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ORIGINAL RESEARCH

Effectiveness of Hyaluronic Acid Gel in Preventing Postoperative Intrauterine Adhesion Formation Following Operative Hysteroscopy

Banu Ciftci[1], Burak Karadag[2]

[1]Department of Obstetrics and Gynecology, Private Gynecology Clinic, Istanbul, Turkey; [2]Department of Obstetrics and Gynecology, University of Health Sciences Antalya Training and Research Hospital, Antalya, Turkey

Correspondence: Burak Karadag, Department of Obstetrics and Gynecology, University of Health Sciences Antalya Training and Research Hospital, Antalya, Turkey, Tel +905055863856, Email drburakkaradag@gmail.com

Objective: To evaluate the effectiveness of intrauterine hyaluronic acid (HA) gel application in preventing postoperative intrauterine adhesion formation following operative hysteroscopy.

Methods: This retrospective comparative study was conducted at a tertiary referral center and included women who underwent operative hysteroscopy between January 2024 and December 2024. Patients were divided into two groups according to postoperative management: those who received intrauterine hyaluronic acid gel application and those who did not receive any adhesion barrier. All patients underwent follow-up evaluation with second-look hysteroscopy between 30 days and 6 months after surgery. The primary outcome was the incidence of postoperative intrauterine adhesion formation. Secondary outcomes included adhesion type, cavity involvement according to the American Fertility Society (AFS) classification, and menstrual pattern changes.

Results: A total of 77 patients were included in the final analysis, including 34 patients in the HA gel group and 43 patients in the control group. Postoperative intrauterine adhesions were detected in 22 patients (28.6%). The incidence of adhesion formation was significantly lower in the HA gel group compared with the control group (8.8% vs. 43.2%, p = 0.001). Adhesions observed in the HA gel group were predominantly filmy in nature, and all observed adhesions involved less than one-third of the uterine cavity. Improvement in menstrual patterns was observed in all patients in the HA gel group and in 78.9% of patients in the control group. The use of hyaluronic acid gel resulted in an absolute risk reduction of 34.4% and a relative risk reduction of approximately 80% in adhesion formation.

Conclusion: Intrauterine application of hyaluronic acid gel following operative hysteroscopy was associated with a lower incidence of postoperative intrauterine adhesions and descriptively milder adhesion characteristics. HA gel may represent a useful adjunct for adhesion prevention; however, larger prospective studies are required to confirm these findings.

Keywords: adhesion prevention, hyaluronic acid, hysteroscopy, intrauterine adhesions, second-look hysteroscopy

Introduction

Intrauterine adhesions (IUAs) result from damage to the basalis layer of the endometrium, leading to fibrotic scarring and partial or complete obliteration of the uterine cavity and/or cervical canal.[1] Clinically, IUAs are associated with menstrual disturbances, infertility, and recurrent pregnancy loss and are commonly referred to as Asherman syndrome.[2]

Operative hysteroscopy is the preferred method for the diagnosis and treatment of IUAs because it allows direct visualization and targeted adhesiolysis while minimizing further endometrial injury.[3]

It should also be noted that the baseline risk of postoperative adhesion formation differs according to the type of hysteroscopic procedure performed.[4] Procedures involving greater endometrial trauma, such as adhesiolysis and myomectomy, are generally associated with a higher risk of adhesion formation than polypectomy.[2,5] Septum resection may represent an intermediate-risk procedure, depending on the extent of endometrial injury and the surgical technique used.[4,5]

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Despite appropriate surgical management, postoperative re-adhesion remains a major limitation, with recurrence rates reported to reach up to 60%.[6] Therefore, effective postoperative strategies to prevent adhesion reformation are of significant clinical importance.

No single strategy has been universally accepted as the gold standard for adhesion prevention. Various strategies have been proposed to prevent postoperative adhesion formation, including mechanical barriers such as intrauterine devices and balloon catheters, as well as pharmacological and bioresorbable anti-adhesion agents. These methods have shown variable effectiveness in reducing adhesion formation, with no universally accepted standard approach. Among these, hyaluronic acid (HA)–based gels have gained increasing attention due to their favorable biocompatibility and barrier function during endometrial healing.[4,7]

Second-look office hysteroscopy is widely recommended following operative hysteroscopy, as it enables early detection and treatment of newly formed adhesions before they progress in extent and density.[8] The American Fertility Society (AFS) classification system is commonly used to assess the severity and extent of IUAs during follow-up hysteroscopy.[9]

