Fluid and pharmacological agents for adhesion prevention after gynaecological surgery (Review)

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[Intervention Review]

Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

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ABSTRACT

Background

Pelvic surgery is associated with high rates of both de novo adhesion formation and adhesion reformation. Since subsequent fertility is reduced with increasing severity of peri adnexal adhesions, pelvic adhesions will remain a clinical problem in infertility patients. Steroids, antihistamines and heparin were amongst the first substances to be advocated for adhesion prevention. More recently icodextrin 4%, hyaluronic acid agents and SprayGel have been used. This review aims to evaluate the role of fluid and pharmacological agents in the prevention of adhesions in fertility-conserving gynaecological surgery.

Objectives

To investigate fluid and pharmacological agents for adhesion prevention when used as adjuvants during pelvic surgery.

Search methods

This review has drawn on the search strategy developed for the Menstrual Disorders and Subfertility Group. The following databases were searched: the Cochrane Menstrual Disorders and Subfertility Group Specialised Register, Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE and EMBASE.

Selection criteria

Randomised controlled trials investigating the use of fluid and pharmacological agents to prevent adhesion formation after fertility-conserving gynaecological surgery.

Data collection and analysis

Data extraction and analysis was performed independently by two authors (Metwally M and Watson A). Two-by-two tables were generated for dichotomous outcomes and expressed as odds ratios (OR) with 95% confidence intervals (CI). For continuous outcomes a standardised mean difference was used.

Main results

There is no evidence of benefit from the use of steroids, dextran or other pharmacological agents in any of the outcomes. The use of hyaluronic acid agents may decrease adhesion formation (OR 0.31, 95% CI 0.19 to 0.51) and prevent the deterioration of pre-existing adhesions (OR 0.28 (95% CI 0.12 to 0.66). There is insufficient evidence for the use of icodextrin 4% or SprayGel as adhesion-preventing agents. None of the studied agents has been shown to improve the pregnancy rate when used as an adjunct during pelvic surgery.

Authors' conclusions

The current evidence for the use of fluid and pharmacological agents for the prevention of adhesions is limited. There is no evidence on any benefit for improving pregnancy outcomes when pharmacological and fluid agents are used as an adjunct during pelvic surgery.

There is insufficient evidence for the use of the following agents: steroids, icodextrin 4%, SprayGel and dextran in improving adhesions following surgery.

There is some evidence that hyaluronic acid agents may decrease the proportion of adhesions and prevent the deterioration of pre existing adhesions. However, due to the limited number of studies available, this evidence should be interpreted with caution and further studies are needed.

PLAIN LANGUAGE SUMMARY

The use of fluids and pharmacological agents (medicinal drugs) to prevent the formation of adhesions (scar tissue) that may interfere with becoming pregnant after surgery of the female pelvis.

Adhesion formation is a condition in which bodily tissues that are normally separate grow together. This can occur after surgical procedures such as operations on the female pelvis to remove a cyst, treat endometriosis, remove a tubal pregnancy, or remove a fibroid (a benign tumour of the womb). This scar tissue can have serious effects on the woman's future fertility as it can lead to blockage of her tubes. Careful tissue handling at the time of surgery and control of the blood loss are important ways of reducing scar tissue, however, over the years other methods have been developed to minimise the risk of scar tissue formation. Surgeons have tried using different types of drugs or leaving different types of fluids inside the pelvis at the end of surgery to prevent tissue surfaces from sticking to each other. Fluids include dextran, icodextrin (Adept), SprayGel, and fluids containing the chemical hyaluronic acid (Intergel, auto-cross linked hyaluronic acid, Sepracoat). Drugs that have been tried include steroids (anti-inflammatory drug), the anti-coagulant heparin, promethazine, and noxytioline.

This review aimed to evaluate the role of these different agents in the prevention of adhesion formation. The results showed that there is currently insufficient evidence to recommend the use of steroids, icodextrin, SprayGel or dextran. The review did show that fluids that contained hyaluronic acid may help lower the chance of scar tissue forming; however, more studies are needed to confirm this. There are also some major safety issues concerning the use of one of these agents (Intergel), which has been withdrawn from the market due to reports of serious side effects such as allergic reactions and pain.

A major problem with studies in this review is that most of them did not look at the rate of pregnancy following the use of these substances. Since the occurrence of pregnancy is the gold standard for measuring how well these agents work to preserve fertility, it is important that future studies take this into consideration.

BACKGROUND

Intraperitoneal adhesions are an important cause of postoperative intestinal obstruction, abdominal discomfort and infertility (Nehez, 2005). Even if careful attention is paid to reducing tissue trauma and ensuring haemostasis, pelvic surgery is associated with both de novo adhesion formation and adhesion reformation.

Adhesions occur following about 80% of gynaecological surgical procedures, and reformation occurs postoperatively in about 85% of patients (Verco 2000; Diamond 2000).

Although there have been considerable improvements in the success of assisted reproductive technologies (ART) cycles, reproductive surgery remains an important option and complement to ART for many couples. A study investigating the effect of tubal and ovarian adhesiolysis on subsequent fertility found the cumulative pregnancy rate in the group that underwent salpingo-ovariolysis was three times higher than in the non-treated group

(Tulandi 1990; Lok 2003). In addition, many gynaecological operations are performed for women of reproductive age for indications unrelated to fertility. Some of these procedures have consequences that may compromise future fertility through various mechanisms, hence the importance of trying to treat or preferably prevent the formation of adhesions.

Microsurgical techniques (the use of magnification, careful haemostasis, continuous irrigation and minimal tissue handling) reduce but do not eliminate the problem (Winston 1991). Adjuvant therapy has been promoted for many years to prevent adhesion formation. Over the years numerous substances have been used experimentally in animal models and many have been advocated for use during human surgery (Holtz 1984; Jansen 1991;

diZerega 1994). Steroids and antihistamines were used in the belief that they would promote fibrinolysis during healing without preventing healing. Fluid agents are said to separate opposing surfaces until after healing has been completed, by means of their flotation effect (Polishuk 1967; Rose 1991). Dextran is a hydrolysed polysaccharide with a molecular weight of 70,000 that is commonly used as a 32% solution (Hyskon (Pharmacia, Uppsala, Sweden)). On instillation into the peritoneal cavity, dextran initiates an osmotically mediated transudation of serum into the cavity which can persist for several days (Krinsky 1984). In addition to its flotation effect, dextran has been claimed to induce a 'siliconising' effect on damaged surfaces (Goldberg 1980).

Hyaluronic acid is a linear polysaccharide with repeating disaccharide units composed of sodium D-glucuronate and N-acetyl-D-glucosamine. It is a major component of many body tissues and fluids where it provides mechanically protective and physically supportive roles (Johns 2001). Hyaluronic acid has been shown in experimental studies to reduce the formation of adhesions following abdominopelvic surgery (Diamond 1998). Intergel (ferric hyaluronate), Sepracoat and auto-cross linked hyaluronic acid gel are all solutions based on the presence of hyaluronic acid and have been studied in this review.

Other fluid agents include SprayGel and icodextrin 4%; SprayGel (Confluent Surgical, Waltham, MA) is a synthetic hydrogel formed when two polyethylene glycol (PEG)-based liquids are sprayed onto target tissue and the precursor liquids crosslink within seconds to form an absorbable, gel barrier (Mettler 2004).

Icodextrin is an alpha-1, 4-glucose polymer of high molecular weight that is rapidly metabolised in the liver. Icodextrin 4% is colourless, non-viscous and iso-osmolar; with an intraperitoneal residence time of at least four days as it is absorbed slowly from the peritoneal cavity (Hosie 2001; diZerega 2002).

Evaluation of the use of these fluid and pharmacological agents value during human surgery has, however, often been poor. Before acceptance in clinical practice can be justified, well controlled, randomised studies are needed.

This is an update of the original review on fluid and pharmacological agents for the prevention of adhesions. It includes a revision of older agents such as steroids and dextran, in addition to a review of the more novel agents such as hyaluronic acid agents, Spray Gel and icodextrin 4%.

OBJECTIVES

To evaluate the role of fluid and pharmacological agents used as adjuvants during fertility preserving pelvic surgery. Individual pharmacological or fluid agents were compared with no treatment or placebo.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials investigating the use of fluid and pharmacological agents to prevent adhesion formation after fertility-conserving gynaecological surgery.

Types of participants

Women in the reproductive period undergoing fertility-preserving pelvic surgery (laparoscopy or laparotomy). Procedures in which fertility is not conserved, such as hysterectomy, are not included.

Types of interventions

1. Pharmacological agents
A. Steroids:
steroids versus no steroids (or placebo);
systemic steroids versus no steroids (or placebo);
intraperitoneal steroids versus no steroids (or placebo);
systemic and intraperitoneal steroids versus no steroids (or placebo);

postoperative hydrotubation with steroids versus no treatment (or placebo);
postoperative steroids (in addition to systemic steroids) versus no steroids (or placebo);
preoperative versus postoperative steroids (in addition to systemic steroids).
B. Intraperitoneal noxytioline versus no noxytioline (or placebo).
C. Intraperitoneal heparin versus no heparin (or placebo).
D. Systemic promethazine versus no promethazine (or placebo).
2. Fluid agents
A. Dextran versus no dextran (or placebo).
B. Hyaluronic acid versus no hyaluronic acid (or placebo).
C. SprayGel versus no SprayGel (or placebo).
D. Isodextrin versus no isodextrin (or placebo).

Types of outcome measures

- Live birth rate
- Clinical pregnancy rate
- Ectopic pregnancy rate (per pregnancy)
- Miscarriage rate (per pregnancy)
- Proportion of adhesions at second-look laparoscopy
- Change in the severity of adhesions at second-look laparoscopy (improvement or deterioration, change in mean adhesion score)

Search methods for identification of studies

This is an update of the review originally performed by Watson A, Vandekerckhove P and Lilford L. Metwally M and Watson A prepared the update.
The review drew on the search strategy developed for the Menstrual Disorders and Subfertility Group. We searched the Cochrane Menstrual Disorders and Subfertility Group Specialised Register (November 2005), Cochrane Central Register of Controlled Trials (last searched November 2005), MEDLINE (1966 to November Week 2, 2005), EMBASE (1980 to 2005, Week 47). We also searched reference lists of articles and contacted experts in the field. For more details see the Menstrual Disorders and Subfertility Group search strategy
See Appendix 1
Bibliographies of included trials were searched for references to further relevant trials. The search was not limited to any one language.

Data collection and analysis

Study selection
Only randomised controlled trials (RCTs)of fluid or pharmacological agents used to prevent adhesions during fertility preserving pelvic surgery were selected.

