

REVIEW ARTICLE

Use of anti-adhesion gel after hysteroscopy for the treatment of female infertility: A systematic review and meta-analysis

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Abstract

This systematic review and meta-analysis assessed the effectiveness of anti-adhesion gels in preventing intrauterine adhesions (IUA) and improving reproductive outcomes following hysteroscopic procedures. Twelve randomized controlled trials involving a total of 1709 patients were included. The results indicated that anti-adhesion gels significantly reduced both the incidence and recurrence of IUA and were associated with a lower American Fertility Society (AFS) score. Furthermore, their use was linked to improved pregnancy and live birth rates. However, no significant effects were found on menstrual improvement or pregnancy loss rates. These findings suggest that anti-adhesion gels may be beneficial in enhancing postoperative reproductive outcomes and reducing adhesion-related complications after hysteroscopy. Further research is needed to clarify the role of anti-adhesion in menstrual recovery and miscarriage prevention. (*Afr J Reprod Health* 2025; 29 [7]: 158-174).

Keywords: Anti-adhesion gel; infertility; intrauterine adhesions; pregnancy rate; American Fertility Society score

Résumé

Cette revue systématique et méta-analyse a évalué l'efficacité des gels anti-adhérences dans la prévention des adhérences intra-utérines (AIU) et l'amélioration des résultats génésiques après hystérocopie. Douze essais contrôlés randomisés, portant sur un total de 1 709 patientes, ont été inclus. Les résultats ont indiqué que les gels anti-adhérences réduisaient significativement l'incidence et la récurrence des AIU et étaient associés à un score AFS (American Fertility Society) plus faible. De plus, leur utilisation était associée à une amélioration des taux de grossesse et de naissances vivantes. Cependant, aucun effet significatif n'a été observé sur l'amélioration des menstruations ou les taux de fausses couches. Ces résultats suggèrent que les gels anti-adhérences pourraient être bénéfiques pour améliorer les résultats génésiques postopératoires et réduire les complications liées aux adhérences après hystérocopie. Des recherches complémentaires sont nécessaires pour clarifier le rôle des gels anti-adhérences dans la récupération menstruelle et la prévention des fausses couches. (*Afr J Reprod Health* 2025; 29 [7]: 158-174).

Mots-clés: Gel anti-adhérence ; infertilité ; adhérences intra-utérines ; taux de grossesse ; score de l'American Fertility Society

Introduction

Intrauterine adhesion (IUA) is a pathological condition that arises from abnormal or incomplete repair of the endometrium following trauma, such as surgical procedures or infections. It is primarily characterized by the development of fibrous adhesions within the uterine cavity, which can vary in extent and severity. These adhesions often result in structural alterations and functional impairment of the uterine cavity^{1,2}. The risk of developing IUA in patients undergoing myomectomy exceeds 9%, while the incidence following hysteroscopic morcellation of retained products of conception can reach up to 20%^{3,4}.

The severity of IUA varies widely, ranging from mild, localized fibrous bands to severe cases

involving partial or complete obliteration of the uterine cavity. Such adhesions can profoundly disrupt the normal physiological function of the endometrium. The clinical manifestations of IUA vary depending on the degree of adhesions, with the most common symptoms including decreased menstrual flow and cyclic abdominal pain, and some patients may present with amenorrhea, especially if the uterine cavity is extensively adherent or completely atretic⁵. In addition, IUA may also affect the environment for embryo implantation and prevent the fertilized egg from implanting, which may lead to infertility or pregnancy failure, further exacerbating the patient's fertility dilemma⁶. In addition, IUA not only affects a woman's fertility, but may also cause long-term negative effects on her physical and mental health.

Hysteroscopic adhesiolysis is currently the main diagnostic and therapeutic tool for IUA by directly separating adhesions and restoring the anatomy of the uterine cavity^{6,7}. It is worth noting that while hysteroscopic surgery has a better therapeutic effect on pre-existing IUA, the regenerative capacity of the endometrium is limited and the IUA recurrence risk after surgery is still high. In addition to hysteroscopic adhesion release for the treatment of IUA, other types of hysteroscopic surgery (e.g., hysteroscopic myomectomy) may also lead to the development of postoperative IUA, and therefore prevent IUA or the recurrence of IUA after hysteroscopic manipulation is an important part of clinical practice⁸. In recent years, a variety of anti-adhesion measures, including mechanical barriers (e.g., uterine balloon stents, intrauterine devices), pharmacological treatments (e.g., estrogens), and anti-adhesion barrier gels, including hyaluronic acid (HA) gels, have been proposed and used in clinical practice to counteract this occurrence^{7,9}.

HA gel is thought to prevent or reduce the occurrence of recurrent IUA and improve fertility problems by forming a physical barrier in the uterine cavity, reducing postoperative traumatic adhesions, and facilitating endometrial repair due to its favorable biocompatibility and adhesive properties². Although the quality of evidence is low, several previous studies have shown that HA gel improves the IUA incidence after various hysteroscopic procedures, and recent meta-analyses have confirmed the role of HA in the prevention of IUA and resulting infertility^{2,7,10}. However, most of the current meta-analyses include different types of surgeries (e.g., curettage), and the use of adhesion-preventive agents and their efficacy for patients undergoing hysteroscopic surgery is still lacking systematic evaluation. Furthermore, previous studies have mainly focused on HA gels, while the effects of other types of anti-adhesion gels have not yet been adequately compared^{2,7,10,11}. Therefore, this study focused on the use of adhesion-preventive agents after hysteroscopic surgery for

the first time, strictly excluding heterogeneity due to surgical procedures such as curettage. It included a study not covered by previous meta-analyses, evaluated the effects of Oxiplex/AP gels in addition to HA gels, and analyzed menstrual improvement to more comprehensively explore the effects of anti-adhesion gels on IUA and reproductive outcomes¹². The findings of this study may serve as a stronger evidence base for clinical practice.