Hyaluronic acid is a naturally occurring glycosaminoglycan that plays an essential role in extracellular matrix structure and tissue repair.[10] Owing to its biocompatibility and viscoelastic properties, HA acts as a temporary physical barrier that separates opposing endometrial surfaces during the critical healing period after surgery. Cross-linked formulations prolong intrauterine persistence of the gel and may enhance its effectiveness in preventing adhesion reformation. Previous studies evaluating HA-based gels after hysteroscopic adhesiolysis have demonstrated variable results, with several reports indicating a reduction in both the incidence and severity of postoperative IUAs.[11–13]

However, despite the availability of randomized studies and meta-analyses, the reported effectiveness of HA gel remains heterogeneous across different patient populations, surgical indications, and follow-up protocols. Accordingly, the objective of the present study was to evaluate the effectiveness of a hyaluronic acid–based anti-adhesion gel in reducing the incidence and severity of intrauterine adhesions following operative hysteroscopy, as assessed by follow-up diagnostic hysteroscopy using the AFS classification system.

Materials and Methods

Study Design

This retrospective, comparative, single-center observational study was conducted at the Department of Obstetrics and Gynecology of the University of Health Sciences Antalya Training and Research Hospital. The study evaluated patients who underwent operative hysteroscopy between January 1, 2024, and December 31, 2024. The study protocol was conducted in accordance with the principles of the Declaration of Helsinki and Good Clinical Practice guidelines. Ethical approval was obtained from the local institutional ethics committee (approval no. 20/26). Written informed consent was obtained from all participants prior to inclusion in the study.

Study Population

Medical records of patients who underwent operative hysteroscopy during the study period were retrospectively reviewed. A total of 82 patients were initially identified, and 77 patients who completed follow-up evaluation with second-look hysteroscopy were included in the final analysis.

Eligible participants were women aged 18 years or older who underwent operative hysteroscopy for intrauterine pathologies, including endometrial polyps, submucosal myomas, intrauterine adhesions, or uterine septa.

Patients were excluded if they were younger than 18 years of age, had a body weight of 100 kg or greater, experienced excessive intraoperative bleeding (>100 mL) or uterine perforation during surgery, had uncontrolled systemic diseases such as diabetes mellitus or coagulation disorders, had a known malignancy or uterovaginal prolapse, underwent concomitant intrauterine device placement, or did not undergo follow-up hysteroscopy. The body weight criterion was applied because of institutional and technical limitations related to operative hysteroscopy equipment and perioperative management protocols during the study period.

Surgical Procedure and Follow-Up

All hysteroscopic procedures were performed by the same experienced surgeon (B.K). Operative hysteroscopy was carried out using standard hysteroscopic techniques depending on the surgical indication. Procedures included hysteroscopic polypectomy, myomectomy, adhesiolysis, or septum resection using appropriate hysteroscopic instruments and energy sources.

After completion of the hysteroscopic procedure, patients were managed according to the postoperative treatment protocol and divided into two groups. In the HA gel group, an intrauterine adhesion barrier gel containing cross-linked hyaluronic acid (40 mg/mL) was applied using a 5-mL prefilled intrauterine applicator through the cervical canal (Semical adhesion barrier gel, AB221; Semical Teknoloji A.Ş., Turkey). The gel was delivered gently into the uterine cavity in a controlled manner. Given the viscous and bioadhesive properties of hyaluronic acid, this application method was considered suitable for intrauterine delivery despite the use of a liquid distention medium. Patients in the control group underwent operative hysteroscopy without the use of any postoperative adhesion barrier agent.

Although early second-look hysteroscopy within the first postoperative weeks is commonly recommended in the literature,[8] follow-up timing in the present retrospective study was based on routine postoperative clinical practice. Because follow-up timing depended on patient availability, appointment scheduling, and clinical logistics, the interval between the initial procedure and second-look hysteroscopy varied among patients. Therefore, a follow-up window of 30 days to 6 months was used in the present study. During follow-up hysteroscopy, the presence of intrauterine adhesions was assessed and documented. The extent and severity of adhesions were classified according to the American Fertility Society (AFS) classification system,[9] which considers the extent of cavity involvement, adhesion characteristics, and menstrual pattern.