Assessment of methodological risk of bias:
The risk of bias of all studies that were deemed eligible for the review was assessed independently by the two authors (Metwally M, Watson A). Any disagreement regarding interpretation of data was settled by consensus. The quality of allocation concealment was graded as adequate (A), unclear (B), or inadequate (C) following the detailed descriptions of these categories provided by the Menstrual Disorders and Subfertility Review Group.
Data extraction:
Data extraction was performed independently by the two authors (Metwally M, Watson A). Any disagreement was settled by consensus. For each individual trial the following information was gathered.

Trial characteristics
1. Allocation of concealment:
a) by a third party (telephone) or trialist (computer, sealed envelope or register);
b) not stated.
2. Method of randomisation:
a) computer generated;
b) random numbers table;
c) not stated;
d) time of randomisation
3. Study design:
a) Presence or absence of blinding;
b) duration of follow up;
4. Size of study with number of women:
a) recruited;
b) randomised;
c) excluded;
d) analysed;
e) lost to follow up.
5. Study setting:
a) single-centre or multi-centre;
b) location;
c) timing.
6. Analyses:
a) power calculation;
b) whether or not by intention to treat.
Characteristics of the study participants
1. Baseline characteristics:
a) age;
b) number randomised;
d) number undergoing second- look laparoscopy ;
d) presence or absence of infertility.
2. Treatment characteristics:
a) indication for surgery;
b) type of surgery: laparoscopy or laparotomy;
c) timing of second-look laparoscopy;
d) type of adhesion score used.
Interventions used

a) type of fluid or pharmacological agent;
b) method of administration;
c) control intervention.

Outcomes

a) pregnancy rate (total);
b) live birth rate;
c) ectopic pregnancy rate (per pregnancy);
d) miscarriage rate (per pregnancy);
e) proportion of adhesions at second look laparoscopy;
f) change in the severity of adhesions at second look laparoscopy (improvement or deterioration or change in mean adhesion score).

Statistical analysis:

Statistical analysis was performed in accordance with the guidelines for statistical analysis developed by The Cochrane Collaboration. Heterogeneity (variations) between the results of different studies was examined by checking the results of the chi-squared and I^2 statistics. A large chi-squared statistic relative to its degrees of freedom or an I^2 statistic with a value greater than 50% provided evidence of heterogeneity of treatment effects. Where appropriate the outcomes were pooled statistically.

The dichotomous data extracted from the individual studies, were expressed as an odds ratio with 95% confidence intervals and combined for meta-analysis with the RevMan software.

A fixed-effect model was used except in the presence of heterogeneity, where a random-effects model was used for analysis. For further information on the statistical methods see the Cochrane Menstrual Disorders and Subfertility Group module on *The Cochrane Library*.

Adhesions at second-look laparoscopy can be assessed in various ways. At the crudest level we used the number of women with an absence or presence of adhesions; or the number of women found to have an improvement or deterioration in adhesions at second-look laparoscopy, where such data were given or could be calculated. A more quantitative way of studying adhesions is the use of adhesion scoring systems. A problem with is the use of different scoring systems by different authors. To solve this problem we used standardised mean difference, which can be used to compare continuous data from different scales, from the mean and standard deviation. Where the standard error of the mean (SEM) was given, it was converted to standard deviation (SD) by multiplying SEM by the square root of the number of women. Where the mean and standard deviation were not obtainable the data were not included in the analysis.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

Sixteen RCTs investigating the role of one or more pharmacological or fluid agents in women undergoing fertility-preserving pelvic surgery were identified. Three trials included in the review (Jansen 1985; Querleu 1989; Jansen 1990a) employed a factorial design where women were randomised twice. Two trials stated that sequential analysis was done during the trial (Rock 1984; Rosenberg 1984); the latter trial was stopped when a beneficial effect of dextran on adhesion score obtained at second-look laparoscopy became significant. One study that was included in the original review (Swolin 1967) has now been excluded from the analysis as it was quasi-randomised.

Intervention assessment

Five studies investigated the role of steroids in preventing adhesion formation or improving pregnancy rates, or both, after pelvic surgery. All studies involved women undergoing elective open microsurgery for infertility. Steroid administration was systemic in three studies (Querleu 1989; Jansen 1990a; Jansen 1990b), intraperitoneal in one (Jansen 1985) and by post-operative hydrotubation in one (Rock 1984). In the latter study there were three treatment arms: hydrotubation with hydrocortisone, hydrotubation without steroids, no hydrotubation; for the purpose of this review the first two arms were compared. Three studies compared steroid administration with no steroid treatment while the other two studies compared two different steroid regimes (Jansen 1990a; Jansen 1990b). The latter two did not analyse pregnancy outcome. All but one study (Rock 1984) assessed adhesions at second-look laparoscopy.

Four RCTs investigated the role of intraperitoneal instillation of 32% dextran 70 before closure of the abdomen (Adhesion SG 1983; Rosenberg 1984; Jansen 1985; Larsson 1985). The control group received a similar volume of Ringer's solution with lactate in two studies (Rosenberg 1984; Jansen 1985) and normal saline in the two other studies (Adhesion SG 1983; Larsson 1985). Adhesions at second-look laparoscopy were assessed in all four studies and pregnancy data were given in three (Adhesion SG 1983; Jansen 1985; Larsson 1985).

Three studies looked at the role of 0.5% ferric hyaluronate gel (Intergel) with a total of 365 women (Thornton 1998; Johns 2001; Lundorff 2001). All three studies used lactated Ringer's solution as control .One study with thirty-six women investigated auto-cross linked hyaluronic acid gel and used 'no treatment' for the control group (Pellicano 2003). One study (Diamond 1998) investigated the role of a dilute hyaluronic acid solution (Sepracoat) with two hundred and forty-five women. Sepracoat was compared to phosphate buffered saline as placebo (Diamond 1998). Only one study stated infertility as an inclusion criterion (Pellicano 2003) and none of the five studies evaluated pregnancy as an outcome. This one study (Pellicano 2003) performed laparoscopy as the primary procedure (laparoscopic myomectomy) whereas the remaining studies involved a laparotomy and peritoneal surgery for a va-

riety of conditions

Two studies investigated the use of SprayGel (Johns 2003; Mettler 2004). In one of these (Johns 2003), the women were randomised to receive SprayGel or no SprayGel during laparoscopic ovarian surgery. In the study by (Mettler 2004), sixty-six women undergoing open or laparoscopic myomectomy were randomised to receive either SprayGel or no SprayGel. The incidence of adhesions at second-look laparoscopy was analysed from one study (Mettler 2004) and the change in the mean adhesion area was analysed from the other (Johns 2003). Neither of these studies reported on pregnancy rates.

One pilot RCT investigated the role of icodextrin 4% (Adept) in the prevention of adhesions (diZerega 2002). This study included women above 18 years of age undergoing laparoscopic peritoneal surgery for pelvic pain, infertility or both. Women were randomised to receive either icodextrin or Ringer's lactated solution. The study commented on incidence of adhesions, the change in adhesion scores and safety; pregnancy rates were not reported.

Individual RCTs investigated the role of intraperitoneal pelvic irrigation with a heparin solution (Jansen 1988); systemic administration of antihistamines (Jansen 1990a); and intraperitoneal instillation of noxytioline (Querleu 1989). These three RCTs studied adhesion formation but only Querleu included pregnancy data.

In some trials, additional adjuvant therapy (apart from the one under investigation) was used for some (Jansen 1988) or all women (Jansen 1990a; Jansen 1990b). A separate, synergistic or antagonistic effect of such agents cannot be excluded.

Timing of intervention

In the studies by Jansen (Jansen 1985; Jansen 1988; Jansen 1990a; Jansen 1990b) second-look laparoscopy was done early (one to three weeks) after initial surgery. Its timing was considerably later in other trials: Mettler 2004 (3 to 16 weeks); Diamond 1998 (40 days); Adhesion SG 1983 (8 to 12 weeks); Larsson 1985 (4 to 10 weeks); Johns 2001, Lundorff 2001, diZerega 2002 (6 to 12 weeks); Pellicano 2003 (60 to 90 days); Querleu 1989 (3 to 6 months); and Rosenberg 1984 (4 to 12 weeks). In one study (Rosenberg 1984) women were advised to use contraceptive measures until the second-look laparoscopy, but only two of the other studies (Adhesion SG 1983; Johns 2001) stated whether patients failing to have second-look laparoscopy did so because of pregnancy.

Outcome Assessment

1. Pregnancy outcomes (live birth rate, clinical pregnancy rate, ectopic pregnancy rate and miscarriage rate)

In total, 791 women were studied for the outcome of pregnancy in RCTs with an untreated control group (steroids: four trials, 481 women; dextran: three trials, 310 women). None stated how pregnancy was determined. The duration of follow up for pregnancy data varied within and between the trials, from one to thirty-six months.

Data specifying the outcome of any pregnancy were given in three studies (Adhesion SG 1983; Jansen 1985; Larsson 1985), for a total of 310 women. In one study (Adhesion SG 1983) pregnancy data were only given for women who conceived prior to second-look laparoscopy, 12 weeks after initial surgery. The two other studies had a follow-up period greater than a year (Jansen 1985; Larsson 1985) and provided data on term pregnancy, miscarriage and ectopic rate.

2. Assessment of adhesions at second-look laparoscopy (proportion of adhesions at second-look laparoscopy and change in the severity of adhesions at second look)

In the studies investigating steroids, no second-look laparoscopy was performed in one study (Rock 1984) and adhesion score change was not an outcome. A total of 323DOES NOT AGREE WITH NUMBERS BELOW? women underwent second-look laparoscopy with adhesion assessment.

In the dextran studies, adhesion score at second-look laparoscopy was an outcome in all four studies; 404 patients were analysed. The difference in the mean adhesion score at second-look laparoscopy was noted from two studies (Adhesion SG 1983; Larsson 1985).

In the hyaluronic acid studies, data regarding the proportion of adhesions found at second-look laparoscopy was reported from four studies (Diamond 1998; Johns 2001; Lundorff 2001; Pellicano 2003). Two studies supplied data regarding the improvement or deterioration of adhesion scores (Johns 2001; Lundorff 2001) and in two studies the mean adhesion score was given (Diamond 1998; Lundorff 2001).

In the two studies investigating SprayGel, data concerning the proportion of adhesions at second-look laparoscopy was obtained from one study (Mettler 2004); the change in the mean extent of adhesions was obtained from the other (Johns 2003).

Changes in the adhesion score (deterioration or improvement) and incidence of adhesions at second-look laparoscopy were reported in the only study investigating icodextrin (diZerega 2002).

Risk of bias in included studies

See Table 1

For fifteen randomised comparisons it appeared that a true method of randomisation was used. The method (an important potential source of bias) was not described in one study (Querleu 1989). Timing of randomisation was on admission to hospital (Rosenberg 1984), the night before surgery (Querleu 1989), at the time of surgery (Thornton 1998; Johns 2001; Lundorff 2001; Johns 2003; Mettler 2004), prior to closure of the peritoneum (Larsson 1985), or up to four weeks before surgery (diZerega 2002). The exact timing of randomisation was not clear in the remaining studies.

