups with a 1:1 allocation ratio: (1) The balloon group receiving IUB dilatation at 2 weeks and 6 weeks after hysteroscopic adhesiolysis, in addition to the standard care; (2) the control group receiving standard care alone.

Standard care

Standard care referred to the usual practice in our department. In all cases, a Foley-catheter filled with 4.5 ml normal saline was inserted into the uterus for 5–7 days after surgery combined with oral antibiotic treatment (Cefaclor 0.375 mg twice daily, Tianjin Central Pharmaceutical Co. Ltd., Tianjin, China). The catheter was removed when the patient was discharged. Hormone therapy also began from the day of operation, consisting of oestradiol valerate at a dose of 4 mg/day for 21 days, with the addition of dydrogesterone at a dose of 10 mg/day for the last 7 days of the oestrogen therapy. After the withdrawal bleed, the hormone therapy was repeated for a further cycle that is 8 weeks in total. A second-look hysteroscopy was carried out in the

early proliferative phase 4 weeks after the index surgery and a third-look hysteroscopy was carried out 8 weeks after the index surgery.

Operation techniques

All patients received hysteroscopic adhesiolysis in their follicular stage. Once the presence of adhesions had been confirmed and uterine anatomy had been assessed, an 8.5-mm rigid resectoscope was introduced into the uterine cavity to divide the adhesions—with the aid of ultrasound guidance as necessary—by one of two experienced endoscopic surgeons (X.H. and Q.Z.). Normal saline was used as the distention medium pressure with a pressure of 120–150 mmHg and a flow rate of 320–360 ml/min. Bipolar energy was used for adhesiolysis with the cutting and coagulating power set at 310 and 90 W, respectively. The filmy and central adhesions were divided first, followed by marginal and dense adhesions.

The second and third look hysteroscopy, at 4 weeks and 8 weeks following the index surgery, respectively, was carried out by another experienced hysteroscopic surgeon (E.X.). A 4.5-mm rigid hysteroscope with normal saline infusion was used under 100 mmHg pressure as an outpatient procedure in the day surgery unit. Ultrasound guidance was routinely available if required. After assessment of the extent and severity of any reformed adhesions, blunt dissection using the tip of the hysteroscope was carried out as reported in the literature.[25]

Intermittent IUB dilatation

Patients randomised into the balloon group received intermittent IUB dilatation therapy according to the methodology previously published in the literature.[19,20] The dilatation therapy was performed at 2 weeks and 6 weeks after the initial surgery in the day surgery unit. In brief, a Foley catheter (size 14fr) was prepared by cutting the excess catheter tip protruding beyond the balloon edge. The balloon catheter was then gently inserted through a Cusco speculum into the uterine cavity under ultrasound guidance. Once the catheter had reached the fundus, 3–4.5 ml of normal saline was slowly introduced into the balloon. The volume introduced was based on the ultrasound images confirming adequate distention (inflation of the Foley balloon with the use of at least 4 ml of saline solution) of the uterine cavity, while ensuring that the patient did not experience too much discomfort. After the procedure, the balloon was deflated and removed immediately.

Outcome measures

A Core Outcome Set was not used in this research. The primary outcome measure was defined as the adhesion reformation rate 8 weeks postoperatively including the ESGE grade at each follow up. Secondary outcomes included (1) the menstrual improvement, which was evaluated according to Pictorial Blood Loss Assessment Chart (PBAC) score[26] at each follow up, (2) the pregnancy rate, miscarriage rate, and ectopic rate, and (3) the patient reported pain scores via use of the Visual Analogue Scale (VAS)[27] from no pain (0) to worst pain imaginable (10). All follow-up data were collected via direct contact or telephone follow up every 2 weeks by one of the investigators (X.S.). The total duration of follow up was 12 months.

Data management

The ESGE Grade before operation and at each follow up was evaluated by X.H. and Q.Z. The PBAC score before operation and at each fellow up was evaluated by X.S. and E.X. All data were recorded on a structured data sheet and entered on the database for storage. The researchers ensured the confidentiality of sensitive data by minimising the number of personnel who handle subject data and encrypted the computer data. To ensure the anonymity, all participants were identified by code number instead of names. All investigators apart from X.S. were blinded to the data.