Methods

Literature sources and criteria for inclusion

The review was conducted using computerized searches of several international databases, including The Cochrane Library, PubMed, Embase, Medline, and ClinicalTrials.gov, to comprehensively collect research literature that satisfied the eligibility criteria. Inclusion criteria: randomized controlled trials (RCT) that included patients undergoing hysteroscopic surgery; trials that included both an anti-adhesive gel group and a control group, and both groups received the same underlying treatment (e.g., a physical barrier, including an intrauterine device or Foley catheter balloon, or neither group received any other intervention). There were no language restrictions. Exclusion criteria: papers that are not RCTs; duplicate papers; publications that provide only abstracts (e.g., conference proceedings); publications that do not provide specific data or where the data have been processed but are still not usable.

Search strategy

The search was conducted in English. The search timeframe was set from the inception of the databases to December 31, 2024, to maximize the inclusion of all potentially relevant studies. A combination of free-text keywords was used to maximize coverage of studies on intrauterine adhesion and anti-adhesion barrier gels. Keywords

included "intrauterine adhesion", "IUA", "endometrial injury", "adhesion", "hysteroscopy", "hysteroscopic surgery", "hysteroscopic adhesiolysis", "gel", "Oxiplex/AP gel", "hyaluronic acid gel", "ACP", "chitosan", and "hyaluronic acid". We also searched other databases for clinical trial data in the unofficial published literature. Two investigators independently conducted literature searches and data extraction to minimize human bias and improve study quality. Discrepancies during the screening process were resolved through discussion with a third investigator.

Data extraction and quality assessment

From each eligible study, two researchers independently extracted the name of the first author, country and region, year of publication, sample size, study design, disease, intervention status of the two patient groups, follow-up, withdrawal, outcome data, and quality information. This review utilized the Cochrane Risk of Bias Assessment Tool to evaluate the methodological quality of all included studies¹³. This tool covers seven aspects of bias, including allocation concealment, random sequence generation, blinding of outcome assessment, blinding of participants and researchers, selective outcome reporting, completeness of outcome data, and other biases. All studies were categorized as low bias, unclear bias, or high bias based on the assessment. The bias assessment was performed independently by two investigators, and in case of disagreement, a third investigator intervened to discuss and reach consensus.

Outcome

Primary outcomes in this analysis consisted of the occurrence and recurrence of IUA, pregnancy rate, and secondary outcomes including American Fertility Society (AFS) score at follow-up, miscarriage rate, live birth rate, and menstrual

improvement rate. IUA incidence was defined as the formation of intrauterine adhesions after hysteroscopic surgery in patients who did not have IUA preoperatively. The IUA recurrence was considered as the recurrence of IUA after hysteroscopic surgery in patients with IUA. The recurrence of IUA was defined as the reappearance of IUA after hysteroscopic surgery in patients with IUA. The pregnancies reported in this study were clinical pregnancies, defined as intrauterine sacs as well as primordial cardiac ductal pulsations detected by ultrasound. Gestational age was greater than 12 weeks. A pregnancy loss was defined as the natural death of an embryo or fetus before it develops to the point where it can survive independently outside the uterus.

Statistical analysis

RevMan 5.4 was utilized to perform all statistical analyses in this study. Risk ratios (RRs) with 95% confidence intervals (CIs) were used for dichotomous outcomes, while mean differences (MDs) with 95% CIs were applied for continuous outcomes. Heterogeneity was assessed using the I^2 statistic, which was judged according to the following criteria: if $I^2 \leq 25\%$, it indicated low heterogeneity and a fixed-effects model was used; if $25\% < I^2 \leq 50\%$, it indicated moderate heterogeneity, and a fixed-effects or random-effects model was chosen, depending on the specific situation; and if $I^2 > 50\%$, it indicated high heterogeneity and random-effects model was used^{10,14}. To assess the risk of publication bias for the primary endpoints, a funnel plot was drawn for visualization in this study.

Results

Characteristics of included studies

In this study, we systematically searched multiple databases, as shown in Figure 1, and obtained a total of 117 relevant literatures.