Allocation concealment was judged as being adequate in ten studies (Adhesion SG 1983; Rock 1984; Rosenberg 1984; Jansen 1985; Jansen 1988; Diamond 1998; diZerega 2002; Johns 2003; Pellicano 2003; Mettler 2004).

A formal power calculation was clearly stated in only five studies (Jansen 1985; Jansen 1988; Querleu 1989; Jansen 1990a; Jansen 1990b) and an intention-to-treat analysis was clearly stated in three studies (Johns 2003; Pellicano 2003; Mettler 2004).

Eight trials had a multi-centre design. The number of participating centres varied from four (Rock 1984) to nine (Adhesion SG 1983). Most studies recruited more than 100 women (range 102 to 281). Three studies included a smaller number of women, ranging from 14 to 77 (Thornton 1998; Lundorff 2001; diZerega 2002; Pellicano 2003; Mettler 2004).

The total number of participants analysed in the included trials was 1779. The sample size in the four studies comparing the use of steroids with an untreated control group varied between 108 and 168 (total 567 women). For the dextran comparison, 310 women were analysed. In the hyaluronic acid group, 623 women were analysed (range 36 to 277). In the two studies investigating SprayGel, 60 women were analysed. A formal power calculation was performed in five trials (Jansen 1985; Jansen 1988; Querleu 1989; Jansen 1990a; Jansen 1990b; diZerega 2002).

Adhesion assessment at second-look laparoscopy can be subjective. To avoid observer bias it was important that the recorder of the findings at second-look laparoscopy was blinded to the group to which the patient was randomised. This was stated to be the case in the studies by Adhesion SG 1983; Rosenberg 1984; Jansen 1985; Jansen 1988; Thornton 1998; Johns 2001; Lundorff 2001; diZerega 2002; and Johns 2003.

Effects of interventions

A) Steroids

Pregnancy outcomes

The meta-analysis did not show any evidence of a significant difference on pregnancy rate (OR 1.10, 95% CI 0.66 to 1.55). No evidence of benefit was found in the outcomes of live birth rate (two trials; OR 0.65, 95% CI 0.26 to 1.62) or ectopic gestation (three studies; OR 0.67, 95% CI 0.08 to 5.7). There was no suggestion that any route of administration was more effective than another.

Assessment of adhesions

Only one study provided data on the number of women where adhesions deteriorated (Querleu 1989) and did not show evidence of a beneficial effect for steroids (OR 0.3, 95% CI 0.08 to 1.15). One study (Jansen 1990b) found no evidence of a significant difference in the improvement or deterioration of adhesions when steroids were given preoperatively compared with postoperatively, in addition to intra-operative steroids (OR 0.4, 95% CI 0.8 to 1.9; OR 1.06, 95% CI 0.37 to 3.04, respectively).

Other effects

Steroids were associated with side effects in three studies (Jansen 1985; Jansen 1990a; Jansen 1990b). Apart from delayed wound healing, Jansen 1985 described transient euphoria with steroid use in some women.

B) Dextran

Pregnancy outcomes

There was no evidence of a significant difference in pregnancy rates (total) associated with the use of dextran (three studies; OR 0.64, 95% CI 0.37 to 1.14). When pregnancy occurred, there was no evidence of benefit in terms of the live birth rate (two studies; OR 0.67, 95% CI 0.29 to 1.58) or ectopic pregnancy rates (two studies; OR 0.38, 95% CI 0.06 to 2.4).

Assessment of adhesions

It was possible to calculate the number of women with an improvement in adhesions at second-look laparoscopy in two trials (Adhesion SG 1983; Jansen 1985); no evidence of significant difference was found (OR 0.93, 95% CI 0.46 to 1.9). In these two studies there was a significantly lower proportion of adhesions in the dextran group at second-look laparoscopy (OR 0.33; 95% CI 0.18 to 0.59).

There was no evidence of benefit in terms of the mean adhesion score at second-look laparoscopy (two studies, combined standardised mean difference (SMD) -0.02, 95% CI -0.37 to 0.33).

Other effects

Only one study described a side effect (labial oedema) attributed to the instillation of dextran (Adhesion SG 1983).

C) Hyaluronic acid-containing solutions (Intergel, auto-cross linked hyaluronic acid gel and Sepracoat)

Pregnancy outcomes

No pregnancy rates were reported in any of the studies.

Assessment of adhesions

Four studies commented on the proportion of adhesions at second-look laparoscopy (Diamond 1998; Johns 2001; Lundorff 2001; Pellicano 2003) and showed a significant decrease in the proportion of adhesions in women treated with hyaluronic acid (OR 0.31, 95% CI 0.19 to 0.51).

Lundorff 2001 and Johns 2001 evaluated improvement or deterioration of adhesion scores and, although there was no evidence of a difference in the chance of having an improved adhesion score in the treatment group (OR 1.55, 95% CI 0.82 to 2.92), there was a significantly higher chance of deterioration of the adhesion score in the control group (OR 0.28, 95% CI 0.12 to 0.66).

The mean adhesion score was calculated from two studies (Diamond 1998; Lundorff 2001). The results showed no evidence of a significant difference between treatment and control groups (SDM -39.8, 95% CI -114.6 to 35).

D) SprayGel

Pregnancy Outcomes

No pregnancy rates were reported in any of the studies.

Assessment of adhesions:

There was no evidence of a significant difference between treatment and control groups in the proportion of adhesions (OR 0.27, 95%CI. 0.05 to 1.5) (Mettler 2004), extent of adhesions (SMD -

0.77, 95%CI. -1.54 to 0) (Johns 2003), the rate of improvement (OR 1.5, 95%CI. 0.12 to 18.54) or rate of deterioration of adhesions
(OR 0.18, 95%CI. 0.03 to 1.06) (Mettler 2004)

E) 4% Icodextrin (ADEPT)

Pregnancy Outcomes

No pregnancy rates were reported in any of the studies.

Assessment of adhesions

There was only one study available at the time of this review that investigated the role of icodextrin in the reduction of adhesions (diZerega 2002). The study did not show any evidence of a significant decrease in the proportion of adhesions (OR 0.48, 95% CI 0.13 to 1.68) or improvement of the adhesion score (OR 3.24, 95% CI 0.86 to 12.1) at second-look laparoscopy with icodextrin.

F) Noxytioline

One RCT investigated the role of intraperitoneal instillation of noxytioline (Querleu 1989).

Pregnancy Outcomes

There was no evidence of benefit in terms of pregnancy rates between the noxytioline and the no treatment group (OR 0.66, 95% CI 0.30 to 1.47).

Assessment of adhesions

There was no evidence of any significant deterioration in the adhesion score in the control compared to the treatment group (OR 0.55, 95% CI 0.17 to 1.76).

G) Heparin

One RCT investigated the role of continuous irrigation of the pelvis during surgery with a solution containing heparin compared with irrigation without heparin (Jansen 1988).

Pregnancy Outcomes

Pregnancy outcomes were not studied.

Assessment of adhesions

No evidence of benefit in terms of the proportion of women with adhesions at second-look laparoscopy was demonstrated (OR 0.87, 95% CI 0.32 to 2.35).

H) Promethazine

One RCT investigated the role of orally administered promethazine in the prevention of post-operative adhesion formation after pelvic surgery (Jansen 1990a).

Pregnancy Outcomes

Pregnancy outcome was not studied as an outcome

Assessment of adhesions

There was no evidence of a significant difference in the number of women with an improvement in adhesions at second look-laparoscopy with promethazine (OR 0.56, 95% CI. 0.22 to 1.42).

Other pharmacological and liquid adjuvants (such as antibiotics, calcium channel blockers, colchicine, crystalloid solutions, non-steroidal anti-inflammatory drugs, progestogens, or salicylates) have been advocated for use during infertility surgery on the basis of data derived from animal work (Holtz 1984; Jansen 1991; diZerega 1994) but no published human RCTs on any of these agents were identified.

DISCUSSION

The use of steroids in infertility surgery has been widespread (Winston 1991; Li 1994), based on their favourable effects on adhesion formation in animal models (Hockel 1987). However, there is no significant evidence from published studies to support steroid use in humans. In addition, the use of systemic steroids can lead to suppression of the pituitary-adrenal axis (Magyar 1984). In order to reduce this (and other) possible side effect(s) of systemic administration it was suggested that steroids be administered by intraperitoneal solution or by flushing through the fallopian tubes postoperatively. Whilst these modes of administration may reduce side effects, their effectiveness remains unproven.

Similarly the use of Dextran 70 is not without complications that may limit its use; pleural effusion (Adoni 1980), anaphylaxis (Borton 1983), labial oedema (Magyar 1985; Sites 1997) and abnormal liver enzymes (Weinans 1990) have all been reported. Cases of peritonitis following intraperitoneal instillation of a combination of dextran and steroids solutions have been reported (Zamir 1989).

Although two studies (Adhesion SG 1983; Jansen 1985) showed fewer adhesions on second-look laparoscopy with dextran, the direction of effect of dextran on both the total birth rate and the live birth rate was negative in all individual RCTs that analysed these outcomes. Although this detrimental effect did not reach statistical significance in any individual trial, or when combined with meta-analysis, a beneficial effect of dextran on pregnancy rate seems unlikely.

We combined all studies of hyaluronic acid fluid agents, namely ferric hyaluronate, auto-cross linked hyaluronic acid and Sepracoat. This yielded a total of five studies. Four out of five studies were included in the meta-analysis, which showed a significant reduction of the proportion of adhesions and a lower chance of deterioration of the adhesion score when hyaluronic acid agents were used. The remaining study (Thornton 1998) was not included in the meta-analysis due to the way the data were presented, which did not allow for combination with the results from the other studies. Further information has been sought from the authors and will be presented when available. The results of this study, nevertheless, agreed with the results of the meta-analysis; it showed a lower proportion of adhesions at second-look laparoscopy in women treated with hyaluronic acid and when adhesions did occur they were significantly less extensive or severe.

Intergel was approved for use in the United States on November 16, 2001 and was intended to be used in open, conservative gynaecological surgery as an adjunct to good surgical technique. Following off license use in laparoscopic surgery, side effects were reported namely pelvic pain and allergic reactions. Intergel was removed from the market in 2003.

Randomised controlled trials on SprayGel are sparse in the literature and only two were included in this review (Johns 2003; Mettler 2004). The currently available evidence does not show any advantage for SprayGel in decreasing the proportion of women with or the extent of adhesions. Similarly only one human randomised controlled pilot study is currently available for icodextrin 4% (diZerega 2002). The study included a relatively small number of women and failed to show any significant benefit for icodextrin over placebo (Ringer's lactated saline). The results of a pivotal phase III study are yet to be reported (diZerega 2002).

