Adhesion Prevention in Minimal Invasive Gynecological Surgery

19

Per Lundorff

Contents

19.1 Epidemiology

The SCAR study (Surgical and Clinical Adhesion Research Study) from 1999 was the first study to verify the extent of problems after open surgery in terms of adhesions. This Scottish database showed that about one-third of almost 30,000 patients who underwent open surgery were readmitted a mean of 2.1 times for complications related to adhesions over a 10-year period. Of all readmissions, 22 % occurred within the first year, but the readmissions continued over the next 10 years of the study period. So adhesions are a consequence of an iatrogenic disease (Ellis et al. 1999).

The SCAR-2 study revealed the overall extent of adhesion-related readmissions following open and laparoscopic gynecological procedures. In this study, it was shown that certain surgical sites are associated with increased risk of adhesions. Also, that adhesion formation results in a large number of readmissions following both open surgery as well as laparoscopy and that risk for adhesion formation and related complications can be seen many years after the surgical procedure (Hawthorn et al. 2003).

19.2 Clinical Aspects

Adhesions develop as a response to a trauma to the peritoneum. This trauma can be induced either after inflammation or after surgery.

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Concomitant factors to increase risk of developing adhesions are inflammation, abrasion, desiccation, ischemia, heat, light, electrocautery, and suturing. Furthermore, bleeding and leaking of plasma proteins can lead to fibrin deposits and concomitant adhesion formation.

Adhesions can have serious consequences as bowel obstruction (Menzies 1993), chronic pelvic pain (Duffy and diZerega 1996), and fertility-related adhesions (Hershlag et al. 1991). It has been shown that the vast majority of small bowel obstructions are related to adhesions, 40 % of patients with chronic pelvic pain are related to adhesions, and 15–20 % of women with secondary infertility are adhesion related (Menzies et al. 2001). Adhesions make reoperation more difficult and may increase complication rate (Coleman et al. 2000). Operating time may be prolonged and risk of bowel or bladder injury may increase. Each additional laparotomy induces de novo adhesion and thereby increases the risk of enterostomy at future surgery.

Some operative procedures are related with greater risk of adhesion developing and consequently reoperation.

In ovarian surgery, 75 of 100 procedures will be readmitted during the first year (Lower et al. 2000), and in myomectomy, 41 of 100 procedures will be readmitted during the first year (Dubuisson et al. 1998).

19.3 Economy

Readmissions due to adhesion-related complications have a major impact on healthcare, and in UK, bed stay for these women represents 2 % of the total bed occupancy per year (Mentiez et al. 2001). The costs of all UK hospital readmissions involved treatment with adhesiolysis are estimated at about 24 million pounds 1 year after surgery and about 95 million pounds 10 years after surgery (Wilson et al. 2002).

To reduce these costs, surgeons should focus upon the surgical procedures with optimizing the techniques and further apply adhesion-preventing adjuvants available for the management and prevention of adhesions.

19.4 Adhesion Prevention

19.4.1 Surgical Techniques

A number of adhesion prevention strategies and techniques were reviewed in 1997 by Risberg, and among these, two strategies were identified (1) good surgical technique and (2) use of antiadhesive adjuvants.

As to good surgical techniques, several factors have been highlighted to illustrate the relationship between adhesion formation and surgery.

First of all, laparoscopy rather than laparotomy is associated with less postoperative adhesions (Mais et al. 1996). In a randomized trial by Lundorff et al. (1991), surgery for ectopic pregnancy by laparotomy showed a significant larger proportions of postoperative adhesions compared with laparoscopy revealed at second-look surgery few months later.

Careful surgical techniques can minimize factors that increase risk for adhesion formation. Well-known factors are ischemia, infection, or serosal trauma associated with increased adhesion formation due to decreased fibrinolytic activity during the postoperative 3–5 days. These factors include traction of the peritoneum, drying of the serosal surface, excessive use of suturing material, or retention of blood clots. The result is increased fibroblast activity with formation of adhesions (Ellis 1971).

Molinas et al. have demonstrated that the use of carbon dioxide (CO_2) during laparoscopic surgery can cause peritoneal hypoxia and thus induce respiratory acidosis leading to metabolic acidosis and metabolic hypoxia (Molinas et al. 2004).

High peritoneal temperature and the use of dry gases can be potential cofactors in adhesion formation, and hypothermia can reduce the toxic effects of hypoxia in mice.