Statistical analysis

Intention-to-treat analysis was conducted on all outcomes. Kolmogorov–Smirnov test was used to test the data distribution. Numerical data with normal distribution were presented as the mean ± standard deviation, whereas data with skewed distribution were presented as the median (interquartile range [IQR]). Student's *t*-test was used to compare normally distributed data between two groups and paired *t*-test was used to compare normally distributed data within two groups. The Mann–Whitney *U*-test was used to compare data with skewed distribution. Contingency table analysis and the Chi-square test along with risk ratios (RR) and 95% confidence intervals (CI) were used to compare categorical data. A *P*-value of <0.05 was considered statistically significant. All statistical analysis was carried out with the use of SPSS 21.0.

Results

A total of 208 women were assessed for eligibility between 15 May 2017 and 22 November 2017. Of these women, 200 were eligible and randomised. Nine patients did not complete the full protocol, resulting in 94 cases in the balloon group and 97 cases in the control group included in the final analysis (Figure 1). The baseline patient demographic characteristics are presented in Table 1. No significant differences were observed between the balloon group and the control group for any of the variables assessed pre-operatively.

At the third-look hysteroscopy, the adhesion reformation rate in the balloon group was significantly lower than the

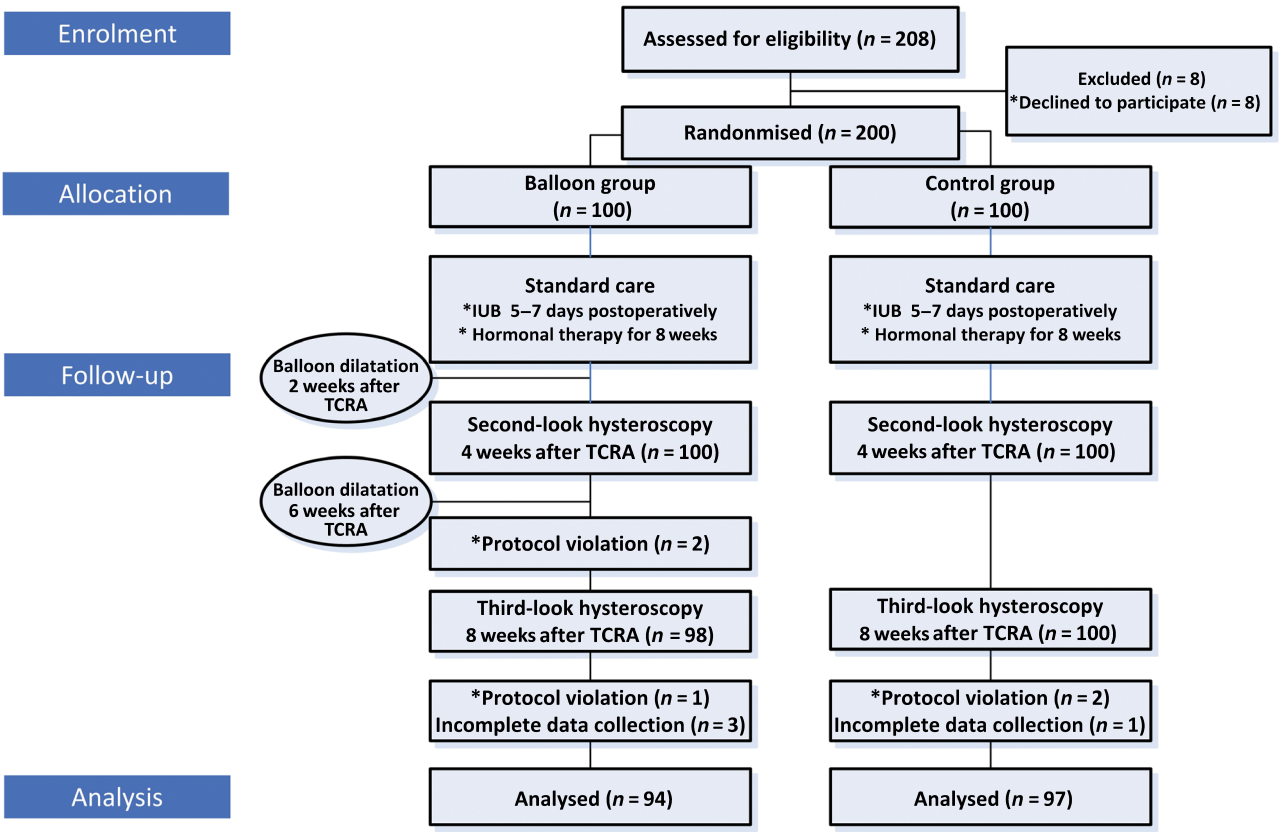

Figure 1. Consort flow diagram. *Protocol violation was defined as not taking hormone therapy as instructed. IUB, intrauterine balloon; TCRA, transcervical resection of adhesion.

