Original Article

Investigating The Role of Hyaluronic Acid Gel as an Antiadhesion Agent in Obstetric and Gynecological Surgeries

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Abstract

Objective: To determine the effectiveness of Hyaluronic acid in reducing adhesion formation during the healing process following major gynecological or obstetrical surgeries.

Methodology: This single-arm observational study was conducted at three hospitals from August 2018 to August 2022. Patients undergoing cesarean section, hysterectomy, myomectomy, and cystectomy, who provided consent for the use of hyaluronic acid gel, were included. Hyaluronic acid gel was injected into the abdominal cavity, covering the raw surfaces after the completion of surgery. Follow-up was conducted in the outpatient department or through phone calls to assess pain, quality of wound healing, and late signs of adhesion formation. Data was entered and analyzed using SPSS version 26.

Results: The ages of the patients ranged from 21 to 62 years. Patients had either no previous cesarean sections 64 (60%), one previous cesarean section 32(30%), two previous cesarean sections 10(9%), or more than two previous cesarean sections 1(1%). The most common indication for surgery was lower segment cesarean section 105(85.4%), followed by laparotomy 9(7.3%), myomectomies 8(6.5%), and one patient had a hysterectomy. Seven patients reported mild to moderate postoperative pain (rated on the NPRS scale) on the 5th to 7th postoperative days. Patients were asked about any symptoms of adhesion-related abdominal pain. Seven patients underwent additional cesarean sections 1-2 years after their initial surgery. We did not find any adhesions during repeat surgery.

Conclusions: The application of hyaluronic acid gel as an anti-adhesion agent was observed to be effective in reducing postoperative symptoms related to adhesion formation, without any reported adverse impacts on wound healing.

Keywords: Gynecological & Obstetrical surgeries, Adhesion formation, Hyaluronic acid, effectiveness

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Introduction

After any surgery, adhesions may form at the surgical site and in the surrounding areas. These are fibrotic bands that form as a result of inflammation, infection, or trauma endured during surgery. Millions of patients are affected by surgical adhesions each year,[1,2] and they suffer from mild to moderate complications.

The severity of adhesions depends on the duration, site, and nature of the surgery. Inflammatory adhesions are found in 10% of patients during surgery even if they have no history of previous surgeries at a particular site, while 90% of patients with previous surgeries show adhesions,[3,4] at the site of the previous surgery. Obstetrical and gynecological surgeries may result in significant adhesion formation, which may lead to small bowel and ureteric obstruction.[5,6] Additionally, in subsequent surgeries, these patients are at high risk for iatrogenic injuries like vascular and bladder injuries.[7]

The important initial steps in adhesion prevention are the use of good surgical technique, meticulous hemostasis, and minimizing tissue handling, resulting in fewer micro-abrasions and prevention of infection.[8] Considering the significant morbidity and high treatment costs associated with adhesion formation, ANGEL (Anti-adhesion in Gynecology Expert Panel) recommends that in medium and high-risk cases, anti-adhesion agents are clinically beneficial and economically justified in reducing further complications and improving the quality of life of patients.[9] Hence, all surgeons should keep in mind that adhesions will form after surgery and adopt anti-adhesion strategies to mitigate this complication.

Preventing adhesion formation after major gynecological or obstetrical surgeries is of paramount importance, and various treatments have been

proposed to address this concern. Among these treatments, hydro-flotation with crystalloid solution, high molecular weight dextrans, or Adapt (Adhesion reduction solution) have been explored. The use of Adapt demonstrated marginal superiority; however, in some instances, it led to vulva and vagina edema.[10] Another approach involves employing adhesion prevention barriers, including Expanded Polytetrafluoroethylene (Gore-Tex Surgical Membranes), which Franklin et al[11] found to significantly reduce post-myomectomy adhesion formation. Regenerated Cellulose (Interceed) has also exhibited effectiveness and safety in open gynecological microsurgical procedures.[12] Additionally, Sodium Hyaluronate has shown promising results, with Bristow and Montz reporting an 84% reduction in mean adhesion scores compared to internal scores.[13] Hyaluronic acid is a glycosaminoglycan found in connective and epithelial tissues,[14] and has been shown to be effective in reducing post-surgery adhesion and improving healing.[15] These diverse treatments offer potential solutions for preventing adhesion formation, emphasizing the need for further research and exploration of their benefits and limitations. However, since no ideal adhesion prevention agent is commonly recommended, therefore the current study has been designed

Methodology

This single-arm observational study was conducted at Al-Ihsan Hospital, Rawalpindi, Rawal General Hospital, Islamabad, and Bangash Hospital, Rawalpindi from August 2018 to August 2022.