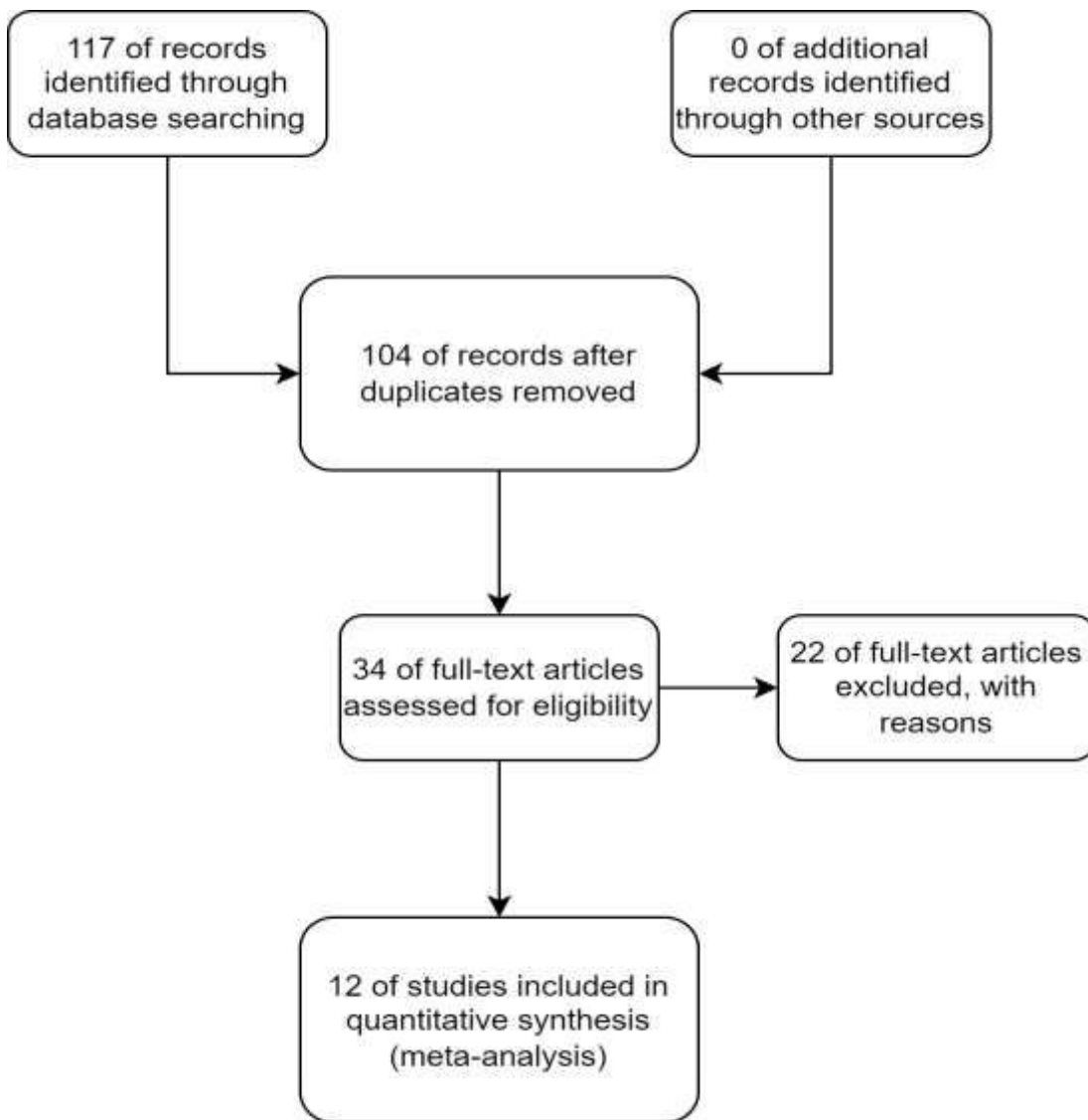


Figure 1: Study flow diagram

Table 1: Characteristics of the included studies

Author year	Study design	Country and region	Language	Patients	Sample size	Dropout patient	Intervention	Control	Gel types	Gel volume	Follow-up	Outcomes
Acunzo 2003	Single-center	Italy	English	IUA	92	8	Hysteroscopic resection of intrauterine adhesions + ACP gel	Hysteroscopic resection of intrauterine adhesions	ACP gel	10 mL	3 months	IUA recurrence
Chen 2022	Multi-center	China	English	Submucosal myoma, endometrial polyp, or uterine septum	200	36	Hysteroscopic electro-surgical resection+ ACP gel	Hysteroscopic electro-surgical resection	ACP gel	3 mL	3 months (IUA), at least 10 months (pregnancy)	IUA, pregnancy rate, live birth rate, pregnancy loss rate
Di Spiezio Sardo 2011	Single-center	Italy	English	Premenopausal women	110	0	Hysteroscopic surgery + Polyethylene oxide-sodium carboxymethylcellulose gel	Hysteroscopic surgery	Polyethylene oxide-sodium carboxymethylcellulose gel	10 mL	1 month	IUA
Fuchs 2014	Single-center	Israel	English	Retained products of conception	52	11	4-mm loop resectoscope as a curette and under	4-mm loop resectoscope as a curette and	Oxiplex/AP gel	Up to 10 mL	1 week (IUA), at least 2	IUA, pregnancy rate

Author	Study Design	Country	Language	Condition	n	Intervention	Control	Intervention	Control	Volume	Outcome	Notes
Guida 2004	Single-center	Italy	English	Submucous myomas, endometrial polyps or uterine septa	138	6	hysteroscopic view + Oxiplex/AP gel Hysteroscopic surgery + ACP gel	under hysteroscopic view Hysteroscopic surgery	ACP gel	10 mL	3 months	IUA
Guo 2022	Single-center	China	English	IUA	188	17	Hysteroscopic adhesiolysis + Foley catheter intrauterine balloon + ACP gel	Hysteroscopic adhesiolysis + Foley catheter intrauterine balloon	ACP gel	5 mL	8 weeks (IUA), 3 months (menstruation)	IUA recurrence, menstrual improvement rate
Huang 2020	Single-center	Taiwan, China	English	Submucosal fibroids	71	1	Hysteroscopic myomectomy + ACP or CHA-P	Hysteroscopic myomectomy	ACP or CHA-P	10 mL	12 weeks	IUA
Mao 2020	Single-center	China	English	IUA	306	35	Hysteroscopic adhesiolysis + CHA gel + embryo transfer	Hysteroscopic adhesiolysis + embryo transfer	CHA gel	N/A	Embryo transfer after 2 months, followed by 12 weeks of pregnancy	Pregnancy rate, live birth rate, pregnancy loss rate

Author	Study Design	Country	Language	Condition	n	Events	Intervention	Control	Volume	Observation	Outcome	
Pabuçcu 2019	Single-center	Turkey	English	IUA	83	11	Hysteroscopic adhesiolysis + NCH gel+ in vitro fertilization	Hysteroscopic adhesiolysis+ in vitro fertilization	NCH gel	5 mL	2nd hysteroscopy after 8-12 weeks, in vitro fertilization after 1 year	Pregnancy rate
Wang 2020	Single-center	China	English	IUA	89	0	Hysteroscopic adhesiolysis + intrauterine device + ACP gel	Hysteroscopic adhesiolysis + intrauterine device	ACP gel	3 mL	1 month	IUA recurrence, pregnancy rate
Xiao 2015	Multi-center	China	Chinese	IUA	120	9	Hysteroscopic adhesiolysis + Foley balloon catheter + ACP gel	Hysteroscopic adhesiolysis + Foley balloon catheter	ACP gel	2 mL	3 months	IUA recurrence
Zhou 2021	Single-center	China	English	IUA	260	15	Hysteroscopic adhesiolysis + standard care + ACP gel	Hysteroscopic adhesiolysis + standard care	ACP gel	3 mL	4 weeks (IUA), 3 months (menstruation)	IUA recurrence, menstrual improvement rate