Timing of second-look laparoscopy after initial open surgery was variable both between and within the RCTs studied (range: eight days to six months). If there is a considerable time interval before second-look laparoscopy, some women will have conceived and, therefore, not undergo laparoscopy. It is likely that the remaining women who were studied for adhesions during a follow-up laparoscopy would have more adhesions than those who became pregnant. For example, in the Adhesion SG 1983 15% of women in the control group (7 out of 47) conceived prior to the second-look laparoscopy compared to 7% of women receiving dextran treatment (4 of 55). Such an imbalance could have caused bias in favour of the dextran-treated group in the analysis of adhesions found at second-look laparoscopy. There are four more studies in which there was a considerable time interval prior to second-look laparoscopy. These they did not specify how many women in each group conceived and, therefore, did not undergo this follow-up procedure.

A further possible confounding factor in the assessment of adhesions is the practice of intraperitoneal instillation of a crystalloid solution in the control group. This was the case in one of the RCTs investigating steroids (Jansen 1985) and in all four RCTs assessing dextran. Some animal data on the role of crystalloid solutions in preventing adhesion formation suggested that such solutions may, in fact, enhance adhesion formation (Yaacobi 1991). If this is indeed the case then any apparent beneficial effect of the tested adjunct may be due to a detrimental effect of the control solution. On the other hand it has also been suggested (Rose 1991) that large volumes of crystalloids, if retained long enough intraperitoneally, may prevent adhesions by limiting contact between pelvic organs; if true this would lead to an underestimation of a beneficial treatment effect.

Lastly, most trials studied a mixture of women with and without pre-existing adhesions. The former are likely to experience an improvement due to the surgery by itself (regardless of any adjuvant treatment), while the situation can only get worse for the latter. If there is an imbalance between the treatment and control groups for such patients (more women with pre-existing adhesions in the treatment group or more women with no adhesions in the control group), or if the patients have more severe adhesions in the treatment group, the scope for improvement is larger for the treatment group and effects can be biased. While such imbalances are unlikely to occur in a large and truly randomised study, this factor should be addressed in the baseline comparison of the study groups and controlled for if present.

AUTHORS' CONCLUSIONS

Implications for practice

The current evidence on the use of fluid and pharmacological agents for the prevention of adhesions is limited. There is no evidence of a benefit for pharmacological and fluid agents used as an adjunct during pelvic surgery for improving pregnancy outcomes.

There is insufficient evidence for the use of steroids, icodextrin 4%, SprayGel and dextran in improving adhesions following surgery.

There is some evidence that hyaluronic acid agents may decrease the proportion of adhesions and prevent the deterioration of pre-existing adhesions. However, due to the limited number of studies available, this evidence should be interpreted with caution and further studies are needed.

Implications for research

Adequately powered, randomised controlled trials using live pregnancy rate as the primary outcome should be performed to investigate all new pharmacological and fluid agents developed to prevent adhesions after pelvic surgery. These agents should be compared to placebo, no treatment or each other.

There is a large void in the literature regarding the role of icodextrin and SprayGel that can only be filled by well-designed large RCTs.

Future studies should avoid the use of any additional adjuvants, apart from the intervention under study, to avoid any possible confounding effects.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Adhesion SG 1983

Methods	Truly randomised trial (computer generated random numbers) Time of randomisation: not stated Double blind Location: Multicentre - 9 centres in the USA (Houston, Indianapolis, Worcester, Bethesda, Nashville, New Haven, Durham, Los Angeles and Seattle) Timing and duration: not stated
Participants	Infertility patients undergoing open pelvic surgery (macro surgery 53, loupe magnification 32, micro-surgery 17) Condition: pelvic inflammatory disease with distal tubal disease (42), endometriosis (14), pelvic adhesions (46) Surgery performed: adhesiolysis; tubal surgery Pre-existing adhesions: all patients Age: 18-35 years (mean not stated) Duration infertility: not stated Infertility workup: semen analysis, postcoital test and confirmation of ovulation (method not stated). Any abnormality was corrected prior to surgery Number randomised: ? (no exclusions stated) Number undergoing treatment: 102 Number undergoing second-look laparoscopy: 91 (11 conceived prior to laparoscopy) Timing second look laparoscopy: 8-12 weeks postoperative Blinding at second-look laparoscopy: yes Females of 18 years and above undergoing laparotomy for gynaecological surgery Exclusion criteria: pregnancy, cancer, PID Number of patients randomised: 277 Number of patients undergoing second-look laparoscopy evaluation: 245
Interventions	Dextran versus normal saline Route of administration: intraperitoneal Dosage/volume: dextran 250 ml; saline 250 ml Prophylactic antibiotics: yes
Outcomes	Analysed in review Pregnancy rate - method of diagnosis: not stated - duration follow up: 8-12 weeks Adhesions at second-look laparoscopy - improvement - change in score OTHER OUTCOMES Adhesions at second-look laparoscopy - present, absent; according to anatomic site Appearance of tube Tubal patency rate

Adhesion SG 1983 (*Continued*)

	Postoperative infection rate
Notes	Adhesion scoring system used Hulka system based on extent of adhesions (scored from 1-4) over fimbriae and ovaries (range 0-16) 1= whole organ seen 2 = >50% seen 3 = <50% seen 4 = totally obscured

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Diamond 1998

Methods	True randomisation (randomisation list) Time of randomisation: preoperative Multicentre study: 23 centres Power calculation: no. Double Blinding: yes
Participants	Females of 18 years and above undergoing laparotomy for gynaecological surgery Exclusion criteria: pregnancy, cancer, PID. Number of patients randomised: 277 Number of patients undergoing second look laparoscopy evaluation:245
Interventions	Sepracoat Versus placebo. Route of administration: intraperitoneal Dosage/Volume: a maximum of 1 litre of Sepracoat or placebo Second look laparoscopy: an average of 40 days later.
Outcomes	Analysed in review 1- Adhesions present at second look laparoscopy 2- mean adhesion score OTHER OUTCOMES 1- mean extent of adhesion score 2-mean incidence of de-novo adhesions at second look laparoscopy 3 mean extent of adhesion score at second look laparoscopy. Pregnancy rates: No.
Notes	Adhesion scoring system used: own system 0= no adhesions 1= up to 25% 2=26-50% 3=more than 50%

Diamond 1998 (*Continued*)

Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Yes	A - Adequate

diZerega 2002

Methods	True randomisation (randomisation list) Pilot study and therefore no power calculation was performed Multicentre (5 centres) Blinding: assessor blind
Participants	Adult females above 18 years and scheduled for pelvic laparoscopic surgery for pelvic pain and infertility Condition: pelvic adhesions, endometriosis Surgery performed: adhesiolysis and tubal/adnexal surgery Mean age: 31 for study group (range 21-40) and 32 for control group (range 18-50) Number eligible: 62 Number undergoing second look laparoscopy: 53
Interventions	Icodextrin 4% versus Ringer's lactated saline Timing second-look laparoscopy: 6-12 months
Outcomes	Analysed in review Adhesions present, improvement or deterioration of adhesion scores at second look laparoscopy Duration follow up: 6-12 months Other outcomesChange in adhesion score at second-look laparoscopy No data on pregnancy rates
Notes	Adhesion scoring system used Modified American Fertility Society endometriosis scoring system

Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Yes	A - Adequate

Jansen 1985

Methods	Truly randomised (random number generated) Time of randomisation: not stated Factorial design Power calculation: yes Location: Sydney, Australia Timing and duration: Feb 1982-Nov 1983
Participants	Adult females above 18 years and scheduled for pelvic laparoscopic surgery for pelvic pain and infertility Condition: pelvic adhesions, endometriosis Surgery performed: adhesiolysis and tubal/adnexal surgery Mean age: 31 for study group (range 21-40) and 32 for control group (range 18-50) Number eligible: 62 Number undergoing second look laparoscopy: 53 Infertility patients undergoing open pelvic microsurgery Condition: peritubal adhesions (76), endometriosis (27), mid tubal occlusion (61) Surgery performed: salpingolysis on its own (92) or with tubal re-anastomosis (20); endometriosis surgery (11); tubal reanastomosis (41) Pre-existing adhesions: 119 patients Mean age: 30 years (range 21-39) Duration infertility: not stated Infertility work-up: not stated Number eligible: 170 Number randomised: 168 Number undergoing SLL: 164
Interventions	1) Dextran versus Hartman's solution Route of administration: intraperitoneal Dosage/volume: dextran 100-200 ml; Hartman's 100 ml or more 2) Steroids versus no treatment Route of administration: intraperitoneal + also systemic (iv and oral) if pre-existing adhesions or endometriosis Dosage/volume: intraperitoneal: 500 mg hydrocortisone in 100-200 ml of dextran or Hartman's; systemic: 8 mg of IV dexamethasone at time of surgery and 30 mg oral prednisolone daily until second-look laparoscopy (SLL) Other adjuvants: perioperative pelvic irrigation with heparinised (5000 IU/L) Ringer's Prophylactic antibiotics: yes Timing SLL: 12-21 days Blinding at SLL: yes
Outcomes	Analysed in review Pregnancy Method of diagnosis: not stated Duration follow up: 1-18 months Live birth Miscarriage rate Ectopic rate Adhesions at second-look laparoscopy - present; absent - improvement; - deterioration

Jansen 1985 (*Continued*)

	Other outcomes Adhesions at second-look laparoscopy - change in score
Notes	Adhesion scoring system used Modified American Fertility Society endometriosis scoring system (range 0-27) Results expressed as medians with their 95% confidence limits Data on adhesions at second-look laparoscopy (absent; present and improvement; no change; deterioration) only available for the dextran comparison No pregnancy outcome data (live birth, ectopic, miscarriage) for patients undergoing re-anastomosis given

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Jansen 1988

Methods	Truly randomised trial (random numbers generated) Time of randomisation: not stated Power calculation done Location: Sydney, Australia Timing and duration: Nov 1983-Oct 1984
Participants	Infertility patients undergoing open pelvic microsurgery Condition: pelvic adhesions; endometriosis; tubal disease; uterine abnormalities Surgery performed: adhesiolysis or treatment for endometriosis (52); tubal anastomosis or uterine surgery (40) Pre-existing adhesions: 63 patients Mean age: 28 years (range 21-42) Duration infertility: not stated Infertility workup: not stated Number eligible: 102 Number undergoing second-look laparoscopy: 92 Timing second-look laparoscopy: 12 days postop Blinding at second-look laparoscopy: yes
Interventions	Heparin containing Ringer's versus Ringer's solution Route of administration: intraperitoneal preoperative pelvic irrigation Dosage/volume: Ringer's solution containing 5000 IU heparin/litre Other adjuvants: 52 patients with pre-existing adhesions or endometriosis received systemic steroids intra- and postoperatively. The first 46 patients of the study received intraperitoneal steroids Prophylactic antibiotics: yes
Outcomes	Analysed in review Adhesions at second-look laparoscopy - improvement; no change; deterioration