control group: 20.2% versus 40.2%, RR 0.50 (95% CI 0.31–0.80), $P = 0.003$ (Table 2). Both groups demonstrated a significant reduction in ESGE grade compared with their pre-operative grade ($P < 0.001$). However, the proportion of subjects with a normal uterine cavity in the balloon group was significantly higher than the proportion in the control group: 75/94 (79.8%) versus 58/97 (59.8%), RR 1.33 (95% CI 1.10–1.62 ($P = 0.003$). In addition, the proportion of subjects with moderate adhesions according to ESGE grade in the balloon group was significantly lower than that of the control group: 7/94 (7.4%) versus 29/97 (29.9%), RR 0.25 (95% CI 0.12–0.54) ($P < 0.001$).

Patient-centred outcomes

In terms of the improvement of menstrual flow, the balloon group again demonstrated a higher rate of improvement in PBAC scores at 8 weeks postoperatively when compared with the control group: 30 (IQR, 20–45) versus 9 (IQR, 0–20), respectively ($P < 0.001$; Table 2). This included all women presenting with amenorrhoea/oligomenorrhoea.

All women wished to conceive after the surgery. At the 12-month follow up, 27/94 (28.7%) women in the balloon group achieved a pregnancy, which was not significantly different from that of 26/97 (26.8%) in the control group. The miscarriage, ectopic pregnancy, ongoing pregnancy (beyond 20 weeks) and live birth rate in the balloon group (8/27 [29.6%], 1/27 [3.8%], and 18/27 [66.6%], respectively) were also not significantly different from the control group (9/26 [34.6%], 1/26 [3.8%] and 16/26 [61.6%], respectively).

In terms of patient-reported pain scores, the VAS was 5.40 ± 1.20 and 1.39 ± 1.03 at 1 and 30 minutes after the balloon dilatation therapy, respectively. No complications (such as uterine perforation, fluid overload, severe bleeding or infection) were observed in either group.

Discussion

Main findings

In the present RCT, we found that patients who received intermittent IUB dilatation therapy following hysteroscopic adhesiolysis experienced a significant reduction in adhesion recurrence and severity (as assessed by the ESGE grade), as well as a significant improvement in menstruation flow (as assessed by PBAC score) when compared with the control

Table 1. Demographic characteristics

Variable	Balloon group (*n* = 94)	Control group (*n* = 97)	Significance
Age (years)[a]	32.0 ± 4.4	32.1 ± 4.7	NS
Gravity[a]	1.2 ± 0.6	1.5 ± 0.5	NS
Parity[a]	0.1 ± 0.3	0.1 ± 0.2	NS
Presenting complaints[b]			
Recurrent miscarriage	15 (16.0%)	22 (22.7%)	NS
Infertility	27 (28.7%)	26 (26.8%)	
Amenorrhoea	17 (18.1%)	11 (11.3%)	
Oligomenorrhoea	77 (81.9%)	86 (88.7%)	
Cyclic pain	17 (18.1%)	11 (11.3%)	
Previous intrauterine operation[b]			
D&C for induced abortion	86 (91.5%)	88 (90.7%)	NS
Postpartum D&C	6 (6.4%)	5 (5.2%)	
No intrauterine operation	2 (2.1%)	4 (4.1%)	
Adhesion grade[b]			
Moderate	41 (43.6%)	47 (48.5%)	NS
Severe	53 (56.4%)	50 (51.5%)	
Duration of operation (min)[a]	21.2 ± 8.6	23.2 ± 8.5	NS
PBAC score before operation[c]	17 (3.75–25)	17 (10–25)	NS

NS, not significant; PBAC, pictorial blood-loss assessment chart. Values are given as mean ± standard deviation, number (percentage) or median (interquartile range), unless otherwise indicated. A *P*-value of <0.05 was considered statistically significant. All patients wished to conceive. Some patients experienced both amenorrhoea/oligomenorrhoea and pelvic pain.
[a]Student's *t*-test.
[b]By $\chi 2$ test and contingency table analysis.
[c]Mann–Whitney *U*test.

group. This was assessed over an 8-week postoperative period which included a second- and third-look hysteroscopy. These surrogate outcomes may prove to have important practical implications for clinicians treating women with IUA.

