

Adhesion Prevention in Operative Gynecology: How Realistic are Our Expectations?

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ABSTRACT

The purpose of this review is to critically analyze the effectiveness of adhesive barriers in adhesion prevention in terms of incidence and extent of postoperative adhesions and to help one choose the best and the most cost-effective, among those available in market today.

Materials and methods: We analyzed 18 published articles to critically look at the effectiveness of adhesive barriers in operative gynecology. A literature research was performed using internet.

Discussion: Oxidized regenerated cellulose (Interceed) was found to be an effective adhesion barrier with treated side-walls showing significantly less area involved with adhesions ($p < 0.05$). With 4% icodextrin solution (ADEPT), no significant reduction of *de novo* adhesions was found in patients undergoing laparoscopic surgery for removal of myomas or endometriotic cysts ($p = 0.909$). With use of hyaluronic acid (Intergel), a significant difference was found in the mean adhesion severity scores ($p < 0.05$). The Sepracoat group had a significantly lower incidence of *de novo* adhesions in terms of proportion of sites involved, percentage of adhesion free patients as well as adhesion extent and severity. Oxiplex was found to prevent an increase in adhesion score when compared to placebo.

Conclusion: The decision whether to use an adhesion barrier or not, need to be a well thought out one after weighing the balance between the efficacy of the material against the cost implications involved. The quest for the best of the adhesive barriers still continues.

Keywords: Adhesion barriers, Oxidized regenerated cellulose, Interceed, Icodextrin, ADEPT, Hyaluronic acid, Intergel/Hyalobarrier, Sepracoat, Viscoelastic gel, Oxiplex.

How to cite this article: Puliyahtinkal S, Vahab KPA, Umadevi N, Geetha KC, Mumtaz P, Govind A, Mahesh P, Hashim A. Adhesion Prevention in Operative Gynecology: How Realistic are Our Expectations? World J Lap Surg 2014;7(2):88-91.

Source of support: Nil

Conflict of interest: None

INTRODUCTION

Abnormal fibrous connections joining tissue surfaces are termed as adhesions.¹ Tissue damage caused by surgical

trauma is the primary contributing factor. Infection, ischemic damage and exposure to foreign materials can significantly contribute to this.²

Adhesions can be primary or *de novo* adhesions vs secondary or reformed adhesions. The former are freshly formed ones, on locations devoid of adhesions before and the latter are those adhesions that undergo adhesiolysis and recur at the same location.³ Adhesions may also be classified based on the location, as intra-abdominal or intrauterine. Virtually, any surgical procedure performed transperitoneally can lead to adhesions ranging from minimal scarring of serosal surface to firm agglutination of structures.

The formation of adhesions following an open approach in gynecology is more than a common entity. It has been reported that intra-abdominal adhesions occur in 60 to 90% of women who have undergone major gynecological procedures.^{4,5} Further, a recent study by⁶ conducted in Scotland reported that women undergoing an initial open surgery for gynecological conditions had a 5% likelihood of being rehospitalized because of adhesions over the next 10 years.

Though many adhesions resulting from gynecological surgery have little or no detrimental effect on patients, a considerable proportion of them can result in serious short and long-term complications, including infertility,⁷ pelvic pain⁸ and intestinal obstruction, resulting in a reduced quality of life⁹ often requiring readmission to hospital and additional more complicated surgical procedures and indeed increased surgical costs.¹⁰

Propensity to form adhesions are thought to be patient specific. The nutritional status, disease entities like diabetes and the presence of concurrent infectious processes also contribute. They impair leukocyte and fibroblast function in these patients, potentially increasing adhesion formation. It has also been shown that postsurgical adhesions increase with the age of the patient, the number of previous surgeries and the type and complexity of surgical procedures.¹¹ When lysed, adhesions have a tremendous propensity to reform.