Jansen 1988 (*Continued*)

	- change in score Other outcomes Blood transfusion requirements Wound healing
Notes	Adhesion scoring system used Modified American Fertility Society endometriosis scoring system (range 0-27) Data for adhesions at SL (improvement; no change; deterioration) derived from scatter plot

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Jansen 1990a

Methods	Truly randomised trial (random number sequence) Timing of randomisation: not stated Factorial design Power calculation: yes Location: Sidney, Australia Timing and duration: not stated
Participants	Infertility patients undergoing open pelvic microsurgery Condition: pelvic adhesions and/or endometriosis Surgery performed: adhesiolysis; excision of endometriosis Pre-existing adhesions: 75 patients Age: not stated Duration infertility: not stated Infertility workup: not stated Number randomised: ?95 (no exclusions stated) Number analysed: 93 for comparison 1; 95 for comparison 2 Timing Second look laparoscopy: 10 or 12 days postop Blinding at second-look laparoscopy: not stated
Interventions	1) Promethazine versus no treatment Route of administration: systemic (po and IM) Dosage/volume: 50 mg po 6 hours pre-operatively and 50 mg IM intra-operatively 2) Postoperative steroids versus no treatment Route of administration: systemic (po) Dosage/volume: postoperative prednisone 25 mg po bd for 4 days, then 25 mg daily until SLL Other adjuvants: all patients received systemic preoperative (50 mg prednisone 8 h preoperatively) and intraoperative (24 mg dexamethasone iv) steroids Prophylactic antibiotics: yes

Jansen 1990a (*Continued*)

Outcomes	Analysed in review Adhesions at Second look laparoscopy -improvement; no change; deterioration Other outcomesAdhesions at second-look laparoscopy - change in score
Notes	Adhesion scoring system used Modified American Fertility Society endometriosis scoring system (range 0-27) Data obtained from review article and investigator himself

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

Jansen 1990b

Methods	Truly randomised controlled trial (random number sequence) Timing of randomisation: not stated Power calculation : yes Location: Sidney, Australia Timing and duration: not stated
Participants	Infertility patients undergoing open pelvic microsurgery Condition: reversal of sterilisation; salpingitis isthmica nodosa Surgery performed: tubal re-anastomosis; tubal resection Pre-existing adhesions: 28 patients Age: not stated Duration infertility: not stated Infertility workup: not stated Number randomised: 75 Number undergoing Second look laparoscopy: 57 Timing second-look laparoscopy: 10 or 12 days postop Blinding at second-look laparoscopy: not stated
Interventions	Preoperative versus postoperative steroids Route of administration: systemic (po) Dosage/Volume: single dose prednisone 50 mg po (8 h pre op versus 24 h postop) Other adjuvants: All patients received systemic intraoperative steroids (24 mg dexamethasone iv) Prophylactic antibiotics: yes
Outcomes	Analysed in review Adhesions at Second look laparoscopy -improvement; no change; deterioration Other outcomesAdhesions at second-look laparoscopy - median adhesion score change

Jansen 1990b (*Continued*)

Notes	Adhesion scoring system used Modified American Fertility Society endometriosis scoring system (range 0-27) Data obtained from review article and investigator himself

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

Johns 2001

Methods	Truly randomised, third part blinded study (randomisation schedule) Multicentre: 16 centres in the USA and Europe. Power calculation: no
Participants	Truly randomised, third part blinded study (randomisation schedule) Multicentre: 16 centres in the USA and Europe. Power calculation: no
Interventions	Intergel versus Ringer's lactate. Volume: 300 ml of Ringer's lactate or Intergel at the end of the procedure Antibiotics: no Second-look laparoscopy: 6-12 weeks after primary procedure
Outcomes	Analysed in review 1. Adhesions present at second look laparoscopy. 2. Improvement of adhesion score (AFS) 3. Deterioration of adhesion score (AFS) Other outcomes1. Shift in mAFS adhesion score. 2. Per cent reduction in mAFS score 3. Severity and extent of adhesions (median and standard deviation) Pregnancy rates: no
Notes	Adhesion scoring system used 1. AFS adhesion score 2. mAFS adhesion score

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

Johns 2003

Methods	Randomised, third part blinded study Time of randomisation: intraoperative. Multicentre: two centres Method of randomisation: sealed envelopes Power calculation: no
Participants	14 patients of 18 years of age or more undergoing laparoscopic ovarian surgery Exclusion criteria: 1. conversion to an open procedure; 2. Evidence of infection, inflammation or malignancy; 3. frozen pelvis; 4. hydrosalpinges; 5. exposure to irrigation solutions other than lactated Ringer's or saline; 6. use of any other adhesion prevention agents, absorbable haemostatic agents, catgut, nonresorbable sutures; 7. gasless laparoscopy; 8. bowel injury or any other non-gynaecological procedure (cholecystectomy); 8- endometriosis stage 4 (ASRM revised classification). Patients acted as their own controls with one ovary receiving SprayGel and the other not receiving SprayGel Number of patients randomised: 14 Number of patients undergoing second look: 14
Interventions	SprayGel versus no SprayGel One ovary received SprayGel and the other good surgical technique alone Second-look laparoscopy: 3-16 weeks after primary procedure
Outcomes	Analysed in review Change in mean extent of adhesions (cm2) Other outcomes1. Frequency of adhesions at first and second-look laparoscopy (mean and SD) 2. Change in adhesion score from first to second-look laparoscopy Pregnancy rates: no
Notes	Adhesion scoring system used Revised American Fertility Society classification

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Larsson 1985

Methods	Truly randomised trial (random number generated) Time of randomisation: at end of surgery Double blind Location: multicenter - 5 centres in Sweden (Huddinge, Umea, Stockholm, Skovde and Molndal) Timing and duration: not stated
Participants	Infertility patients undergoing open pelvic microsurgery Condition: tubal and/or peritoneal adhesions Surgery performed: adhesiolysis; tubal surgery (cases without adhesions excluded) Pre-existing adhesions: all patients Mean age: 31 years (range 21-39) Duration infertility: not stated Infertility workup: semen analysis, postcoital test, confirmation of ovulation (not specified) and laparoscopy; some also had hysterosalpingogram and/or sperm-mucus penetration test Number randomised: 109 4 exclusions (lost to follow up) Number analysed: 105 Timing second-look laparoscopy: 4-10 weeks postop Blinding at second-look laparoscopy: not stated
Interventions	Dextran versus saline Route of administration: intraperitoneal Dosage/volume: dextran 250 ml; 0.9% saline 250 ml Prophylactic antibiotics: yes
Outcomes	Analysed in review Pregnancy rate - method of diagnosis: not stated - duration follow up: 12-36 months Full term pregnancy rate Miscarriage rate Ectopic rate Adhesions at SLL - change in score (ovaries, tubes, fimbriae) Other outcomesAdhesions at SLL - change in score according to anatomical site (total, Pouch of Douglas, pelvic sidewall, colon, small bowel, anterior abdominal wall) - change in score according to etiology of adhesions Tubal patency Laboratory tests
Notes	Adhesion scoring system used Own scoring system based on extent of adhesions (scored from 1-4) over tubes, fimbriae and ovaries (range 4-24) 0 = none 1 = minimal 2 = mild (one or two simple thin strands less than 1 cm in width) 3 = moderate (more than two adhesions of type 2 or at least one solid adhesion) 4 = severe (more than type 3)

Larsson 1985 (*Continued*)

Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Unclear	D - Not used

Lundorff 2001

Methods	Randomised trial (computer generated schedule) Third party blind Multicentre: five European centres. Time of randomisation: at the time of the procedure. Power calculation: no
Participants	14-42 year-old females undergoing laparotomy were including any patient with systemic disease or inflammatory pelvic condition or receiving any other form of adhesion prevention agents was excluded 77 patients were analysed, not clear how many patients were randomised Not clear if intention-to-treat analysis was used
Interventions	Intergel versus lactated Ringer's Route of administration: intraperitoneal Dosage/volume: 300 ml of either Intergel or Ringer's lactated Prophylactic antibiotics: no Second-look laparoscopy performed 6-12 weeks after the initial procedure
Outcomes	Analysed in review 1. Presence of adhesions at second look 2. Improvement or deterioration of adhesion scores at second look 3. Change in mean adhesion score Other outcomes1. Severity and extent of adhesions 2. mAFS score categorized by surgical procedure Pregnancy rates: no
Notes	Adhesion scoring system used mAFS

Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	No	C - Inadequate

Mettler 2004

Methods	Truly randomised trial (computer generated). Blinding: yes Time of randomisation: not stated
Participants	64 patients with a mean age of 34.9 undergoing laparoscopy or laparotomy for treatment of fibroids Exclusion criteria: 1. patients under 18 years of age; 2. cannot adequately communicate in German or English; 3. unwilling to undergo a second-look laparoscopy. Number of patients randomised: 64 Number of patients undergoing second-look laparoscopy: 62.5% return rate for second look
Interventions	SprayGel versus no treatment
Outcomes	Analysed in review Presence or absence of adhesions at second-look laparoscopy Other outcomes Change in severity of adhesions at second-look laparoscopy
Notes	Adhesion scoring system used Mean adhesion tenacity score

Risk of bias

Item	**Authors' judgement**	**Description**
Allocation concealment?	Yes	A - Adequate

Pellicano 2003

Methods	Truly randomised trial (computer generated central randomisation) Double blinded (known by correspondence with author) Power calculation: no Intention-to-treat analysis: yes
Participants	Infertile patients undergoing laparoscopic myomectomy 36 patients randomised and analysed Inclusion criteria: 1. history of infertility more than or recurrent miscarriages; 2. lack of pedunculation of the main myoma; 3. presence of not more than four myomas; 4. absence of submucosal fibroids as screened by hysteroscopy; 5. no calcification of the main myoma; 6. absence of abnormal cervical smear; 7. negative urine pregnancy test. Exclusion criteria: patients who did not fulfil the inclusion criteria Mean age 26.8 Both groups demographically similar at the start of the study

Pellicano 2003 (*Continued*)

	Number of patients randomised: 36 Number of patients analysed after second-look laparoscopy: 36
Interventions	Auto-crosslinked hyaluronic acid (HA) gel, 5 ml, versus no treatment Time of application: at the end of the procedure Second-look laparoscopy performed: 60-90 days after the primary procedure
Outcomes	Analysed in reviewPresence of adhesions at second-look laparoscopy Other outcomes Incidence of adhesions with regards to the site of the primary myoma Pregnancy rates: no
Notes	Scoring system not used, only rate of presence or absence of adhesions