Furthermore, the use of humidified gases has been demonstrated to minimize adhesion formation induced by desiccation. So the combination of controlled intraperitoneal cooling with a rigorous prevention of desiccation can be important for adhesion prevention (Binda et al. 2004); (Binda et al. 2006).

Other animal studies have demonstrated that the addition of 3 % oxygen to the CO_2

pneumoperitoneum further decreases adhesion formation (Elkelani et al. 2004).

Further improvement in adhesion prevention during surgery should always be based upon the use of good surgical techniques, using newly developed instruments, based on the basic principles of microsurgery, liberal irrigation of the abdominal cavity and may be installation of large amount of Ringer's lactate or saline at the end of the surgical procedure (Tulandi 1997).

19.4.2 Antiadhesive Adjuvants

A number of antiadhesive adjuvants are increasingly available, and especially in high-risk procedures, precautions should be taken.

Procedures at high risk for developing postoperative adhesions are as follows:

- Ovarian surgery
- Endometriosis surgery
- Tubal surgery
- Myomectomy
- Adhesiolysis

Several agents have been tested to decrease adhesion formation after surgery.

19.4.3 Anti-inflammatory Drugs

NSAIDs interferes the postsurgical inflammatory response by affecting the metabolism of arachidonic acid, prostaglandins, and thromboxane. Animal studies have shown that NSAIDs administered intraperitoneally are effective, yet not proven in clinical studies. In an animal model, the agents must be administered continuously for 2–3 days with a miniosmotic pump to be efficient (Gomel et al. 1996).

However, there is no significant evidence from any published study to recommend their use in humans (Wiseman 1994).

19.4.3.1 Corticosteroids

Immunosuppression and prolonged healing of wound are the backgrounds for using corticosteroids. Older studies show mixed results and are difficult to interpret, as it is often used parallel with antihistamine. Serious side effects minimize the use for the prevention of adhesions (Swolin 1967; Querleu et al. 1989).

As a conclusion, corticosteroids show poor efficacy, delayed wound healing, do not remain in the body during the process of wound healing (4–5 days).

19.4.4 Fibrinolytics

It has been hypothesized that an imbalance between fibrin-forming and fibrin-dissolving activities in the peritoneum is a major pathogenetic factor in adhesion formation in animals (diZerega and Campeau 2001).

Fibrinolytic agents act by reducing the fibrinous mass directly and indirectly by stimulating the plasminogen activator (PA) activity and thereby have been suggested to reduce adhesion formation (Hellebrekers et al. 2000).

Studies to reveal safety and side effects are still awaiting.

19.4.5 Anticoagulants

In animal studies, heparin has been widely used for the purpose of adhesion prevention. Nevertheless, no study has been able to demonstrate reduced adhesion formation when heparin was administered alone or in combination with other agents such as Interceed TC7 barrier (Jansen 1988; Reid et al. 1997).

Furthermore, compared to Ringer's lactate no significant reduction in adhesion formation was found (Fayez and Schneider 1987).

19.4.6 Barriers Adjuvants

19.4.6.1 Preclude and Seprafilm

Preclude Peritoneal membrane (Goretex) 0.1-mm thin membrane consisting of polytetrafluorethylene. The microporous structure inhibits the ingrowth of cells and thus convenient as a barrier method. It is not absorbed and gives no inflammatory response. Not easy to handle, should be

sutures in place, and removed later. Studies show reduction of de novo adhesions as well as reformation of adhesions (Goldberg et al. 1987; The Surgical Membrane Study Group 1991).

19.4.6.2 Seprafilm II

Is a derivate of hyaluronic acid and carboxymethylcellulose. The membrane separates the injured surfaces during the first day of wound healing and is resorbed within 7 days. Promising results have been described (Diamond 1996; Becker et al. 1996).

19.4.6.3 Interceed

Interceed (Gynecare, Johnson & Johnson) is an oxidized regenerated cellulose woven into a special net. When the net has been applied to the peritoneal surface, it adheres without sutures and turns into a gel within few hours, thus serving as a barrier between two surfaces. It has been shown to reduce adhesion formation, both in animal studies and in human studies (Marana et al. 1997; Franklin 1995).

The efficacy of Interceed is reduced in an environment of blood and liquid and is only effective when a good hemostasis has been obtained.

Several clinical studies have demonstrated the positive effect of Interceed [Sekiba 1992; Nordic Adhesion Prevention Study Group 1995; Interceed (TC7) Adhesion Barrier Study Group II 1993; Adhesion (TC7) Barrier Study Group 1989].