Since, its first introduction in gynecological surgery in 1986, laparoscopy with its minimal access to the peritoneal cavity has been claimed to be associated with reduced rates of adhesion formation¹² and related complications, compared with open approach. Conclusive evidence is available from current studies, that a comparable or

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reduced adhesion formation rate is seen in women who undergo laparoscopic procedures. An epidemiologic study by Lower et al (2004)¹³ reported on data from 24,046 patients undergoing laparoscopy or laparotomy for gynecological conditions and partially contrasted with the results from the previous studies. Data from this study have supported the concept that laparoscopy is less adhesiogenic than laparotomy but this stands only with respect to laparoscopic tubal sterilization procedures, which represented a considerable proportion of laparoscopies (59%), and the vast majority of those categorized as having 'low-risk' of directly adhesion-related readmission within the first year of surgery. However, for 'high-risk' (laparoscopic adhesiolysis and cyst drainage) and 'medium-risk' (other interventions not otherwise categorized) laparoscopies, which constituted 40% of gynecological procedures, the risk of adhesion-related readmission has been shown to be considerable (1 in 80 and 1 in 70 respectively) and substantially higher than for the conventional approach (1 in 170). In the background of such controversies related to the occurrence of more or comparable or lesser incidence of adhesions in laparoscopy, this article specifically attempts to look at the realistic expectations from adhesion barriers in the field of gynecological laparoscopy.

Adhesion Barriers

It was quite a logical thought process of the initial days that mechanical separation of peritoneal surfaces of the pelvic organs during the early days of the healing postoperatively, is a way to prevent postoperative adhesions. Intra-abdominal instillates and solid barriers were the options available. The ideal barrier should be noninflammatory, nonimmunogenic, persist during the remesothelialization, remain in place without suture, remain active in the presence of blood and be completely biodegradable.

MATERIALS AND METHODS

A literature search was performed using Google, Yahoo, Springerlink and Highwire Press.

The following search terms were used: adhesion barriers, oxidized regenerated cellulose, Interceed, icodextrin, ADEPT, hyaluronic acid (HA), intergel/hyalobarrier, sepracoat, viscoelastic gel, oxiplex.

Though there are numerous adhesion barrier agents and devices available in market today (Table 1), we decided to critically evaluate the evidence available about the most commonly used ones in the field of operative gynecology.

DISCUSSION

Oxidized regenerated Cellulose (Interceed)

The most relevant data related to this comes from a study conducted by Sekiba K (1992).¹⁴ They evaluated Interceed (TC7) in a randomized, multicenter clinical study. Sixty-three infertility patients had bilateral pelvic sidewall adhesions removed at laparotomy. One pelvic sidewall was covered by Interceed and the other was left uncovered. The deperitonealized areas (N = 205) of all sidewalls were divided into three groups: less than 100 mm², N = 72; 100-1000 mm², N = 95; and more than 1000 mm², N = 38. The effectiveness of interceed was evaluated at laparoscopy 10 to 98 days after laparotomy. Significantly more adhesions were observed at laparoscopy on the control pelvic sidewalls (48 of 63, 76%) than on the treated sides (26 of 63, 41%) (p < 0.0001). The interceed treated sidewalls also had significantly less area involved with adhesions at laparoscopy (p < 0.05, p < 0.001 and p < 0.001 in the three groups, respectively) (Table 2). Twenty-eight women with severe endometriosis also had significantly more adhesions on the control side (23 of 28, 82%) than on the treated side (14 of 28, 50%) (p < 0.05).

Icodextrin (ADEPT)

The best of the available evidence regarding this adhesion barrier comes from a study done in 2011 by Trew et al.¹⁵ This randomized, double-blind study comprising of 498 subjects was designed to assess the efficacy and safety of 4% icodextrin solution (ADEPT) in the reduction of *de novo* adhesion compared to lactated Ringer's solution (LRS)

Table 1: List of commercially available adhesion barriers

Materials	Trade name	Mechanism
Oxidized regenerated cellulose	Interceed	Changes into a gelatinous mass covering the injured peritoneum
Icodextrin	ADEPT	Gets metabolized to glucose by α -amylase in the circulation and gets slowly absorbed from the peritoneal cavity
Hyaluronic acid	Intergel/hyalobarrier	Transformation into a highly viscous solution coating serosal surfaces (application before injury)
Solution of HA	Sepracoat	Transforms into a viscous liquid or gel coating serosal surfaces and minimizing desiccation (application before injury)
Viscoelastic gel	Oxiplex/AP	Transformation into a viscous gel coating surgical sites
Hydrogel	Spray Gel	Solidification after spraying into a gel strongly adherent to the sites of application
Fibrin sealants	Beriplast	Rolled fibrin sheets to be placed on surgical wounds

in patients undergoing laparoscopic surgery for removal of myomas or endometriotic cysts. The mean number of *de novo* adhesions was 2.58 (2.11) for ADEPT and 2.58 (2.38) for LRS. This difference was not found to be significant (Table 3).