Risk of bias

Item	**Authors' judgement**	**Description**
Allocation concealment?	Yes	A - Adequate

Querleu 1989

Methods	Truly randomised trial (computer generated central randomisation) Double blinded (known by correspondence with author) Power calculation: no Intention-to-treat analysis: yes Randomised trial (method not stated) Time of randomisation: evening before surgery Factorial design Power calculation done Location: multicenter - 5 centres in France (Clermond-Ferrand, Montpellier, Paris, Roubaix and Lyon) and 1 centre in the Netherlands (Nijmegen) Timing and duration: 1984 Sponsored by Laboratories Chanterau, France
Participants	Infertility patients undergoing open pelvic microsurgery Condition: distal tubal obstruction and/or pelvic adhesions (active PID, endometriosis, proximal tubal obstruction cases excluded) Surgery performed: tubal surgery; adhesiolysis (19) Pre-existing adhesions: analysis done according to pre-existing adhesion status but number not stated Age: not stated Duration infertility : not stated Infertility work-up: not stated Number randomised: 131 5 lost to follow up Number analysed: 126 Number undergoing second look laparoscopy: 88 Timing Second look laparoscopy: 3-6 months postop

Querleu 1989 (*Continued*)

	Blinding at second-look laparoscopy: not stated
Interventions	Auto-crosslinked hyaluronic acid (HA) gel, 5 ml, versus no treatment Time of application: at the end of the procedure Second-look laparoscopy performed: 60-90 days after the primary procedure 1) Steroids versus no steroids Route of administration: systemic (IM) Dosage/volume: dexamethasone 2 mg day before surgery, 8 mg on day of surgery and day after, 2 mg the 5 following days 2) noxytioline versus no treatment Route of administration: intraperitoneal Dosage/volume: noxytioline (Noxyflex) 5 mg diluted in 250 ml of normal saline instilled in the pelvis via a removable drain Other adjuvants: perioperative pelvic irrigation with heparinised (5000 IU/L) normal saline Prophylactic antibiotics: yes (doxycycline)
Outcomes	Analysed in review Pregnancy - method of diagnosis: not specified - duration follow up: 36 months Ectopic pregnancy rate Adhesions at second-look laparoscopy - improvement; deterioration or no change - change in score Other outcomesAdhesions at second-look laparoscopy - change in score according to initial score - change in score according to grade of adhesions - change in score in subgroup of pure adhesiolysis - grade of adhesions - per cent of ovarian surface free of adhesions - fimbrial status - mobility of the tube
Notes	Adhesion scoring system used Modified American Fertility Society endometriosis scoring system (range 0-84) Adhesions were graded as filmy, vascular or dense The power calculation envisaged participation of 10 centres, entering 32 patients each Only 4 centres reached this number, and 2 more centres entered fewer patients Pregnancy rates also presented in a cumulative conception curve using life-table analysis for the steroid and no-treatment groups

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	D - Not used

Rock 1984

Methods	Randomised trial (method not stated) Time of randomisation: evening before surgery Factorial design Power calculation done Location: multicenter - 5 centres in France (Clermond-Ferrand, Montpellier, Paris, Roubaix and Lyon) and 1 centre in the Netherlands (Nijmegen) Timing and duration: 1984 Sponsored by Laboratories Chanterau, France Truly randomised (pack of cards) Time of randomisation: not stated Sequential analysis Location: multicenter - 4 centres in the USA (2 units in New York, Norfolk, Durham), 1 in the Netherlands (Amsterdam) and 1 in Colombia (Bogota) Timing and duration: Jan 1978-Dec 1981
Participants	Infertility patients undergoing open pelvic microsurgery Condition: bilateral distal tubal obstruction (unilateral if only one residual tube) Surgery performed: tubal surgery Pre-existing adhesions: not stated Age: < 36 years (mean 28) Mean duration infertility: 10.7 years (range 1-18) Infertility workup: semen analysis, PCT, documentation of ovulation (method not stated), HSG and laparoscopy (90% of patients) Number randomised: ? (no exclusions stated) Number analysed: 120
Interventions	Steroids versus Ringer's lactated solution Route of administration: postoperative hydrotubation on the first 3 postoperative days and on day of discharge Dosage/volume: 50 ml Ringer's lactate with or without 150 mg hydrocortisone Prophylactic antibiotics: yes
Outcomes	Analysed in review Pregnancy rate (total and live birth) - method of diagnosis: not stated - duration follow up: > 2 years Miscarriage rate Ectopic rate Other outcomesInfection rates and complications after hydrotubation
Notes	Three-way trial comparing postoperative hydrotubation with or without steroids or no hydrotubation; also included in review on postoperative procedures following tubal surgery

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Rosenberg 1984

Methods	Truly randomised (randomised code) Time of randomisation: on admission for surgery Sequential analysis Double blind Location: Richmond, USA Timing and duration: Aug 1981-Aug 1982
Participants	Infertility patients undergoing open pelvic microsurgery Condition: "requirement for infertility surgery" Surgery performed: ovarian cystectomy (10); tubal re-anastomosis (17); tubal surgery (12); adhesiolysis (16); endometriosis surgery (10); myomectomy (8) Pre-existing adhesions: 29 patients Age: not stated Duration infertility: not stated Infertility work-up: not stated Number randomised: 46 Number undergoing second-look laparoscopy: 44 Timing second-look laparoscopy: 4-12 weeks postop (mean 7.5) Blinding at second-look laparoscopy: yes
Interventions	Dextran versus Ringer's lactate Route of administration: intraperitoneal Dosage/volume: dextran 200 ml; Ringer's 200 ml Prophylactic antibiotics: yes
Outcomes	Analysed in review Adhesion score at second-look laparoscopy - change in score Other outcomes Adhesion score at second-look laparoscopy - change in score according to adhesion status
Notes	Adhesion scoring system usedModified American Fertility Society endometriosis scoring system Sequential analysis trial; the randomisation code was broken after 1 year and the trial terminated because dextran appeared significantly better

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Mettler 2003(a)	This is an interim analysis the completed study (Mettler 2004) has been included
Mettler 2003(b)	This is an interim analysis the completed study (Mettler 2004) has been included
Rose 1991	RCT comparing intraperitoneal dextran with Ringer's lactated solution in 15 patients undergoing laparoscopic pelvic surgery Reason for exclusion: weight change was the measured outcome
Sites 1997	RCT comparing intraperitoneal dextran with Ringer's lactated solution in 13 patients undergoing laparoscopic pelvic surgery Reason for exclusion: rate of fluid absorption from the peritoneal cavity as measured by ultrasound was the measured outcome
Swolin 1967	Quasi-randomised trial of steroids versus non-steroids Reason for exclusion: quasi-randomised trial (case record numbers)
Tulandi 1985	RCT comparing intraperitoneal dextran with saline in 22 infertility patients undergoing open pelvic surgery Reason for exclusion: non-infertility related outcomes (coagulation, serum electrolytes)
Tulandi 1991	Patients randomised at reversal of sterilisation to receiving fibrin glue or standard sutures

DATA AND ANALYSES

Comparison 1. Steroids (any route) versus no steroids

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 live birth	2	223	Odds Ratio (M-H, Fixed, 95% CI)	0.65 [0.26, 1.62]
2 clinical pregnancy rate	3	410	Odds Ratio (M-H, Fixed, 95% CI)	1.01 [0.66, 1.55]
3 ectopic rate (per pregnancy)	3	83	Odds Ratio (M-H, Random, 95% CI)	0.67 [0.08, 5.70]
4 deterioration of adhesion score	1	87	Odds Ratio (M-H, Random, 95% CI)	0.30 [0.08, 1.15]

Comparison 2. Systemic steroids versus no steroids

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 clinical pregnancy rate	1	126	Odds Ratio (M-H, Fixed, 95% CI)	1.18 [0.55, 2.54]
2 ectopic rate (per pregnancy)	1	37	Odds Ratio (M-H, Fixed, 95% CI)	0.28 [0.03, 2.96]
3 deterioration of adhesion score	1	87	Odds Ratio (M-H, Fixed, 95% CI)	0.30 [0.08, 1.15]

Comparison 3. Intraperitoneal steroids versus no steroids

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 pregnancy (total)	1	61	Odds Ratio (M-H, Fixed, 95% CI)	1.22 [0.42, 3.50]

Comparison 4. Systemic and intraperitoneal steroids versus no steroids

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 live birth	1	103	Odds Ratio (M-H, Fixed, 95% CI)	0.82 [0.25, 2.73]
2 clinical pregnancy rate	1	103	Odds Ratio (M-H, Fixed, 95% CI)	1.03 [0.39, 2.75]
3 ectopic rate (per pregnancy)	1	20	Odds Ratio (M-H, Fixed, 95% CI)	0.13 [0.01, 3.11]

Comparison 5. Postoperative hydrotubation with steroids versus no postoperative hydrotubation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 live birth	1	120	Odds Ratio (M-H, Fixed, 95% CI)	0.47 [0.11, 1.99]
2 clinical pregnancy rate	1	120	Odds Ratio (M-H, Fixed, 95% CI)	0.82 [0.34, 1.96]
3 ectopic rate (per pregnancy)	1	26	Odds Ratio (M-H, Fixed, 95% CI)	3.67 [0.67, 20.19]

Comparison 6. Postoperative steroids (in addition to systemic intraoperative steroids) versus no postoperative steroids

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 improvement of adhesion score	1	75	Odds Ratio (M-H, Fixed, 95% CI)	4.83 [1.71, 13.65]
2 deterioration of adhesion score	1	95	Odds Ratio (M-H, Fixed, 95% CI)	0.25 [0.10, 0.65]

Comparison 7. Pre- versus postoperative steroids (in addition to systemic intraoperative steroids)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 improvement of adhesion score	1	28	Odds Ratio (M-H, Fixed, 95% CI)	0.4 [0.08, 1.91]
2 deterioration of adhesion score	1	57	Odds Ratio (M-H, Fixed, 95% CI)	1.06 [0.37, 3.04]

Comparison 8. Dextran versus no dextran

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 live birth	2	208	Odds Ratio (M-H, Fixed, 95% CI)	0.67 [0.29, 1.58]
2 clinical pregnancy rate	3	310	Odds Ratio (M-H, Fixed, 95% CI)	0.64 [0.36, 1.14]
3 ectopic pregnancy rate (per pregnancy)	2	50	Odds Ratio (M-H, Random, 95% CI)	0.38 [0.06, 2.40]
4 proportion of adhesions at second- look laparoscopy	2	268	Odds Ratio (M-H, Fixed, 95% CI)	0.33 [0.18, 0.59]
5 improvement of adhesion score	2	210	Odds Ratio (M-H, Random, 95% CI)	0.93 [0.46, 1.90]
6 deterioration of adhesion score	1	166	Odds Ratio (M-H, Fixed, 95% CI)	1.7 [0.86, 3.37]
7 mean adhesion score	2	196	Std. Mean Difference (IV, Random, 95% CI)	-0.02 [-0.37, 0.33]