Patients aged 18 to 50 years undergoing cesarean section, hysterectomy, myomectomy, and cystectomy, who provided consent to use hyaluronic acid gel, were included. Pregnant or lactating women, patients with a history of previous pelvic or abdominal surgeries, patients with severe systemic diseases that may affect wound healing, and those who did not provide consent to use hyaluronic acid gel were excluded.

After obtaining verbal informed consent, the surgical procedure was planned according to the protocol and routine surgical steps. Hyaluronic acid gel was injected into the abdominal cavity, specifically covering the raw surfaces (Figure 1). The abdomen was closed in layers with Vicryl #1 sutures. The skin was closed with Prolene 2/0 sutures, and patients were transferred to the post-operation ward where routine post-operative management was carried out according to the surgical procedure.

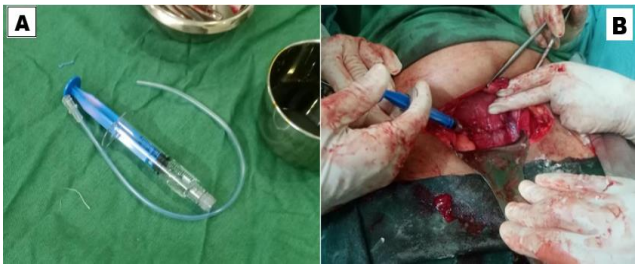

Figure 1. A= The Hibbary applicator prepared for use, B= HIbbary being applied to the surgical site.

Follow-up in the outpatient department (OPD) or through phone calls was conducted at 5-7 days' post-operative and at 1, 3, and 6-month intervals. Patients were asked to indicate any abdominal pain using a Numerical Pain Rating Scale (NPRS).16 Wounds were inspected on the 7th post-operative day, and abdominal examination was performed; the findings were recorded in the performa. Some patients underwent repeat surgery after 1-2 years. During this surgery, the surgical site was inspected for signs of adhesions. Qualitative data were expressed as percentages.

Results

The patients' ages range was between 21 and 62 years, and most of them belonged to the reproductive age category (20-40 years), with an average age of 29.12 years and a standard deviation of 4.23 years. Out of the total patients, 64 (60%) underwent their first surgery, 32 (30%) had previously undergone one cesarean section, making it their second surgery. Additionally, 10 patients (9%) had a history of two previous cesarean sections. Most of the surgeries took less than 40 minutes, however, approximately a quarter of them went on for longer period as shown in table I.

Table I: Distribution of Patient Demographics and Surgical Characteristics

Variables		Statistics	
Age (mean ±SD)		29.12±4.23 years	
Operative history	Previous 1 C-section	32	(30.2%)
	Previous 2 C-sections	10	(9.4%)
	First time operated	64	(60.4%)
Duration of surgery	≤ 40 minutes	26	(24.5%)
	> 40 minutes	80	(75.5%)

The most common indication of surgery in our study group was lower segment cesarean section i.e., 105 patients (85.4%), followed by laparotomy in 9 patients (7.3%). 8 patients (6.5%) had myomectomy, and a single patient had a hysterectomy. Figure.2

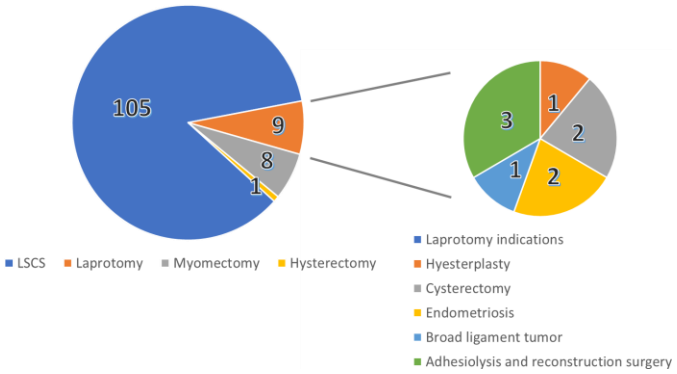

Figure 2. Indication for surgery for selected population of patients.