Previous RCTs have shown improvements in reducing IUA reformation rates using solid barriers,[12] semi-solid barriers,[13,14] and tissue barriers.[15–17] In fact, solid and semi-solid barriers are the only methods to receive Level A grade of recommendation from the AAGL and ESGE for use within this context.[18] Typically, most studies describe the insertion of a balloon catheter (such as a Foley) at the end of the primary hysteroscopic adhesiolysis procedure, with a view to it being removed after a total of 3–30 days.[8,28,29] However, our study is the first to use intermittent IUB dilatation as an additional barrier prevention method for reducing adhesion reformation rates. Intermittent IUB dilatation may divide early reformed adhesions via simple blunt dissection along the physiological uterine cavity plane, before denser adhesion bands are formed. We elected to perform IUB dilatation 2 and 6 weeks after the index hysteroscopic surgery, as studies have reported that IUA can form as early as 2 weeks following hysteroscopic adhesiolysis.[30] Our preliminary observations prior to this RCT have shown favourable outcomes and patient acceptability when using this technique.[19,20] In addition to the improved outcomes outlined above, the VAS pain scores reported by patients after dilatation therapy were 5.40 ± 1.20 and 1.39 ± 1.03 at 1 and 30 minutes, respectively, which are similar to the scores reported during office hysteroscopy (5.20 ± 2.10 and 1.33 ± 6.73, at 1 and 30 minutes, respectively).[31] It is worth pointing out that although the intermittent balloon therapy appeared effective in reducing recurrence of adhesions over above what might be achieved with the use of standard care, the extra cost incurred to the patient is minimal: the procedure and consumable cost for each episode of balloon therapy in China is only around UK£20. The advantages are that it is simple, quick, of low-cost and can be performed in the outpatient office setting without the need for hysteroscopic equipment, analgesia or anaesthesia.

There was significant difference in the incidence of adhesion reformation and adhesion score at 8 weeks between the groups but not at 4 weeks postoperatively, raises the question of whether the beneficial effect of the intermittent balloon therapy was primarily due to the second balloon treatment and whether the first balloon treatment at 2 weeks was unnecessary. If this was the case, it could mean the postoperative balloon therapy could be simplified to consist of only one balloon dilation at 6 weeks. Further clinical studies will be needed to address this question.

Strengths and limitations

In terms of strengths, to our knowledge, this is the first RCT to use an additional barrier method (intermittent IUB dilatation therapy) for the prevention of adhesion reformation. In addition, it appears to be the largest of all RCTs that have been identified by a recent meta-analysis.[11] Furthermore, a relatively comprehensive follow-up protocol was devised, which included second- and third-look hysteroscopies, measurements of adhesion grade (ESGE classification), menstrual flow (PBAC score), pain scores and preliminary reproductive outcome data.

In terms of limitations, this study was not designed or powered and did not include a long enough follow-up period to assess specifically the question of reproductive outcomes for the patients undergoing treatment. In contrast, like most studies to date, it used the surrogate outcomes of adhesion reformation rates and improvement of menstrual

Table 2. Comparison of the incidence of intrauterine adhesion reformation, the reduction of adhesion grade, and the increase of PBAC score at second- and third-look hysteroscopy