Comparison 9. Hyaluronic acid versus no hyaluronic acid

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 proportion of adhesions at second- look laparoscopy	4	623	Odds Ratio (M-H, Fixed, 95% CI)	0.31 [0.19, 0.51]
2 improvement of adhesion score	2	342	Odds Ratio (M-H, Fixed, 95% CI)	1.55 [0.82, 2.92]
3 deterioration of adhesion score	2	342	Odds Ratio (M-H, Fixed, 95% CI)	0.28 [0.12, 0.66]
4 mean adhesion score	2	322	Std. Mean Difference (IV, Random, 95% CI)	-39.76 [-114.58, 35.07]

Comparison 10. SprayGel versus no SprayGel

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 proportion of adhesions at second-look laparoscopy	1	40	Odds Ratio (M-H, Fixed, 95% CI)	0.27 [0.05, 1.50]
2 improvement of adhesion score	1	31	Odds Ratio (M-H, Fixed, 95% CI)	1.5 [0.12, 18.54]
3 deterioration of adhesion score	1	31	Odds Ratio (M-H, Fixed, 95% CI)	0.18 [0.03, 1.06]
4 mean adhesion extent (cm2)	1	28	Std. Mean Difference (IV, Fixed, 95% CI)	Not estimable

Comparison 11. Icodextrin versus no icodextrin

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 proportion of adhesions at second look laparoscopy	1	53	Odds Ratio (M-H, Fixed, 95% CI)	0.48 [0.13, 1.68]
2 improvement of adhesion score	1	53	Odds Ratio (M-H, Fixed, 95% CI)	3.24 [0.86, 12.12]
3 deterioration of adhesion score	1	53	Odds Ratio (M-H, Fixed, 95% CI)	0.28 [0.07, 1.21]

Comparison 12. Intraperitoneal noxytioline versus no treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 clinical pregnancy rate	1	126	Odds Ratio (M-H, Fixed, 95% CI)	0.66 [0.30, 1.47]
2 ectopic pregnancy rate (per pregnancy)	1	33	Odds Ratio (M-H, Fixed, 95% CI)	4.91 [0.45, 53.27]
3 deterioration of adhesion score	1	87	Odds Ratio (M-H, Fixed, 95% CI)	0.55 [0.17, 1.76]

Comparison 13. Intraperitoneal heparin solution versus no intraperitoneal heparin

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 improvement of adhesion score	1	63	Odds Ratio (M-H, Fixed, 95% CI)	0.87 [0.32, 2.35]
2 deterioration of adhesion score	1	92	Odds Ratio (M-H, Fixed, 95% CI)	1.27 [0.56, 2.91]

Comparison 14. Systemic promethazine versus no promethazine

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 improvement of adhesion score	1	75	Odds Ratio (M-H, Fixed, 95% CI)	0.56 [0.22, 1.43]
2 deterioration of adhesion score	1	93	Odds Ratio (M-H, Fixed, 95% CI)	0.59 [0.25, 1.42]

Analysis 1.1. Comparison 1 Steroids (any route) versus no steroids, Outcome 1 live birth.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 1 Steroids (any route) versus no steroids

Outcome: 1 live birth

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Jansen 1985	6/56	6/47		50.5 %	0.82 [0.25, 2.73]
Rock 1984	3/60	6/60		49.5 %	0.47 [0.11, 1.99]
Total (95% CI)	**116**	**107**		**100.0 %**	**0.65 [0.26, 1.62]**

Total events: 9 (Treatment), 12 (Control)

Heterogeneity: Chi^2 = 0.33, df = 1 (P = 0.57); I^2 =0.0%

Test for overall effect: Z = 0.93 (P = 0.35)

Analysis 1.2. Comparison 1 Steroids (any route) versus no steroids, Outcome 2 clinical pregnancy rate.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 1 Steroids (any route) versus no steroids

Outcome: 2 clinical pregnancy rate

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Jansen 1985	32/87	28/77		44.7 %	1.02 [0.54, 1.92]
Querleu 1989	19/61	18/65		28.6 %	1.18 [0.55, 2.54]
Rock 1984	12/60	14/60		26.7 %	0.82 [0.34, 1.96]
Total (95% CI)	**208**	**202**		**100.0 %**	**1.01 [0.66, 1.55]**

Total events: 63 (Treatment), 60 (Control)

Heterogeneity: Chi^2 = 0.38, df = 2 (P = 0.83); I^2 =0.0%

Test for overall effect: Z = 0.06 (P = 0.96)

Analysis 1.3. Comparison 1 Steroids (any route) versus no steroids, Outcome 3 ectopic rate (per pregnancy).

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 1 Steroids (any route) versus no steroids

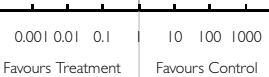
Outcome: 3 ectopic rate (per pregnancy)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Jansen 1985	0/11	2/9		25.2 %	0.13 [0.01, 3.11]
Querleu 1989	1/19	3/18		33.4 %	0.28 [0.03, 2.96]
Rock 1984	6/12	3/14		41.4 %	3.67 [0.67, 20.19]
Total (95% CI)	**42**	**41**		**100.0 %**	**0.67 [0.08, 5.70]**

Total events: 7 (Treatment), 8 (Control)

Heterogeneity: Tau^2 = 2.13; Chi^2 = 4.98, df = 2 (P = 0.08); I^2 =60%

Test for overall effect: Z = 0.37 (P = 0.71)



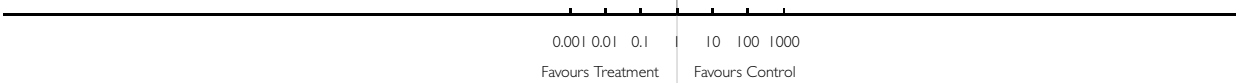
Analysis 1.4. Comparison 1 Steroids (any route) versus no steroids, Outcome 4 deterioration of adhesion score.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 1 Steroids (any route) versus no steroids

Outcome: 4 deterioration of adhesion score

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Querleu 1989	3/38	11/49		100.0 %	0.30 [0.08, 1.15]
Total (95% CI)	**38**	**49**		**100.0 %**	**0.30 [0.08, 1.15]**
Total events: 3 (Treatment), 11 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.76 (P = 0.079)					



Analysis 2.1. Comparison 2 Systemic steroids versus no steroids, Outcome 1 clinical pregnancy rate.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 2 Systemic steroids versus no steroids

Outcome: 1 clinical pregnancy rate

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Querleu 1989	19/61	18/65		100.0 %	1.18 [0.55, 2.54]
Total (95% CI)	**61**	**65**		**100.0 %**	**1.18 [0.55, 2.54]**
Total events: 19 (Treatment), 18 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.43 (P = 0.67)					

Analysis 2.2. Comparison 2 Systemic steroids versus no steroids, Outcome 2 ectopic rate (per pregnancy).

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 2 Systemic steroids versus no steroids

Outcome: 2 ectopic rate (per pregnancy)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Querleu 1989	1/19	3/18		100.0 %	0.28 [0.03, 2.96]
Total (95% CI)	**19**	**18**		**100.0 %**	**0.28 [0.03, 2.96]**
Total events: 1 (Treatment), 3 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.06 (P = 0.29)					

Analysis 2.3. Comparison 2 Systemic steroids versus no steroids, Outcome 3 deterioration of adhesion score.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 2 Systemic steroids versus no steroids

Outcome: 3 deterioration of adhesion score

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Querleu 1989	3/38	11/49		100.0 %	0.30 [0.08, 1.15]
Total (95% CI)	**38**	**49**		**100.0 %**	**0.30 [0.08, 1.15]**
Total events: 3 (Treatment), 11 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.76 (P = 0.079)					

Analysis 3.1. Comparison 3 Intraperitoneal steroids versus no steroids, Outcome 1 pregnancy (total).

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 3 Intraperitoneal steroids versus no steroids

Outcome: 1 pregnancy (total)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Jansen 1985	21/31	19/30		100.0 %	1.22 [0.42, 3.50]
Total (95% CI)	**31**	**30**		**100.0 %**	**1.22 [0.42, 3.50]**
Total events: 21 (Treatment), 19 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.36 (P = 0.72)					

Analysis 4.1. Comparison 4 Systemic and intraperitoneal steroids versus no steroids, Outcome 1 live birth.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 4 Systemic and intraperitoneal steroids versus no steroids

Outcome: 1 live birth

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Jansen 1985	6/56	6/47		100.0 %	0.82 [0.25, 2.73]
Total (95% CI)	**56**	**47**		**100.0 %**	**0.82 [0.25, 2.73]**
Total events: 6 (Treatment), 6 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.32 (P = 0.75)					

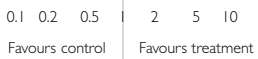
Analysis 4.2. Comparison 4 Systemic and intraperitoneal steroids versus no steroids, Outcome 2 clinical pregnancy rate.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 4 Systemic and intraperitoneal steroids versus no steroids

Outcome: 2 clinical pregnancy rate

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Jansen 1985	11/56	9/47		100.0 %	1.03 [0.39, 2.75]
Total (95% CI)	**56**	**47**		**100.0 %**	**1.03 [0.39, 2.75]**
Total events: 11 (Treatment), 9 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.06 (P = 0.95)					



Analysis 4.3. Comparison 4 Systemic and intraperitoneal steroids versus no steroids, Outcome 3 ectopic rate (per pregnancy).

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 4 Systemic and intraperitoneal steroids versus no steroids

Outcome: 3 ectopic rate (per pregnancy)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Jansen 1985	0/11	2/9		100.0 %	0.13 [0.01, 3.11]
Total (95% CI)	**11**	**9**		**100.0 %**	**0.13 [0.01, 3.11]**
Total events: 0 (Treatment), 2 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.26 (P = 0.21)					

Analysis 5.1. Comparison 5 Postoperative hydrotubation with steroids versus no postoperative hydrotubation, Outcome 1 live birth.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 5 Postoperative hydrotubation with steroids versus no postoperative hydrotubation

Outcome: 1 live birth

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Rock 1984	3/60	6/60		100.0 %	0.47 [0.11, 1.99]
Total (95% CI)	**60**	**60**		**100.0 %**	**0.47 [0.11, 1.99]**
Total events: 3 (Treatment), 6 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.02 (P = 0.31)					

Analysis 5.2. Comparison 5 Postoperative hydrotubation with steroids versus no postoperative hydrotubation, Outcome 2 clinical pregnancy rate.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 5 Postoperative hydrotubation with steroids versus no postoperative hydrotubation

Outcome: 2 clinical pregnancy rate

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Rock 1984	12/60	14/60		100.0 %	0.82 [0.34, 1.96]
Total (95% CI)	**60**	**60**		**100.0 %**	**0.82 [0.34, 1.96]**
Total events: 12 (Treatment), 14 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.44 (P = 0.66)					

Analysis 5.3. Comparison 5 Postoperative hydrotubation with steroids versus no postoperative hydrotubation, Outcome 3 ectopic rate (per pregnancy).