19.4.6.4 Spray Gel (Confluent Surgical, Waltham, MA, USA)

Is a solid polymer, acting as an adhesion barrier. It consists of two synthetic liquid precursors that rapidly cross-link to form an absorbable, flexible hydrogel, when it is applied and mixed during laparoscopy. No reports so far have shown evidence that there is decreased adhesion formation using Spray Gel Specialist equipment and technique (Dunn et al. 2001; Mettler et al. 2004).

19.4.6.5 Oxiplex/AP Gel (FzioMed, San Louis Obispo, CA, USA)

Is a viscoelastic gel composed of polyethylene oxide and carboxymethyl cellulose stabilized with calcium chloride. Preclinical studies were encouraging (Berg et al. 2003).

In a randomized multicenter European trial, the results concluded that the viscoelastic gel significantly reduced adnexal adhesions in patients undergoing gynecologic laparoscopic surgery (Lundorff et al. 2005).

Furthermore, another prospective randomized trial evaluated efficacy of Oxiplex/QP gel and could conclude that the gel was easy to use, safe, and reduce adhesion scores (Young et al. 2005).

Recently approved as site-specific agent.

19.4.6.6 Crystalloids (LRS)

Rapidly reabsorbed, ineffective in reducing adhesions.

Crystalloids, including saline solution and Ringers acetate solution, have been widely used to minimize the risk of postoperative adhesion formation. Yet, no significant improvement can be shown in clinical studies (diZerega 1994; Gomel et al. 1996).

As peritoneal healing takes place within 5–7 days after surgery, crystalloids are absorbed long ago. The peritoneal surface absorbs 15–30 ml of crystalloids per hour, so even if you leave 1 l of crystalloids, it will be absorbed within 24 h.

19.4.6.7 Hyscon

Hyscon is a 32 % solution of Dextran 70. It creates an osmotic gradient in the peritoneal cavity, producing transient ascites. Adverse results, and serious side effects such as anaphylaxis, coagulopathy and vulvar edema have disqualified the agent (Adhesion Study Group 1983).

19.4.6.8 Icodextrin (Adept, Baxter, USA)

Is a glucose polymer of high molecular weight, rapidly metabolized to glucose but slowly absorbed by the peritoneal cavity. Because the 4 % Icodextrin solution has a longer resorption time from the peritoneal cavity (>4 days) compared to crystalloids, it will give the internal organs a longer hydroflotation time and thereby theoretical a better adhesion protection after surgery.

Animal studies have shown a decreased reformation of adhesions and decreased de novo adhesion formation postoperatively after irrigation with Icodextrin 4 % (Verco et al. 2000).

A randomized pilot study and later a clinical trial have confirmed these observations (diZerega et al. 2002; Brown et al. 2007).

Geneva study (Gynaecological ENdoscopic EValuation of Adept), a double-blind randomized study with 25 European centers enrolling patients to assess the safety and efficacy of Adept compared with lactated ringers solution when used as an intraoperative irrigation solution. Safety of Adept was confirmed, but overall there was no evidence of clinical effect (Trew et al. 2011).

19.4.7 Hyaloronic Acid

Hyaluronan (HA) is a naturally occurring component of the extracellular matrix and peritoneal fluid that has received much attention because of its possible application as an adhesion–prevention adjuvant in a variety of surgical procedures. Indeed, several authors in different experimental and clinical settings have proposed that deposition of HA around surgically treated tissues reduces postoperative adhesion formation (Chen and Abatangelo 1999). Moreover, native HA has a high degree of biocompatibility and a favorable safety profile (Laurent and Fraser 1992).

19.4.8 Hyalobarrier

A highly viscous gel of HA derivatives obtained through an autocross-linking process that does not introduce foreign bridge molecules, namely Hyalobarrier®, has recently been developed. The autocross-linked polymer is an inter and intramolecular ester of HA in which a proportion of the carboxyl groups are esterified with hydroxyl groups belonging to the same and/or different molecules of the polysaccharide, thus forming a mixture of lactones and intermolecular ester bonds. The level of cross-linking can be varied by modulating the reaction conditions. The absence of foreign bridge molecules ensures the release of native HA only during degradation, while the autocross-linking process improves the viscoelastic properties of the gel compared with unmodified HA solutions of the same molecular weight (Renier et al. 2005).

Preclinical trials in animal models have shown that Hyalobarrier® gel reduces the incidence and severity of postoperative adhesions (Belluco et al. 2001; Pucciarelli et al. 2003; Mais et al. 2006).