Variable	Balloon group (*n* = 94)	Control group (*n* = 97)	Risk ratio (95% CI)	*P*-value
Adhesion reformation rate[a]	19 (20.2%)	39 (40.2%)	0.50 (0.31–0.80)	0.003
ESGE Grade before operation[a]				
Moderate	41 (43.6%)	47 (48.5%)	0.90 (0.66–1.23)	0.56
Severe	53 (56.4%)	50 (51.5%)	1.09 (0.84–1.24)	0.56
ESGE Grade after operation 4 weeks[a]				
Normal	42 (44.7%)	40 (41.2%)	1.08 (0.78–1.50)	0.66
Mild	33 (35.1%)	34 (35.1%)	1.00 (0.68–1.47)	1.00
Moderate	19 (20.2%)	23 (23.7%)	0.85 (0.50–1.50)	0.60
Severe	0 (0%)	0 (0%)		
ESGE Grade after operation 8 weeks[a]				
Normal	75 (79.8%)	58 (59.8%)	1.33 (1.10–1.62)	0.003
Mild	12 (12.8%)	10 (10.3%)	1.24 (0.56–2.73)	0.66
Moderate	7 (7.4%)	29 (29.9%)	0.25 (0.12–0.54)	<0.001
Severe	0 (0%)	0 (0%)		
PBAC score before operation[b]	17 (10–25)	17 (4–25)		0.34
PBAC score after operation 4 weeks[b]	50 (35–60)	34 (19–42)		<0.001
PBAC score after operation 8 weeks[b]	50 (35–60)	30 (18–40)		<0.001
Increase of PBAC score[b]	30 (20–45)	9 (0–20)		<0.001

Abbreviations: NS, not significant; ESGE, European Society for Gynaecological Endoscopy; PBAC, pictorial blood-loss assessment chart. Values are given as number (percentage) or median (interquartile range), unless otherwise indicated. A p value of <0.05 was considered statistically significant.
[a]By $\chi 2$ test and contingency table analysis.
[b]Mann-Whitney *U* test.

flow which are considered to affect reproductive outcomes. In addition, the investigator (X.S.) who prepared the data was not blinded to the randomization, which could constitute a bias. Finally, the trial included a spherical Foley catheter balloon rather than a purpose-designed catheter such as a heart-shaped balloon, which fits better into the uterine cavity,[32] which may produce even more favourable results.

Interpretation

When reviewing the literature regarding the use of solid barriers for the prevention of IUA reformation, to our knowledge, there is only one previous RCT in the literature comparing the use of an intrauterine balloon versus an intrauterine coil in the immediate postoperative period.[12] Interestingly, our control group, which also received an intrauterine balloon in the immediate postoperative period, displayed similar adhesion reformation rates to both treatment arms of the study by Lin[12] (40% versus 30–35%, respectively), whereas our study group showed a lower adhesion reformation rate in comparison with only 20%. When considering semi-solid barrier use, two RCTs have assessed the use of auto-crosslinked hyaluronic acid gel.[13,14] In the larger study of Xiao et al.,[13] the adhesion reformation rate was 52% for the control group (balloon catheter only) and only 24% for the study group (balloon catheter and auto-crosslinked hyaluronic acid gel), which was similar to our study group (20%). Other RCTs have reported the use of tissue barrier methods such as fresh and freeze-dried amnion grafts.[15,17] The largest of these trials is that of Gan et al.,[15] where the control group of 40 patients received an intrauterine balloon for the first 5 postoperative days, similar to our control group, whereas the intervention group of 40 patients received a balloon in a similar fashion that was coated with a sterile, freeze-dried amnion graft. The reported rate of adhesion reformation in their control group was similar to our control group (40% versus 40%, respectively); however, that of their treatment group was slightly higher than our intermittent IUB dilatation group (28% versus 20%, respectively). It is worth noting that comparisons between trials are limited by the heterogeneity in both the study populations and data collected. We have shown in this study that intermittent balloon therapy postoperatively is of benefit in reducing adhesion reformation, but it would be of interest in future to conduct further clinical trials to see whether a combination of intermittent balloon with semi-solid barriers (e.g. auto cross-linked hyaluronic acid gel) and tissue barriers (e.g. freeze-dried amnion grafts) would produce additional benefit.

In our study we have followed up our patients for at least 1 year, similar to a recently published cohort study from the Sydney group[33]; however, future studies could follow up the reproductive outcome of patients including live birth and obstetric complications for up to 2 years, as the more than 68% majority will be expected to have conceived by then.[34] In addition, purpose-designed balloon catheters with a shape more compatible with the uterine cavity could be considered as a refinement, as they may prove to be less painful for the patient and more effective in terms of reaching the more distal areas of the uterine cavity, such as the tubal ostia and lower part of the uterus.

Conclusions

The present RCT has demonstrated that following hysteroscopic adhesiolysis, the use of intermittent dilatation balloon therapy can significantly reduce adhesion reformation rates, while improving menstruation flow. Further trials are required to clarify whether the improved benefits in these surrogate outcomes can be translated into improved reproductive outcomes.