After de-duplication, 104 papers were included in the initial screening and then screened based on title and abstract, and the remaining 34 full texts were further evaluated to see if they met the inclusion criteria. After excluding 22 studies that did not meet the inclusion criteria, 12 studies were finally included in the meta-analysis^{5,6,8,12,15-22}. Figure 1

Table 1 shows that the 12 included RCTs were published from 2003 to 2022 and included a total of 1709 subjects, with the majority of studies including subjects with predominantly IUA patients^{5,6,15,18-21}, while some of the studies included patients with combined endometrial polyps, submucous fibroids, or uterine septum who underwent hysteroscopic surgery^{8,12,16,17,22}. These studies were carried out in multiple countries and regions, including seven from China^{5,6,8,16,19-21}, three from Italy^{15,17,22}, one from Israel¹², and one from Turkey¹⁸. Except for Xiao's study, which was published in Chinese, the literature was in English²⁰. Of these studies, ten were single-center studies^{5,6,8,12,15,17-19,21,22} and two were multicenter studies^{16,20}. The types of antiadhesive gels used in the studies were more varied, with the most common being auto-crosslinked hyaluronic acid (ACP) gel^{5,8,15-17,19-21}, and the remaining studies using Oxiplex/AP gel¹², crosslinked hyaluronic acid (CHA) gel⁶, crosslinked hyaluronic acid platform (CHA-P) gel⁸, new crosslinked hyaluronic acid (NCH) gel¹⁸, and polyethylene oxide–sodium carboxymethylcellulose gel²². The amount of gel used varied between studies, ranging from 2 mL to 10 mL, and one study did not report the amount of gel used⁶. Follow-up time varied widely between studies, ranging from 1 week to 3 months for IUA recurrence and longer for pregnancy outcomes (e.g., pregnancy rate, live birth rate, miscarriage rate, etc.), with some studies exceeding 1 year, with a high completion rate of follow-up in the majority of studies, but a high loss to follow-up rate of 21% in the Fuchs study¹².

Risk of bias assessment of included studies

To evaluate study quality and potential bias, the Cochrane Risk of Bias Tool was applied to all 11 included trials. As shown in Figure 2, most of the studies performed well in terms of allocation concealment and blinding and random sequence generation, but some of them still had some risk of bias.

In terms of allocation concealment and random sequence generation, all studies used computerized random numbers and described their allocation concealment methods in detail, except for two studies that did not specify the exact method^{18,20}. In terms of blinding, two studies^{6,18} did not clearly report blinding of subjects and researchers, which may have led to performance bias, while four studies may not have provided the blinding of outcome assessment, which may have led to detection bias in the results^{6,17,18,22}. Finally, one of the studies¹⁸ may have had attrition bias.

Incidence of IUA and changes in AFS scores

A total of 11 studies^{5,6,8,12,15-17,19-22} (n = 1248) were included to assess the incidence of postoperative IUA, as shown in Figure 3A. According to the meta-analysis, the intervention group had a significantly lower rate of IUA than the control group (RR = 0.64, P < 0.00001). Heterogeneity analysis showed moderate heterogeneity in this outcome (I² = 45%, P = 0.05), the fixed-effects model was selected for the combined analysis due to its consistency with the random-effects model results. This result suggests that anti-adhesion gel can significantly reduce the incidence of IUA after hysteroscopy.

As shown in Figure 3B, for patients who had developed uterine adhesions and underwent hysteroscopic treatment, Meta-analysis included six studies^{5,6,15,19-21} (n = 728) to assess the recurrence rate of IUA.