Moreover, preliminary clinical studies in hysteroscopic surgery as well as laparotomic and laparoscopic myomectomy have suggested that Hyalobarrier® gel may reduce the incidence and severity of postoperative adhesions in pelvic surgery (Pellicano et al. 2003; Guida et al. 2004) with improvement in the pregnancy rate in infertile patients who were submitted to laparoscopic myomectomy (Pellicano et al. 2005).

For a clinical point of view, recommendations for the use of antiadhesion agents can be summarized as:

Site-specific agent (Intercoat, Interceed, Hyalobarrier), to be used preferably in connection with:

- Ovarian surgery
- Tubal surgery
- Minor endometriotic lesions
- Myomectomy

Nonsite-specific agent (Adept), to be used preferably in connection with:

- Major endometriosis surgery
- Adhesiolysis
- Myomectomy

References

Adhesion (TC7) Barrier Study Group (1989) Prevention of postsurgical adhesions by Interceed (TC79, an absorbable adhesion barrier: a prospective, randomised multicenter clinical study. Fertil Steril 51:933–938

Adhesion Study Group (1983) Reduction of post operative pelvic adhesions with intraperitoneal 32 % dextran 70: a prospective randomized clinical study. Fertil Steril 40:612–619

Becker JM, Dayson MT, Fazio VW, Beck DE, Stryker SJ, Wexner SD, Wolff BG, Roberts PL, Smith

LE, Sweeney SA, Moore M (1996) Prevention of postoperative abdominal adhesions by sodium hyaluronate-based bioabsorbable membrane: a prospective randomized, double-blind multicenter study. J Am Coll Surg 183:297–306

Belluco C, Meggiolaro F, Pressato D, Pavesio A, Bigon E, Dona M, Forlin M, Nitti D, Lise M (2001) Prevention of postsurgical adhesions with an autocrosslinked hyaluronan derivative gel. J Surg Res 100:217–221

Berg RA, Rodgers KE, Cortese S et al (2003) Postsurgical adhesion reformation is inhibited by Oxiplex adhesion barrier gel. In: Marana R, Busacca M, Zupi E (eds) International proceedings. World meeting on Minimal invasive surgery in gynecology, Rome, pp 17–21

Binda MM, Molinas CR, Mailova K et al (2004) Effect of temperature upon adhesion formation in a laparoscopic mouse model. Hum Reprod 19:2626–2632

Binda MM, Molinas CR, Hansen P et al (2006) Effect of desiccation and temperature during laparoscopy on adhesion prevention in mice. Fertil Steril 86:166–175

Brown CB, Luciano AA, Martin D, Peers E, Scrimgeour A, diZerega GS (2007) Adept (icodextrin 4% solution) reduces adhesions after laparoscopic surgery for adhesiolysis: a double-blind, randomized, controlled study. Fertil Steril 5:1413–1426, Epub 26 Mar 2007

Chen WY, Abatangelo G (1999) Functions of hyaluronan in wound repair. Wound Repair Regen 7(2):79–89

Coleman MG, McLain AD, Moran BJ (2000) Impact of previous surgery on time taken for incision and division of adhesions during laparotomy. Dis Colon Rectum 43:1297–1299

Diamond MP, Seprafilm Adhesion Study Group (1996) Reduction of adhesions after uterine myomectomy by Seprafilm membrane (Hal-F), a blinded, prospective, randomized, multicenter clinical study. Fertil Steril 66(6):904–910

diZerega GS (1994) Contemporary adhesion prevention. Fertil Steril 64:219–235

diZerega GS, Campeau JD (2001) Peritoneal repair and postsurgical adhesion formation. Hum Reprod Update 7:547–555

diZerega GS, Verco SJ, Young P et al (2002) A randomized, controlled pilot study of the safety and efficacy of 4% icodextrin solution in the reduction of adhesions following laparoscopic gynaecological surgery. Hum Reprod 17:1031–1038

Dubuisson JB, Fauconnier A, Chapron C, Kreiker G, Norgaard C (1998) Second look after laparoscopic myomectomy. Hum Reprod 13:2102–2106

Duffy DM, diZerega GS (1996) Adhesion controversies: pelvic pain as a cause of adhesions, crystalloids in preventing them. J Reprod Med 41:19–26