Disclosure of interests

None declared. Completed disclosure of interests forms are available to view online as Supporting Information.

Contribution to authorship

TCL designed the study. QZ, XH, and EX conducted the trial. XS conducted the dilatation therapy and prepared the data. XS and SHS analysed the data and drafted the manuscript. All of the authors critically revised the manuscript, contributed to the final draft of the manuscript, and approved the version to be published.

Details of ethics approval

The study was approved by Institutional review board of Capital Medical University (reference No. 2016FXHEC-KY, 20 October 2016). The study was registered at Clinicaltrials.gov. Clinical trial identification number: NCT03131596. URL of the registration site: https://clinicaltrials.gov/show/NCT03131596.

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References

1 Valle RF, Sciarra JJ. Intrauterine adhesions: hysteroscopic diagnosis, classification, treatment, and reproductive outcome. *Am J Obstet Gynecol* 1988;158:1459–70.
2 Orhue AA, Aziken ME, Igbefoh JO. A comparison of two adjunctive treatments for intrauterine adhesions following lysis. *Int J Gynaecol Obstet* 2003;82:49–56.
3 Schenker JG. Etiology of and therapeutic approach to synechia uteri. *Eur J Obstet Gynecol Reprod Biol* 1996;65:109–13.
4 Song D, Liu Y, Xiao Y, Li TC, Zhou F, Xia E. A matched cohort study comparing the outcome of intrauterine adhesiolysis for Asherman's syndrome after uterine artery embolization or surgical trauma. *J Minim Invasive Gynecol* 2014;21:1022–8.
5 Deans R, Abbott J. Review of intrauterine adhesions. *J Minim Invasive Gynecol* 2010;17:555–69.
6 Yu D, Wong YM, Cheong Y, Xia E, Li TC. Asherman syndrome—one century later. *Fertil Steril* 2008;89:759–79.
7 Fedele L, Vercellini P, Viezzoli T, Ricciardiello O, Zamberleti D. Intrauterine adhesions: current diagnostic and therapeutic trends. *Acta Eur Fertil* 1986;17:31–7.
8 Pabuccu R, Atay V, Orhon E, Urman B, Ergun A. Hysteroscopic treatment of intrauterine adhesions is safe and effective in the restoration of normal menstruation and fertility. *Fertil Steril* 1997;68:1141–3.
9 Hanstede M, van der Meij E, Goedemans L, Emanuel M. Results of centralized Asherman surgery, 2003-2013. *Fertil Steril* 2015;104:1561–8 e1.
10 Guo EJ, Chung JPW, Poon LCY, Li TC. Reproductive outcomes after surgical treatment of asherman syndrome: a systematic review. *Best Pract Res Clin Obstet Gynaecol* 2019. https://doi.org/10.1016/j.bpobgyn.2018.12.009
11 Yan Y, Xu D. The effect of adjuvant treatment to prevent and treat intrauterine adhesions: a network meta-analysis of randomized controlled trials. *J Minim Invasive Gynecol* 2018;25:589–99.
12 Lin XN, Zhou F, Wei M, Yang Y, Li Y, Li TC, et al. Randomized, controlled trial comparing the efficacy of intrauterine balloon and intrauterine contraceptive device in the prevention of adhesion reformation after hysteroscopic adhesiolysis. *Fertil Steril* 2015;104:235–240.
13 Xiao S, Wan Y, Zou F, Ye M, Deng H, Ma J, et al. Prevention of intrauterine adhesion with auto-crosslinked hyaluronic acid gel: a prospective, randomized, controlled clinical study [in Chinese]. *Zhonghua Fu Chan Ke Za Zhi* 2015;50:32–6.
14 Acunzo G, Guida M, Pellicano M, Tommaselli GA, Di Spiezio Sardo A, Bifulco G, et al. Effectiveness of auto-cross linked hyaluronic acid gel in the prevention of intrauterine adhesions after hysteroscopic adhesiolysis: a prospective, randomized, controlled study. *Hum Reprod* 2003;18:1918–21.
15 Gan L, Duan H, Sun FQ, Xu Q, Tang YQ, Wang S. Efficacy of freeze-dried amnion graft following hysteroscopic adhesiolysis of severe intrauterine adhesions. *Int J Gynaecol Obstet* 2017;137:116–22.
16 Wang X, Duan H. Clinical evaluation of amniontic products after transcervical resection of intensive degree of intrauterine adhesions [in Chinese]. *Zhonghua Fu Chan Ke Za Zhi* 2016;51:27–30.
17 Amer MI, Abd-El-Maeboud KH. Amnion graft following hysteroscopic lysis of intrauterine adhesions. *J Obstet Gynaecol Res.* 2006;32:559–66.
18 AAGL Elevating Gynecologic Surgery. AAGL practice report: practice guidelines on intrauterine adhesions developed in collaboration with the European Society of Gynaecological Endoscopy (ESGE). *J Minim Invasive Gynecol* 2017;24:695–705.