Treatment allocation was not randomized. All hysteroscopic procedures were performed by the same experienced surgeon (B.K)., and the decision to apply HA gel was based on routine clinical practice and material availability during the study period rather than random allocation. Although this approach reduces inter-operator variability, potential selection bias and residual confounding cannot be excluded.

Outcome Measures

The primary outcome of this study was the incidence of postoperative intrauterine adhesion formation detected during second-look hysteroscopy.

Secondary outcomes included the extent of adhesion spread within the uterine cavity, adhesion type (filmy, dense-filmy, or dense), menstrual pattern changes following surgery, and operative parameters such as operation time and perioperative hemoglobin levels.

Statistical Analysis

Statistical analysis was performed using SPSS software (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation, and categorical variables were presented as frequencies and percentages. The normality of distribution was assessed using the Kolmogorov–Smirnov test. Comparisons between groups were performed using the independent samples *t*-test or Mann–Whitney *U*-test, as appropriate, for continuous variables, and the chi-square or Fisher's exact test for categorical variables. A p-value of <0.05 was considered statistically significant.

Results

Patient Selection

During the study period, a total of 82 patients who underwent operative hysteroscopy were initially evaluated. Five patients were excluded due to the absence of follow-up hysteroscopy. Consequently, 77 patients who completed second-look hysteroscopy were included in the final analysis. Among these patients, 34 received postoperative intrauterine hyaluronic acid (HA) gel application, while 43 patients served as the control group.

Baseline Characteristics

The mean age of the patients was 36.96 ± 6.93 years, and the mean body mass index was 24.05 ± 2.11 kg/m^2. Baseline demographic and operative characteristics, including perioperative hemoglobin change (Hb difference), were comparable between the HA gel and control groups (Table 1). No statistically significant differences were observed between the groups with respect to age, BMI, parity, previous dilation and curettage procedures, size of intrauterine pathology, operation time, or perioperative hemoglobin change (all $p > 0.05$). Endometrial polyp was the most common indication for operative hysteroscopy (51.9%). The distribution of surgical indications and energy sources used during hysteroscopic procedures was similar between the two groups. All patients who underwent hysteroscopic myomectomy had a single myoma. However, detailed myoma location was not consistently documented in all cases and therefore was not included in the statistical analysis.

Primary Outcome: Postoperative Adhesion Formation

At second-look hysteroscopy, postoperative intrauterine adhesions were detected in 22 patients (28.6%). The incidence of postoperative adhesion formation was significantly lower in the HA gel group than in the control group (8.8% vs. 43.2%, $p = 0.001$). The relative risk (RR) of adhesion formation in the HA gel group compared with the control group was 0.20, corresponding to an absolute risk reduction of 34.4% and a relative risk reduction of approximately 80%. The number needed to treat (NNT) to prevent one case of adhesion formation was three patients.

Secondary Outcomes

Adhesion Severity and Cavity Involvement

Adhesion characteristics differed between the two groups. In the HA gel group, adhesions were predominantly filmy in nature, whereas the control group demonstrated a higher proportion of more severe adhesions.

All adhesions observed in the HA gel group involved less than one-third of the uterine cavity. In contrast, adhesions in the control group involved less than one-third of the cavity in 13 patients, one-third to two-thirds in two patients, and

Table 1 Baseline Characteristics and Operative Indications of the Study Groups

		Control (n=43)	HA Gel (n=34)	p
Age (years)		37.3 ± 7.09	36.44 ± 6.77	0.562
BMI (kg/m^2)		24.05 ± 2.25	24.04 ± 1.94	0.991
Parity		1 (0–4)	0 (0–4)	0.507
D&C		0 (0–3)	0 (0–2)	0.444
Size of pathology (mm)		16.03 ± 4.91	16.43 ± 4.55	0.683
Operation time (min)		21.98 ± 4.10	21.91 ± 5.22	0.844
Hb difference		1.34 ± 0.86	1.14 ± 0.83	0.295
Indication for hysteroscopy	Endometrial polyp	22 (51.2%)	18 (52.9%)	0.946
	Submucosal myoma	7 (16.3%)	4 (11.8%)	
	Intrauterine adhesion	11 (25.6%)	9 (26.5%)	
	Uterine septum	3 (7%)	3 (8.8%)	
Energy source	Cold scissors	10 (23.3%)	9 (26.5%)	0.948
	Bipolar	16 (37.2%)	12 (35.3%)	
	Morcellator	17 (39.5%)	13 (38.2%)	

Notes: Values are presented as mean ± SD, median (range), or n (%), as appropriate.
Abbreviations: D&C, dilation and curettage; Hb, haemoglobin.