A small fraction of patients indicated mild to moderate pain in the days following surgery (Table II). 7 patients had repeat caesarean sections, during which the initial surgical site was inspected for presence of adhesions. We did not find any adhesions on repeat surgery in any of these patients and the previous incision site was clean, therefore hyaluronic acid gel was instilled again. 3 patients stated that they would like to repeat the use of hyaluronic acid.

Table II. Post-operative pain and wound complications (n=106)

Post-operative Pain and wound complications			
Early Pain (5th to 7th day of surgery)		**Late Pain**	**Wound Complications**
Yes= 5(4.7%)	No= 101(95.3%)	N/A	N/A
Pain Rating (NPRS)			
1-3	4-6		
2(1.9%)	3(2.8%)		

Discussion

Studies conducted in the USA show that the economic impact of this morbidity exceeds $3 billion annually.[17] This fact suggests that adhesion prevention should be a priority for every surgeon. Adhesion formation begins immediately after surgery or following tissue damage, and becomes increasingly vascular and organized from the 5th to 7th day.[9] Hence, intervention for the prevention of adhesion formation should occur within the first 7 days. If adhesions are allowed to form, they can result in morbidities such as chronic pelvic pain, dyspareunia, subfertility, and small bowel problems.[18] Long-term effects may involve complications in subsequent surgeries, such as bowel perforation and vascular injuries. Adhesions are also a major cause of iatrogenic urinary tract injuries.[19] These complications can even lead to lawsuits against surgeons if patients are not adequately counseled.[20]

Adhesion formation is a frequent complication arising from different surgical procedures. According to a recent literature review, around 90% of patient's experience lesions after abdominal surgery, while the percentage ranges from 55% to 100% for patients undergoing pelvic surgery.[21] However, in our study, we observed that patients who had undergone repeat operations showed minimal adhesions, demonstrating the effectiveness of hyaluronic acid gel as an anti-adhesion agent.

As the presence of pain at the surgical site is a typical indication of adhesion formation.[22] In our study, only 5 patients reported mild and moderate pain, suggesting that very few adhesions were formed after the use of hyaluronic acid gel, an outcome that is consistent with previous literature using similar methodologies.[22] Zheng F et al[23] reported that the hyaluronic acid gel led to a notable decrease in the occurrence of moderate and severe intrauterine adhesions. Huang CY et al[24] observed that the application of hyaluronic acid gels in women undergoing a hysteroscopic myomectomy resulted in substantial therapeutic advantages. However, one study conducted by Carta et al[25] reported that approximately 25% of patients developed abdominal adhesions after pelvic surgeries even when hyaluronic acid preparation was used. This could be due to either difference in the product formulation used or, more likely, the fact that they were able to observe the original surgical sites in repeat surgeries for all study participants. In our study instillation of hyaluronic acid gel at surgical site did not cause any delay in wound healing or wound infection which is consistent with the study carried out by González-Quintero et al.[10]

Despite the promising outcome of this study, it must be noted that it had limitations; primarily, the study had a relatively small sample size with subjects selected using convenience sampling. Out of the sample, only 7 patients were directly observed for adhesion formation during repeat surgery – this necessitates future studies with larger sample sizes to confirm the

effectiveness of hyaluronic acid gel. Our study is one of the few studies carried out in Pakistan evaluating the role of hyaluronic acid in the prevention of adhesion formation in obstetric and gynecological patients. Given the rising rate of childbirth using caesarean sections, adhesion prevention will result in decreased morbidity by decreasing postoperative pain and mitigating blood loss, and decreasing the duration of surgery for subsequent operations.

Conclusion

As per the study conclusion, the use of hyaluronic acid gel as an antiadhesion agent in obstetric and gynecological surgeries has shown promising results. The application of hyaluronic acid gel as an anti-adhesion agent has proven effectiveness in reducing postoperative symptoms related to adhesion formation, without any reported adverse impacts on wound healing.

This observation implies that hyaluronic acid gel holds potential as a valuable intervention for the prevention of adhesions and related complications subsequent to surgical interventions within this specific patient population. Nonetheless, further investigations and larger-scale clinical trials are requisite to establish its long term safety and efficacy. The preliminary evidence, however, is encouraging and justifies deliberation for its integration into surgical protocols.

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