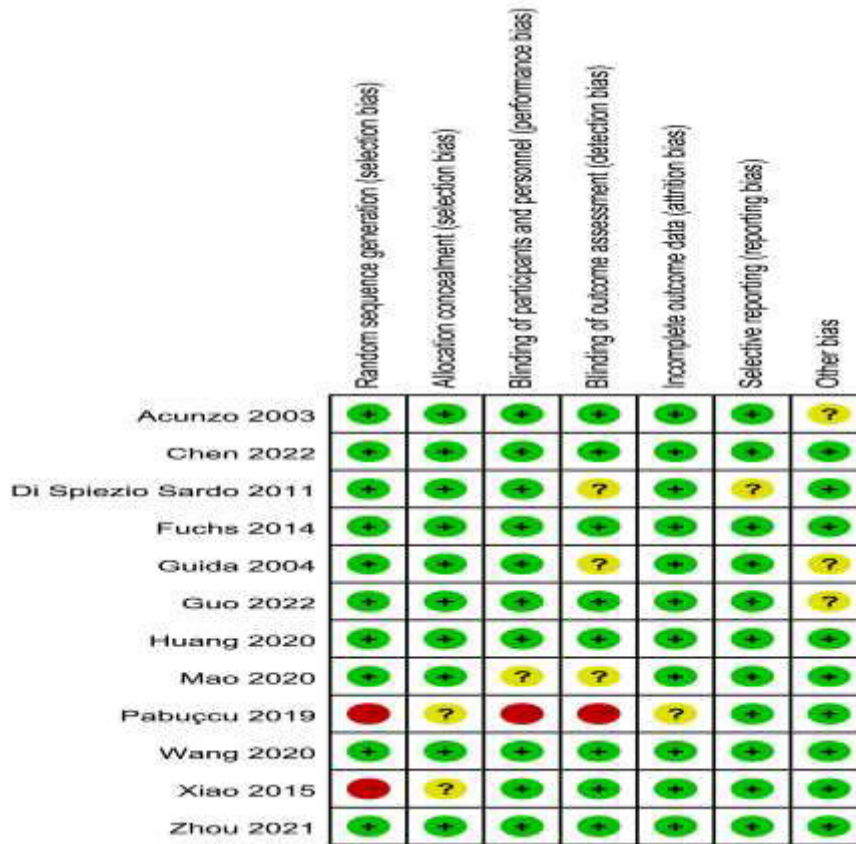


Figure 2: Risk of bias summary

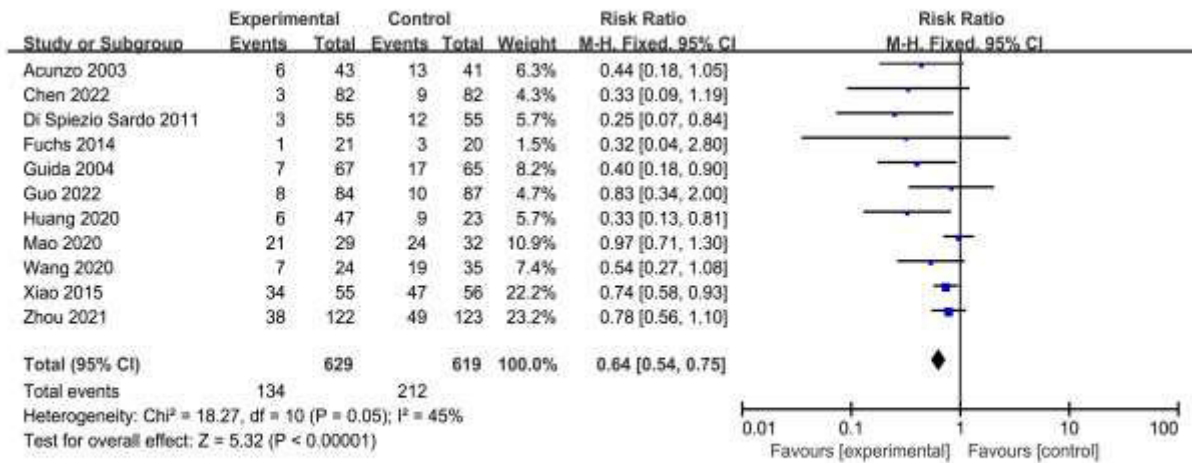
A lower recurrence rate of IUA was observed in the intervention group compared to the control group, according to the meta-analysis (RR = 0.75, P = 0.001) and no significant heterogeneity (I² = 0%, P = 0.47). This part of the results suggests a clearer protective effect of anti-adhesion gel in reducing IUA recurrence.

As shown in Figure 3C, a total of five studies^{6,15,17,18,20} (n = 439) were included to assess the change in postoperative AFS scores. A significant decrease in AFS scores was observed in the intervention group relative to the control group, based on the meta-analysis (MD = -1.12, P =

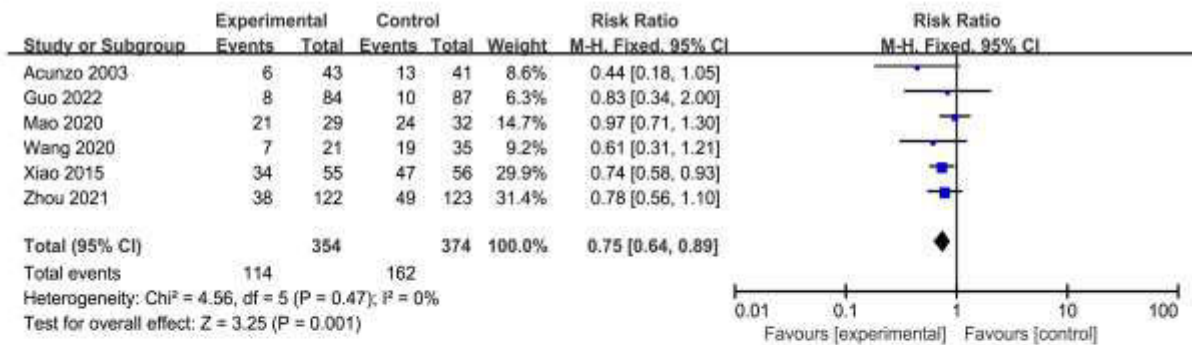
0.0008). Heterogeneity analysis revealed high heterogeneity in this outcome (I² = 65%, P = 0.03). We conducted a sensitivity analysis to explore the origin of heterogeneity among studies, and when Mao's study⁶ was excluded, the I² decreased to 0%, suggesting that this study may be the main source of heterogeneity. However, the intervention effect remained statistically significant regardless of its exclusion (MD = -1.12 vs. -1.44), suggesting that the results were robust, and thus all studies were ultimately included in the combined analysis.

Overall, our results in this study suggest that anti-adhesion gel may improve the severity of IUA after hysteroscopy and reduce AFS scores.