Table 2 Postoperative Intrauterine Adhesion Outcomes in the Study Groups

		Control (n=43)	HA Gel (n=34)	p
Adhesion formation		19 (43.2%)	3 (8.8%)	0.001
Adhesion type	Filmy	9 (47.4%)	2 (66.7%)	0.711
	Dense–filmy	7 (36.8%)	1 (33.3%)	
	Dense	3 (15.8%)	0	
Cavity involvement	<1/3	13 (68.4%)	3 (100%)	0.521
	1/3–2/3	2 (10.5%)	0	
	>2/3	4 (21.1%)	0	
Menstrual pattern	Normal	15 (78.9%)	3 (100%)	0.116
	Hypomenorrhea	4 (21.1%)	0	

Notes: Values are presented as n (%) unless otherwise indicated. Percentages for adhesion type and cavity involvement were calculated among patients with postoperative adhesions.

more than two-thirds in four patients. The extent of cavity involvement appeared lower in the HA gel group; however, the difference was not statistically significant (p = 0.521).

Detailed comparisons of adhesion formation and characteristics between the groups are presented in Table 2.

Menstrual Pattern

Improvement in menstrual patterns following hysteroscopic surgery was observed in all patients in the HA gel group and in 78.9% of patients in the control group; however, the between-group difference was not statistically significant.

No intraoperative or postoperative complications related to hyaluronic acid gel application were observed.

Discussion

The present study showed that intrauterine application of hyaluronic acid gel following operative hysteroscopy was associated with a lower incidence of postoperative intrauterine adhesion formation. In our cohort, the adhesion rate decreased from 43.2% in the control group to 8.8% in patients receiving HA gel. Beyond the reduction in adhesion incidence, HA gel use was descriptively associated with milder adhesion characteristics, with a predominance of filmy adhesions and limited cavity involvement. This observation may be clinically relevant because milder adhesions are generally associated with better reproductive outcomes and may be easier to manage if re-intervention is required.[2,5] In addition, the improvement in menstrual patterns observed in both groups, particularly in the HA gel group, may reflect enhanced endometrial healing, although this finding did not reach statistical significance.[5] Taken together, these findings suggest that HA gel may have benefits beyond reducing adhesion incidence. However, these observations should be interpreted cautiously because severity-related outcomes did not reach statistical significance. Intrauterine adhesions are a well-recognized complication of intrauterine surgical procedures and may result in menstrual abnormalities, infertility, and recurrent pregnancy loss. Damage to the basalis layer of the endometrium during surgical procedures is considered the primary mechanism underlying adhesion formation, leading to fibrosis and partial or complete obliteration of the uterine cavity.[2] Despite advances in hysteroscopic techniques, postoperative adhesion recurrence remains a significant clinical challenge, with reported rates reaching up to 60% following hysteroscopic adhesiolysis.[2,6]

The overall postoperative adhesion rate in our cohort was 28.6%, which may appear relatively high compared with some previous reports. This may be explained by the heterogeneous nature of the study population, as postoperative adhesion risk varies according to the type and extent of hysteroscopic surgery performed.[4] Procedures such as simple endometrial polypectomy generally carry a lower risk of adhesion formation compared with more extensive procedures such as hysteroscopic adhesiolysis, myomectomy, or septum resection. In particular, patients undergoing adhesiolysis

represent a distinct high-risk group because of pre-existing endometrial damage and the propensity for adhesion recurrence.[2,5] Recent randomized studies and meta-analyses have suggested that anti-adhesion strategies, including hyaluronic acid–based barriers, may reduce postoperative intrauterine adhesion formation; however, the magnitude of benefit appears to vary according to the surgical indication and baseline adhesion risk.[14,15] Importantly, intrauterine adhesions are clinically relevant not only as an anatomical outcome but also because of their potential negative effects on reproductive outcomes, including pregnancy and live birth rates following hysteroscopic adhesiolysis.[16]

The type of hysteroscopic energy modality may also influence postoperative adhesion formation by affecting the degree of thermal or mechanical endometrial injury.[4,5] In the present study, cold scissors, bipolar energy, and morcellation systems were used according to surgical indication. Although the distribution of energy sources was similar between the groups, the relatively small sample size did not allow a separate analysis of adhesion outcomes according to energy modality.