Dunn R, Lyman MD, Edelman PG et al (2001) Evaluation of SprayGel adhesion barrier in the rat cecum abration and rabbit uterine horn adhesion models. Fertil Steril 75:411–416

Elkelani OA, Binda MM, Molinas CR et al (2004) Effect of adding more that 3% of oxygen to carbon dioxide pneumoperitoneum upon adhesion formation in a laparoscopic mouse model. Fertil Steril 82:1616–1622

Ellis H (1971) The cause and prevention of postoperative intraperitoneal adhesions. Surg Gynecol Obstet 133: 497–511

Ellis H, Moran BJ, Thompson JN, Parker MC, Wilson MS, Menzies D et al (1999) Adhesion-related hospital readmissions after abdominal and pelvic surgery: a retrospective cohort study. Lancet 353:1476–1480

Fayez JA, Schneider PJ (1987) Prevention of pelvic adhesion formation by different modalities of treatment. Am J Obstet Gynecol 157:1184–1188

Franklin RR, Ovarian Adhesion Study Group (1995) Reduction of ovarian adhesions by the use of Interceed. Obstet Gynecol 86:335–340

Goldberg JM, Toledo AA, Mitchell PE (1987) An evaluation of the Goretex surgical membrane for the postoperative peritoneal adhesions. Obstet Gynecol 70:846–848

Gomel V, Urman B, Gurgan T (1996) Pathology of adhesion formation and strategies for prevention. J Reprod Med 41:35–41

Guida M, Acunzo G, Di Spiezio Sardo A, Bifulco G, Piccoli R, Pellicano M, Cerrota G, Cirillo D, Nappi C (2004) Effectiveness of auto-crosslinked hyaluronic acid gel in the prevention of intrauterine adhesions after hysteroscopic surgery: a prospective, randomized, controlled study. Hum Reprod 19:1461

Hawthorn RJS, Lower A, Clark D, Knight AD, Crowe AM (2003) Adhesion-related readmissions following gynaecological laparoscopy in Scotland, an epidemiological study of 24,046 patients. Rev Gynaecol Pract 3(1) Supplement:1

Hellebrekers BW, Trimbos-Kember TC, Trimbos JB et al (2000) Use of fibrinolytic agents in the prevention of post-operative adhesion formation. Fertil Steril 74:203–212

Hershlag A, Diamond MP, DeCherney AH (1991) Adhesiolysis. Clin Obstet Gynecol 34:395–402

Interceed (TC7) Adhesion Barrier Study Group II (1993) Pelvic sidewall adhesion reformation: microsurgery alone or with Interceed absorbable adhesion barrier. Surg Gynecol Obstet 177:135–139

Jansen RP (1988) Failure of peritoneal irrigation with heparin during pelvic operations upon young women to reduce adhesions. Surg Gynecol Obstet 166: 154–160

Laurent TC, Fraser JR (1992) Hyaluronan. FASEB J 6:2397–2404

Lower AM, Hawthorn RJS, Ellis H, O'Brien F, Buchan S, Crowe AM (2000) The impact of adhesions on hospital readmissions over ten years after 8849 open gynaecological operations: an assessment from the Surgical and Clinical Adhesions Research Study. BJOG 107:855–862

Lundorff P, Hahlin M, Kallfelt B et al (1991) Adhesion formation after laparoscopic surgery in tubal pregnancy: a randomized trial versus laparotomy. Fertil Steril 55:911–915

Lundorff P, Donnez J, Korell M et al (2005) Clinical evaluation of a viscoelastic gel for reduction of adhesions following gynaecological surgery by laparoscopy in Europe. Hum Reprod 20:514–520

Mais V, Ajossa S, Mascia M et al (1996) Laparoscopy versus abdominal muomectomy: a prospective randomized trial to evaluate benefits on early outcome. Am J Obstet Gynecol 174:654–658

Mais V, Bracco GL, Litta P, Gargiulo T, Melis GB (2006) Reduction of postoperative adhesions with an auto-crosslinked hyaluronan gel in gynaecological laparoscopic surgery: a blinded, controlled, randomized, multicentre study. Hum Reprod 21(5): 1248–1254

Marana R, Catalano GF, Caruana P et al (1997) Postoperative adhesion formation and reproductive outcome using Interceed after ovarian surgery: a randomized trial in the rabbit model. Hum Reprod 12:1935–1938

Menzies D (1993) Postoperative adhesion: their treatment and relevance in clinical practive. Ann R Coll Surg Engl 75:147–153