Hyaluronic Acid (Intergel)

The study which investigated the efficacy of this autocross-linked barrier was done in 2006 by Mais et al.¹⁶ Fifty-two patients aged 22 to 42 years, undergoing surgery at four centers, were randomly allocated to receive either the gel or no adhesion prevention. The incidence and severity of postoperative adhesions were assessed laparoscopically after 12 to 14 weeks in a blinded, scored fashion.

A higher proportion of patients receiving the gel were free from adhesions compared with control patients. In subjects undergoing myomectomy without any concomitant surgery, though there was no significant difference in the proportion of adhesion free patients, a significant difference was found in the mean severity scores (Table 4). In subjects without uterine adhesions prior to myomectomy, a significant difference was found in the severity of uterine adhesions.

Solution of HA (Sepracoat)

It was the study by Diamond¹⁷ in 1998 which looked at patients who underwent gynecologic procedures by means of a prospective, randomized, blinded, placebo-controlled multicenter study. Surgeons assessed their adhesions during second-look laparoscopy approximately 40 days later. The Sepracoat group had a significantly lower incidence of *de novo* adhesions than the placebo group as assessed by the proportion of sites involved and the percentage of patients without *de novo* adhesions as well as significantly reduced adhesion extent and severity (Table 5).

Oxiplex

The study of 2005 by Young et al¹⁸ was aimed at patients undergoing laparoscopic surgery with pelvic adhesions,

tubal occlusion, endometriosis, and/or dermoids. They were randomized to receive Oxiplex or no further treatment after surgery.

The mean baseline (American Fertility Society adhesion score) AFS score for each group was 8.0 (Table 6). At second look, treated adnexa had the same score (8.1), whereas in control adnexa the score increased (8.0-11.6).

CONCLUSION

The decision whether to use an adhesion barrier or not, need to be well thought out one. We need to weigh the balance between the efficacy of the material used against the cost implications involved. The reasonable conclusions that we were able to reach in the light of the available evidence are mentioned below.

Oxidized regenerated cellulose (Interceed) effectively helps to reduce the incidence and extent of postoperative adhesions, even in high risk groups (including patients with severe endometriosis). Though icodextrin (ADEPT) was found to be safe in laparoscopic surgery, no beneficial clinical effects could be established with its use. Auto-cross linked hyaluron gel appears to have a favorable safety profile as well as an efficacious antiadhesive action following laparoscopic gynecological procedures with the available data. Sepracoat appears to be one of the most promising adhesive barriers, in not only being safe but also significantly reducing the incidence, extent and severity of *de novo* adhesions at

Table 2: Sekiba K (1992)

Parameter assessed	Interceed	Control	p-value
Percentage of patients with adhesions	41%	76%	<0.0001
Area involved in adhesions	Significantly less	NA	<0.001
Percentage of patients with adhesions in high risk group	50%	82%	<0.05

Table 3: Trew et al (2011)

Parameter assessed	Icodextrin	Ringer's lactate	p-value
Mean number of <i>de novo</i> adhesions	2.58 (2.11)	2.58 (2.38)	0.909

Table 4: Mais et al (2006)

Parameter assessed	Hyaluron gel	No barrier	p-value
Percentage of patients free of adhesions	62%	41%	NS
Mean severity scores for adhesions (for myomectomy alone)	Less severe		<0.05
Mean severity scores for adhesions (in adhesion free patients prior to myomectomy)	Less severe		<0.05

NS: Nonsignificant

Table 5: Diamond (1998)

Parameter assessed	Sepracoat	Placebo	p-value
Percentage of adhesion free patients	13%	4.6%	<0.05
Proportion of sites involved	0.23	0.30	<0.05
Adhesion severity	Significantly less		<0.05

Table 6: Young et al (2005)

Parameter assessed	Oxiplex	Placebo	p-value
Increase in AFS score	8-8.1	8-11.6	
Percentage of patients with increase in AFS score	34%	67%	

multiple sites indirectly traumatized by gynecologic surgery. Oxiplex too appears to be an adhesion barrier for the future with its safety and efficacy being demonstrated, though larger study results are still being awaited.

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