A



B



C

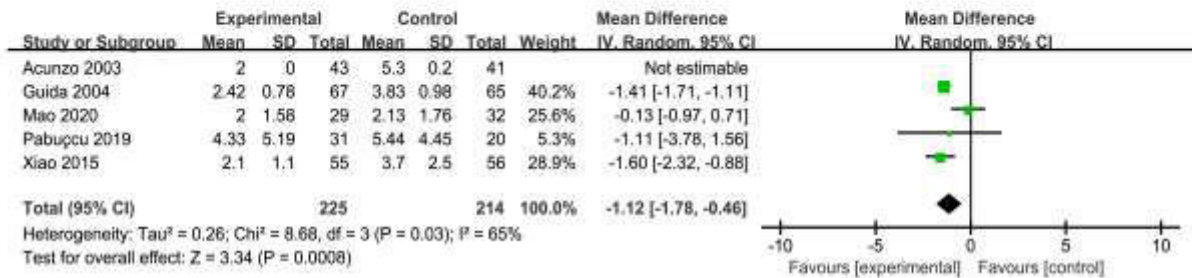


Figure 3: Meta-analysis of IUA occurrence, recurrence, and AFS scores A. IUA occurrence. B. IUA recurrence. C. AFS score

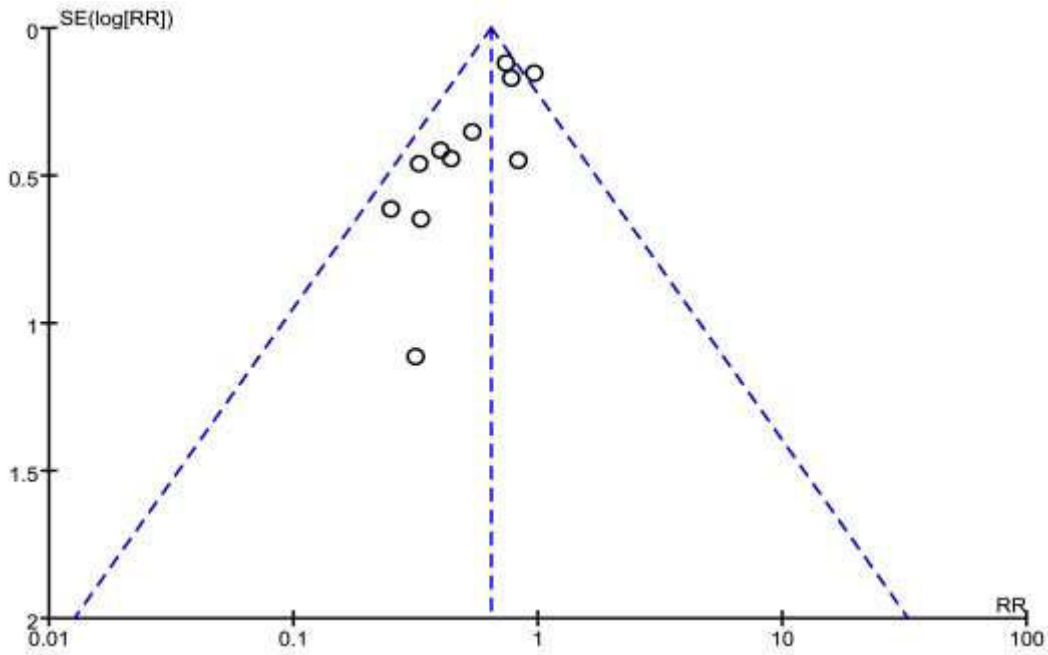


Figure 4: Funnel plot of risk of publication bias for IUA occurrence

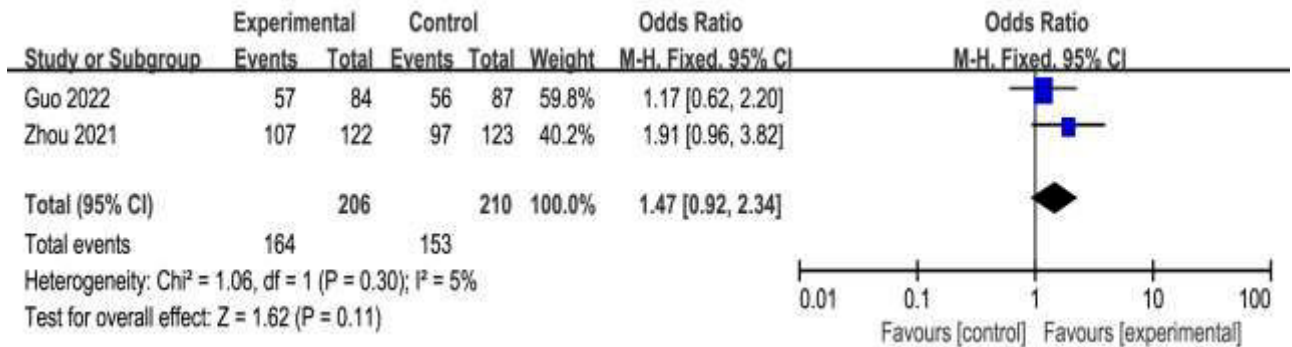
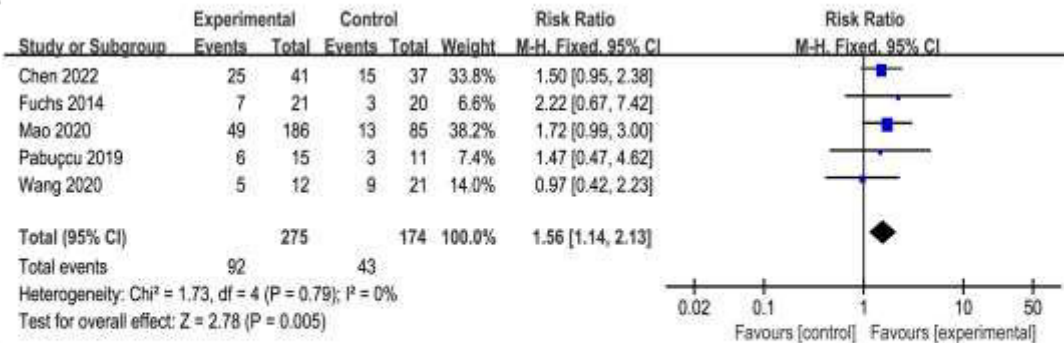
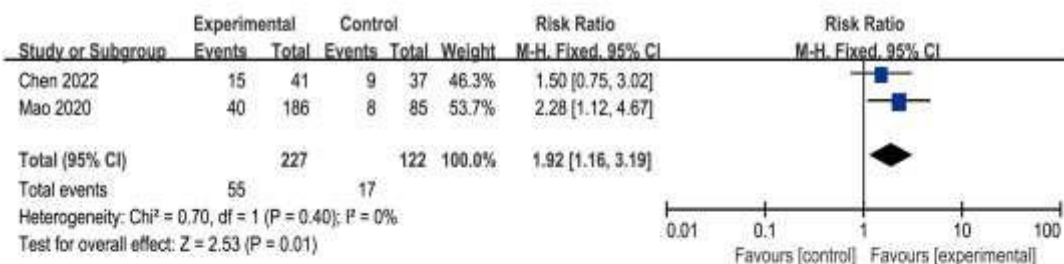