19 Saravelos SH, Li TC. Ultrasound guided treatment of intrauterine adhesions in the outpatient setting. *Ultrasound Obstet Gynecol* 2017;50:278–80.

20 Saravelos SH, Li TC. Intrauterine balloon therapy: a novel ultrasound guided treatment for intrauterine adhesions. *Gynecol Surg* 2016;13:403–7.

21 Yu D, Li TC, Xia E, Huang X, Liu Y, Peng X. Factors affecting reproductive outcome of hysteroscopic adhesiolysis for Asherman's syndrome. *Fertil Steril* 2008;89:715–22.

22 Peng X, Li TC, Zhao Y, Guo Y, Xia E. Safety and efficacy of amnion graft in preventing reformation of intrauterine adhesions. *J Minim Invasive Gynecol* 2017;24:1204–10.

23 Wamsteker K, De Block S. Diagnostic hysteroscopy: technique and documentation. In: Sutton C, Diamond M, eds. *Endoscopic Surgery for Gynecologists*. London: WB Saunders; 1998. pp 511–24.

24 Lin X, Wei M, Li TC, Huang Q, Huang D, Zhou F, et al. A comparison of intrauterine balloon, intrauterine contraceptive device and hyaluronic acid gel in the prevention of adhesion reformation following hysteroscopic surgery for Asherman syndrome: a cohort study. *Eur J Obstet Gynecol Reprod Biol* 2013;170:512–6.

25 Robinson JK, Colimon LM, Isaacson KB. Postoperative adhesiolysis therapy for intrauterine adhesions (Asherman's syndrome). *Fertil Steril* 2008;90:409–14.

26 Higham JM, O'Brien PM, Shaw RW. Assessment of menstrual blood loss using a pictorial chart. *Br J Obstet Gynaecol* 1990;97:734–9.

27 Breivik H, Borchgrevink PC, Allen SM, Rosseland LA, Romundstad L, Hals EK, et al. Assessment of pain. *Br J Anaesth* 2008;101:17–24.

28 Yasmin H, Nasir A, Noorani KJ. Hystroscopic management of Asherman's syndrome. *J Pak Med Assoc.* 2007;57:553–5.

29 Amer MI, Abd-El-Maeboud KH, Abdelfatah I, Salama FA, Abdallah AS. Human amnion as a temporary biologic barrier after hysteroscopic lysis of severe intrauterine adhesions: pilot study. *J Minim Invasive Gynecol* 2010;17:605–11.

30 Yang JH, Chen MJ, Wu MY, Chao KH, Ho HN, Yang YS. Office hysteroscopic early lysis of intrauterine adhesion after transcervical resection of multiple apposing submucous myomas. *Fertil Steril* 2008;89:1254–9.

31 Fouda UM, Gad Allah SH, Elshaer HS. Optimal timing of misoprostol administration in nulliparous women undergoing office hysteroscopy: a randomized double-blind placebo-controlled study. *Fertil Steril* 2016;106:196–201.

32 March C. Management of Asherman's syndrome. *Reprod Biomed Online* 2011;23:63–76.

33 Deans R, Vancaillie T, Ledger W, Liu J, Abbott J. Live birth rate and obstetric complications following the hysteroscopic management of intrauterine adhesions including Asherman syndrome. *Hum Reprod* 2018;33:1847–53.

34 Hanstede M, Emanuel M. Reproductive outcomes of 10 years Asherman's surgery. *J Minim Invasive Gynecol* 2015;22:s1.