Various strategies have been proposed to prevent adhesion formation after intrauterine surgery, including mechanical barriers, intrauterine devices, balloon catheters, and pharmacologic agents. Among these, hyaluronic acid–based anti-adhesion gels have attracted considerable attention due to their favorable biological properties and biocompatibility.[7] Hyaluronic acid acts as a temporary physical barrier that separates opposing endometrial surfaces during the early postoperative healing phase, thereby reducing the likelihood of fibrotic adhesion formation.[4]

Several previous clinical studies have evaluated the efficacy of HA-based gels in preventing intrauterine adhesions. In a randomized controlled trial, Acunzo et al demonstrated that the application of auto-cross-linked hyaluronic acid gel significantly reduced adhesion recurrence following hysteroscopic adhesiolysis.[11] Similarly, Guida et al reported lower rates of postoperative adhesion formation and improved uterine cavity healing in patients treated with HA gel compared with untreated controls.[12] More recently, Hooker et al reported that the use of hyaluronic acid gel following intrauterine procedures reduced the incidence of newly formed adhesions during follow-up hysteroscopy.[13]

Our findings are consistent with these studies, showing a lower rate of adhesion formation among patients receiving HA gel. In addition, adhesions observed in the HA gel group were predominantly filmy in nature and, descriptively, were confined to less than one-third of the uterine cavity in all affected patients. This observation may be clinically relevant because milder adhesions are generally considered easier to treat and potentially less likely to impair reproductive outcomes.[2,5]

In contrast, some studies have reported less pronounced effects of HA gel in adhesion prevention. Chen et al[17] observed a lower incidence of postoperative IUAs in patients treated with auto-cross-linked hyaluronic acid gel; however, the difference did not reach statistical significance. Differences between studies may be explained by variations in patient populations, surgical indications, sample sizes, follow-up intervals, and concomitant postoperative treatments. In addition, differences in hysteroscopic energy modalities may also influence postoperative endometrial injury and subsequent adhesion formation.

An additional noteworthy finding of the present study is the improvement in menstrual patterns following hysteroscopic surgery, particularly among patients who received HA gel. Restoration of normal menstrual flow may reflect improved endometrial healing and a lower degree of intrauterine scarring.[5] Although the difference between groups did not reach statistical significance, the observed trend supports the potential clinical benefit of adhesion prevention strategies.

The present study has several limitations. First, the retrospective and non-randomized design may introduce selection bias and limit the ability to control for confounding factors. Although all procedures were performed by the same experienced surgeon, treatment allocation was based on routine clinical practice rather than randomization. Second, the broad follow-up window for second-look hysteroscopy may have influenced adhesion detection, as timing varied according to patient availability and clinical logistics. Third, the heterogeneous surgical indications may have influenced baseline adhesion risk, since adhesiolysis and myomectomy generally carry a higher risk of postoperative adhesion formation than polypectomy. Although postoperative adhesions were evaluated using the American Fertility Society (AFS) classification system[9] during second-look hysteroscopy, detailed preoperative adhesion grading in patients who underwent adhesiolysis was not consistently available because of the retrospective design. In addition, although previous dilation and curettage history was evaluated, postoperative estrogen therapy, detailed surgical risk stratification, detailed myoma location in patients who underwent hysteroscopic myomectomy, and the potential effects of different

hysteroscopic energy modalities were not consistently available or could not be evaluated separately. Finally, the sample size was relatively small, and fertility outcomes, including pregnancy and live birth rates, were not evaluated.

Despite these limitations, the strengths of the study include the use of standardized hysteroscopic evaluation with second-look hysteroscopy and the assessment of adhesion severity using the American Fertility Society classification system.[9] These methodological aspects enhance the reliability of the findings.

In conclusion, the intrauterine application of hyaluronic acid gel following operative hysteroscopy was associated with a lower incidence of postoperative intrauterine adhesions and descriptively milder adhesion characteristics. However, given the retrospective and non-randomized design and the relatively small sample size, these findings should be interpreted with caution. Larger prospective studies are required to confirm these findings. The calculated number needed to treat of three patients suggests potential clinical relevance, although this estimate should be validated in larger populations.

Data Sharing Statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Ethics Approval

The study was approved by the Ethics Committee of University of Health Sciences Antalya Training and Research Hospital (Approval No: 20/26).

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Disclosure

The authors declare no conflicts of interest in this work.

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