Figure 5: Meta-analysis of menstrual improvement

A



B



C

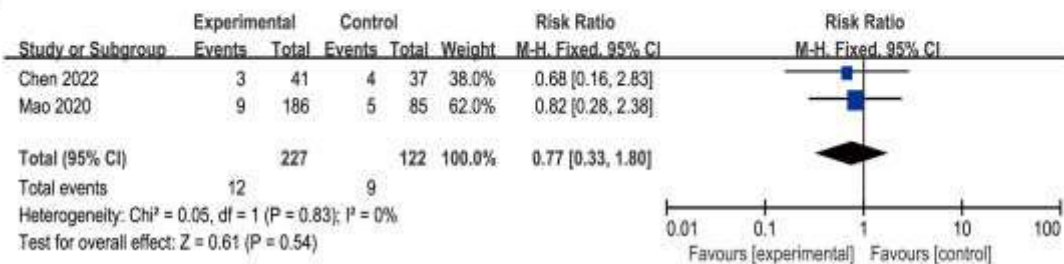


Figure 6: Meta-analysis of pregnancy rates, live birth rates and pregnancy loss rates A. Pregnancy rate. B. Live birth rate. C. Pregnancy loss rate.

To evaluate the potential for publication bias for the outcome of IUA incidence, a funnel plot was generated in this study. As shown in Figure 4, the funnel plot was approximately symmetric and no evidence of significant publication bias was detected. However, given the limited number of included studies, the potential for publication bias could not be completely excluded.

Improvement of menstruation

As shown in Figure 5, meta-analysis included two studies^{5,21} ((n = 416) assessing the menstrual improvement rate in patients after hysteroscopy. No significant difference in menstrual improvement rate was observed between the intervention and control groups (OR = 1.47, P = 0.11) and no

significant heterogeneity ($I^2 = 5\%$, $P = 0.30$). Although Zhou's study²¹ suggested that anti-adhesion gel may help menstrual recovery, the overall combined analysis did not reach statistical significance.

Improvements in pregnancy rates and pregnancy outcomes

Here, a total of five studies^{6,12,16,18,19} ($n = 449$) were included to assess the effect of anti-adhesion barrier gel on pregnancy rate after hysteroscopy.

As shown in Figure 6A, according to the meta-analysis, the intervention group exhibited a significantly higher pregnancy rate compared to the control group ($RR = 1.56$, $P = 0.005$), and there was no heterogeneity ($I^2 = 0\%$, $P = 0.79$). Our results suggest that anti-adhesion gel can significantly increase the pregnancy rate in patients after hysteroscopy.

As shown in Figure 6B, meta-analysis included two studies^{6,16} ($n = 349$) evaluating the effect of anti-adhesion barrier gel on the live birth rate after hysteroscopy. The results showed that the live birth rate was higher in the intervention group than in the control group ($RR = 1.92$, $P = 0.01$), and there was no heterogeneity ($I^2 = 0\%$, $P = 0.40$). This result suggests that anti-adhesion gel not only improves pregnancy rate but also may improve the final reproductive outcome.

As shown in Figure 6C, meta-analysis included two studies^{6,16} ($n = 349$) assessing abortion rates.

Statistical analysis revealed that the difference between the intervention and control groups was not significant ($RR = 0.77$, $P = 0.54$) and no heterogeneity ($I^2 = 0\%$, $P = 0.83$). This result may be related to the limited sample size or the multifactorial effect of pregnancy outcome, suggesting that the effect of anti-adhesion agents on miscarriage rate is unclear and still needs to be validated in further studies.

Discussion

Anti-adhesion gel is a physical barrier agent composed of polymeric materials such as hyaluronic acid, polyethylene oxide, or carboxymethylcellulose. It acts by forming a temporary protective film over the endometrial surface after hysteroscopic surgery, thereby reducing direct tissue contact, mechanical irritation, and microbial invasion. This physical isolation helps to suppress the local inflammatory response, inhibit fibroblast proliferation and collagen deposition, and ultimately reduce the risk of IUA formation. Anti-adhesion gel is currently considered one of the most important strategies for the prevention and management of IUA, and remains a major focus of clinical research^{10,23,24}. In this review, 12 RCTs with 1709 patients were systematically included to evaluate the effects of anti-adhesion gel application on the incidence and recurrence of IUA and reproductive outcomes after hysteroscopy. The meta-analysis showed that anti-adhesion gel significantly reduced the incidence and recurrence of IUA after hysteroscopy, improved AFS scores, and significantly increased the live birth rate and pregnancy rate, suggesting that it has important clinical value in aiding anti-adhesion and improving fertility prognosis. Given the increasing demand for reproductive health services in developing countries, the findings of this study have important implications for both policy and clinical practice.