Mentiez D, Parker M, Hoare R, Knight A (2001) Small bowel obstruction due to postoperative adhesions: treatment patterns and associated costs in 110 hospital admissions. Ann R Coll Surg Engl 83:40–46

Mettler L, Audeberg A, Lehmann-Willenbrock E et al (2004) A randomized, prospective, controlled, multicenter clinical trial of a sprayable, site-specific adhesion barrier system in patients undergoing myomectomy. Fertil Steril 82:398–404

Molinas CR, Tjwa M, Vanacker B et al (2004) Role of CO2 pneumoperitoneum-induced acidosis in CO2 pneumoperitoneum-enhanced adhesion formation in mice. Fertil Steril 81:708–711

Nordic Adhesion Prevention Study Group (1995) The efficacy of Interceed (TC7) for prevention of reformation of postoperative adhesions on ovarie, fallopian tubes and fimbriae in microsurgical operations for fertility: a multicenter study. Fertil Steril 63:709–714

Pellicano M, Bramante S, Cirillo D, Palomba S, Bifulco G, Zullo F, Nappi C (2003) Effectiveness of autocrosslinked hyaluronic acid gel after laparoscopic myomectomy in infertile patients: a prospective, randomized, controlled study. Fertil Steril 80:441–444

Pellicano M, Guida M, Bramante S, Acunzo G, Di Spiezio Sardo A, Tommaselli GA, Nappi C (2005) Reproductive outcome after autocrosslinked hyaluronic acid gel application in infertile patients who underwent laparoscopic myomectomy. Fertil Steril 83:498

Pucciarelli S, Codello L, Rosato A, Del Bianco P, Vecchiato G, Lise M (2003) Effect of antiadhesive agents on peritoneal carcinomatosis in an experimental model. Br J Surg 90:66

Querleu D, Vankeerberghen DF, Deffense F, Boutteville C (1989) The effect of noxytiolin and systemic corticosteroids in infertility surgery; a prospective randomised study. J Gynecol Obstet Biol Reprod 18:935–940

Reid RL, Hahn PM, Spence JE et al (1997) A randomized trial of oxidized regenerated cellulose adhesion barrier (Interceed TC7) alone or in combination with heparin. Fertil Steril 67:23–29

Renier D, Bellato P, Bellini D, Pavesio A, Pressato D, Borrione A (2005) Pharmacokinetic behaviour of ACP gel, an autocrosslinked hyaluronan derivative, after intraperitoneal administration. Biomaterials 26: 5368–5374

Risberg B (1997) Adhesions: preventive strategies. Eur J Surg Suppl 163:32–39

Sekiba K, The Obstetrics and Gynecology Adhesion Prevention Commiteé (1992) Use of Interceed (TC7) absorbable adhesion barrier to reduce post operative adhesion reformation in infertility and endometrioses surgery. Obstet Gynecol 79:518–522

Swolin K (1967) Die Einwirkung von Grossen Intraperitonealen Dosen Glucocorticoid auf die Bildung von Postoperative Adhaisionen. Acta Obstet Gynecol Scand 46:204–209

The Surgical Membrane Study Group (1991) Prophylaxis of pelvic sidewall adhesions with Gore-Tex surgical membrane; a multicenter clinical investigation. Fertil Steril 57:921–923

Trew J, Pistofides G, Pados G et al (2011) Gynaecological endoscopic evaluation of 4 % icodextrin solution: a European, multicentre, double-blind, randomized study of the efficacy and safety in the reduction of de novo adhesions after laparoscopic gynaecological surgery. Hum Reprod 26:2015–2027

Tulandi T (1997) How can we avoid adhesions after laparoscopic surgery? Curr Opin Obstet Gynecol 9:239–243

Verco SJ, Peers EM, Brown CB et al (2000) Development of a novel glucose polymer solution (Icodextrin) for adhesion prevention: preclinical studies. Hum Reprod 15:1764–1772

Wilson MS, Menzies D, Knight AD, Crowe AM (2002) Demonstrating the clinical and cost effectiveness of adhesion reduction strategies. Colorectal Dis 4:355–360

Wiseman DM (1994) Polymers for the prevention of surgical adhesions. In: Domb AJ (ed) Polymeric site-specific pharmacotherapy. Wiley, Chichester, pp 369–421

Young P, Johns A, Templeman C et al (2005) Reduction of post-operative adhesions after laparoscopic gynaecological surgery with Oxiplex/AP gel: a pilot study. Fertil Steril 84:1450–1456