Anti-adhesion gels not only improve patients' reproductive prognosis but may also help reduce the long-term financial and psychological burdens associated with infertility. Therefore, policymakers and clinicians should consider incorporating anti-adhesion gels into standard postoperative management for appropriate patient populations. Notably, the effect of anti-adhesion gel on menstrual improvement and miscarriage rate is unclear.

Compared with previous studies, the most important feature of this study is that the inclusion was strictly limited to women who underwent hysteroscopic surgery, thus avoiding the interference of clinical heterogeneity caused by differences in surgical procedures. The meta-analysis published by Liu¹⁰ and Luo² included different surgical procedures, such as curettage and hysteroscopy, in the same analytical framework. As a less invasive and more precise endoscopic technique, the mechanism of postoperative IUA and recurrence risk of hysteroscopy is not clear, may be more different from that of traditional curettage^{25,26}. Therefore, the results of this study are more relevant and can provide a more informative evidence base for postoperative hysteroscopic management. In addition, almost all Earlier meta-analyses exploring the role of anti-adhesion gels on the occurrence of IUA and reproductive outcomes after hysteroscopic manipulation were limited to hyaluronic acid gels^{2,10,27,28}. The present study included the first RCT of Oxiplex/AP gel, which broadened the scope of evaluation of anti-adhesion barrier gels and showed that other types of gels besides hyaluronic acid also have some anti-adhesion effects, suggesting that there is still room for optimization in the selection of gel types in the future¹².

Regarding the prevention and treatment of IUA, the findings of this study showed that the anti-adhesion gel could reduce the risk of postoperative IUA by 34% and the risk of recurrence by 25%, and it could significantly reduce the AFS scores at follow-up, suggesting that it not only reduces the adhesion formation but also helps to reduce the adhesion severity. The findings were basically consistent with the conclusions of the meta-analysis by Luo et al. However, the present study was more advantageous in terms of the number of included studies, the consistency of surgical background, and the control of heterogeneity, which enhanced the credibility of the conclusions². Notably, in this study, there was some heterogeneity in the analysis of AFS scores, and the sensitivity analysis

suggested that the Mao's study⁶ was the main source of heterogeneity, and the heterogeneity was significantly reduced after its exclusion from analysis, however, the direction and statistical significance of the effect remained unchanged, further validating the robustness of the results. Similar to the results of this study, a previous meta-analysis also found high heterogeneity in AFS scores². We speculate that one of the reasons for this finding may be that the study by Mao et al. included subjects with moderate to severe IUA who underwent assisted reproduction therapy, a population with a complex baseline profile and generally high AFS scores, suggesting that assisted reproduction patients should be analyzed as a separate subgroup when designing relevant studies in the future. In addition, because AFS scores, as continuous variables, do not have consistent data distribution characteristics across studies, some studies reported medians and interquartile ranges instead of means and standard deviations. Conversion of such data to means and standard deviations may introduce some estimation error, thereby exacerbating heterogeneity^{29,30}.

IUA is a major contributor to female infertility and pregnancy failure, significantly affecting a woman's reproductive prognosis. Previous studies have shown that hyaluronic acid-based gels can optimize the embryo implantation environment and improve pregnancy success and pregnancy outcomes by forming a physical barrier, reducing direct contact and inflammatory responses at the endometrial surface of the uterine cavity after surgery, promoting endothelial repair, and improving endothelial tolerance^{10,31}. In this meta-analysis, we observed that the use of anti-adhesion gels was associated with notable improvements in both pregnancy and live birth rates. Specifically, the results indicated a 56% increase in pregnancy rate and a 92% increase in live birth rate in the intervention group compared to the control group, findings that are consistent with those reported in previous studies. Although the previous study by

Luo et al. showed that anti-adhesion gel had a facilitating effect on pregnancy rate, the results were not as significant as those of the present study, which may be related to the greater heterogeneity of their included studies². Our combined analysis did not show a significant effect of the anti-adhesion gel on menstrual improvement, but some studies suggested that the gel contributed to menstrual recovery, a trend that may not have been significant owing to the limited number of included studies and the relatively short follow-up duration²¹. Considering that patients with IUA often complain of menstrual abnormalities and that menstrual improvement directly reflects the restoration of endothelial function, future studies should pay more attention to this outcome and extend the follow-up period to comprehensively evaluate the role of anti-adhesion gels in improving menstruation and fertility.

The limitations of this review are mainly reflected in the modest sample size of some of the included studies, the different duration of follow-up, and the differences in the combined interventions, which may have some impact on the results. In addition, several studies did not adequately report randomization and blinding procedures, with some risk of bias, and further improvement is still warranted, especially in terms of outcome assessment and data completeness. Nevertheless, the results of the robustness analysis of the main outcomes were good, and the direction of the main effects was consistent, suggesting that the conclusions of this study have high reliability and generalizability. High-quality RCT with robust sample sizes and long-term observational periods are still needed in the future to further optimize the anti-adhesion strategy after hysteroscopy and improve the reproductive health and quality of life of patients.

Conclusion

Evidence from this meta-analysis supports that anti-adhesion gel has a good anti-adhesion effect after hysteroscopy, which can reduce the IUA occurrence and recurrence risk, and significantly increase the rate of pregnancy and live birth, which has important clinical application value. Although the effects on menstrual improvement and miscarriage rate are still unclear, the results suggest that anti-adhesion gel has greater potential to improve reproductive prognosis, and future studies with large samples and long-term follow-up should be intensified to optimize the anti-adhesion strategy after hysteroscopy to further improve women's reproductive outcomes and quality of life.

Authors' contributions

YFW and JL conceptualized this study. YFW and LPL worked on the literature review. YFW and LPL worked on the data analysis and interpretation of results. All authors worked on the discussion of the findings. All the authors read and approved the final manuscript.

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Declaration of conflicting interests

The authors declare no competing interests

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