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 5 Postoperative hydrotubation with steroids versus no postoperative hydrotubation

Outcome: 3 ectopic rate (per pregnancy)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Rock 1984	6/12	3/14		100.0 %	3.67 [0.67, 20.19]
Total (95% CI)	**12**	**14**		**100.0 %**	**3.67 [0.67, 20.19]**
Total events: 6 (Treatment), 3 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.49 (P = 0.14)					

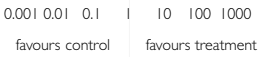
Analysis 6.1. Comparison 6 Postoperative steroids (in addition to systemic intraoperative steroids) versus no postoperative steroids, Outcome 1 improvement of adhesion score.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 6 Postoperative steroids (in addition to systemic intraoperative steroids) versus no postoperative steroids

Outcome: 1 improvement of adhesion score

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Jansen 1990a	29/36	18/39		100.0 %	4.83 [1.71, 13.65]
Total (95% CI)	**36**	**39**		**100.0 %**	**4.83 [1.71, 13.65]**
Total events: 29 (Treatment), 18 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.97 (P = 0.0029)					



Analysis 6.2. Comparison 6 Postoperative steroids (in addition to systemic intraoperative steroids) versus no postoperative steroids, Outcome 2 deterioration of adhesion score.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 6 Postoperative steroids (in addition to systemic intraoperative steroids) versus no postoperative steroids

Outcome: 2 deterioration of adhesion score

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Jansen 1990a	8/45	23/50		100.0 %	0.25 [0.10, 0.65]
Total (95% CI)	**45**	**50**		**100.0 %**	**0.25 [0.10, 0.65]**
Total events: 8 (Treatment), 23 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.84 (P = 0.0045)					

Analysis 7.1. Comparison 7 Pre- versus postoperative steroids (in addition to systemic intraoperative steroids), Outcome 1 improvement of adhesion score.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 7 Pre- versus postoperative steroids (in addition to systemic intraoperative steroids)

Outcome: 1 improvement of adhesion score

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Jansen 1990b	4/14	7/14		100.0 %	0.40 [0.08, 1.91]
Total (95% CI)	**14**	**14**		**100.0 %**	**0.40 [0.08, 1.91]**
Total events: 4 (Treatment), 7 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.15 (P = 0.25)					

Analysis 7.2. Comparison 7 Pre- versus postoperative steroids (in addition to systemic intraoperative steroids), Outcome 2 deterioration of adhesion score.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 7 Pre- versus postoperative steroids (in addition to systemic intraoperative steroids)

Outcome: 2 deterioration of adhesion score

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Jansen 1990b	17/29	16/28		100.0 %	1.06 [0.37, 3.04]
Total (95% CI)	**29**	**28**		**100.0 %**	**1.06 [0.37, 3.04]**
Total events: 17 (Treatment), 16 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.11 (P = 0.91)					

Analysis 8.1. Comparison 8 Dextran versus no dextran, Outcome 1 live birth.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 8 Dextran versus no dextran

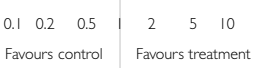
Outcome: 1 live birth

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Jansen 1985	4/50	8/53		54.4 %	0.49 [0.14, 1.74]
Larsson 1985	6/51	7/54		45.6 %	0.90 [0.28, 2.87]
Total (95% CI)	**101**	**107**		**100.0 %**	**0.67 [0.29, 1.58]**

Total events: 10 (Treatment), 15 (Control)

Heterogeneity: Chi^2 = 0.47, df = 1 (P = 0.49); I^2 =0.0%

Test for overall effect: Z = 0.91 (P = 0.36)



Analysis 8.2. Comparison 8 Dextran versus no dextran, Outcome 2 clinical pregnancy rate.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 8 Dextran versus no dextran

Outcome: 2 clinical pregnancy rate

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Adhesion SG 1983	4/55	7/47		24.0 %	0.45 [0.12, 1.64]
Jansen 1985	9/50	11/53		30.1 %	0.84 [0.31, 2.23]
Larsson 1985	12/51	18/54		45.9 %	0.62 [0.26, 1.45]
Total (95% CI)	**156**	**154**		**100.0 %**	**0.64 [0.36, 1.14]**

Total events: 25 (Treatment), 36 (Control)

Heterogeneity: Chi^2 = 0.59, df = 2 (P = 0.75); I^2 =0.0%

Test for overall effect: Z = 1.51 (P = 0.13)

Analysis 8.3. Comparison 8 Dextran versus no dextran, Outcome 3 ectopic pregnancy rate (per pregnancy).

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 8 Dextran versus no dextran

Outcome: 3 ectopic pregnancy rate (per pregnancy)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Jansen 1985	1/9	1/11		38.2 %	1.25 [0.07, 23.26]
Larsson 1985	1/12	6/18		61.8 %	0.18 [0.02, 1.76]
Total (95% CI)	**21**	**29**		**100.0 %**	**0.38 [0.06, 2.40]**

Total events: 2 (Treatment), 7 (Control)

Heterogeneity: $Tau^2 = 0.09$; $Chi^2 = 1.05$, df = 1 (P = 0.31); I^2 =5%

Test for overall effect: Z = 1.03 (P = 0.30)

Analysis 8.4. Comparison 8 Dextran versus no dextran, Outcome 4 proportion of adhesions at second- look laparoscopy.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 8 Dextran versus no dextran

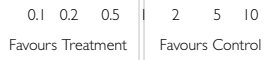
Outcome: 4 proportion of adhesions at second- look laparoscopy

Study or subgroup	Control n/N	Treatment n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Adhesion SG 1983	13/55	24/47		49.2 %	0.30 [0.13, 0.69]
Jansen 1985	56/78	77/88		50.8 %	0.36 [0.16, 0.81]
Total (95% CI)	**133**	**135**		**100.0 %**	**0.33 [0.18, 0.59]**

Total events: 69 (Control), 101 (Treatment)

Heterogeneity: $Chi^2 = 0.12$, df = 1 (P = 0.73); I^2 =0.0%

Test for overall effect: Z = 3.73 (P = 0.00019)

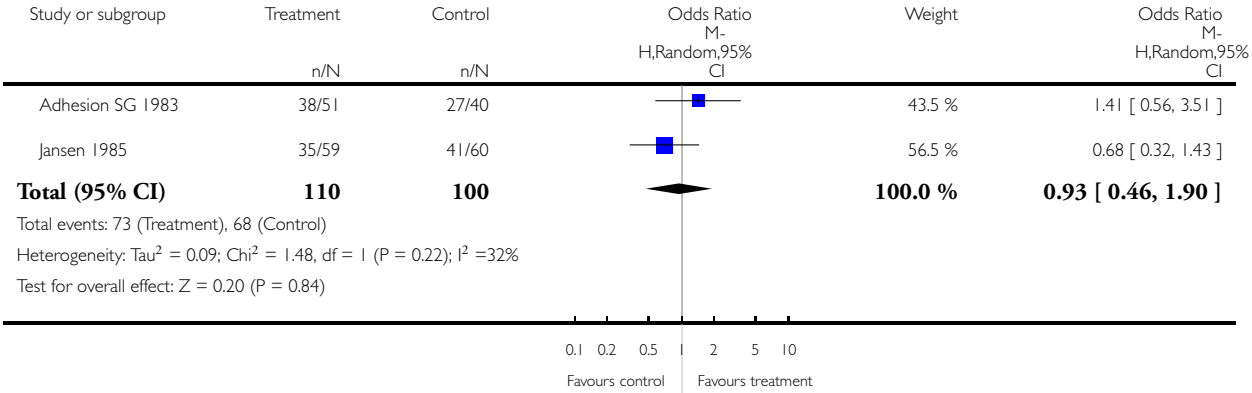


Analysis 8.5. Comparison 8 Dextran versus no dextran, Outcome 5 improvement of adhesion score.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 8 Dextran versus no dextran

Outcome: 5 improvement of adhesion score

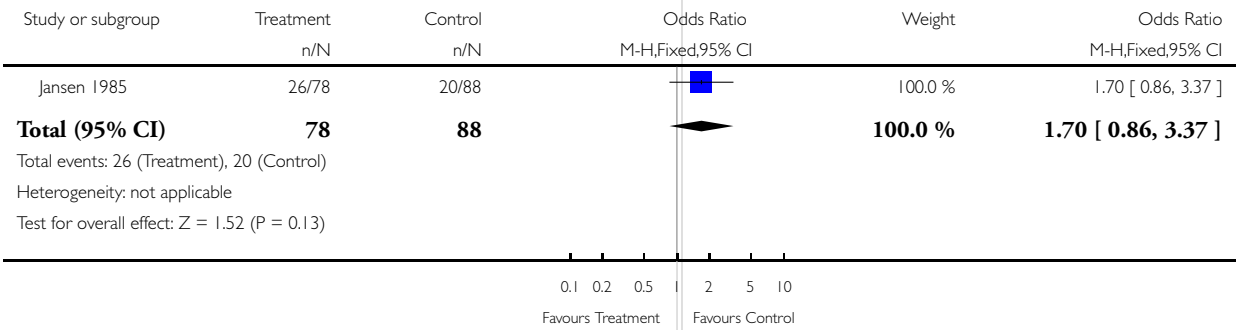


Analysis 8.6. Comparison 8 Dextran versus no dextran, Outcome 6 deterioration of adhesion score.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 8 Dextran versus no dextran

Outcome: 6 deterioration of adhesion score



Analysis 8.7. Comparison 8 Dextran versus no dextran, Outcome 7 mean adhesion score.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

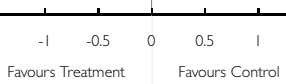
Comparison: 8 Dextran versus no dextran

Outcome: 7 mean adhesion score

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Adhesion SG 1983	51	3.63 (5.78)	40	4.83 (5.75)		47.4 %	-0.21 [-0.62, 0.21]
Larsson 1985	51	6.92 (5.68)	54	6.07 (5.58)		52.6 %	0.15 [-0.23, 0.53]
Total (95% CI)	**102**		**94**			**100.0 %**	**-0.02 [-0.37, 0.33]**

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 1.53$, df = 1 (P = 0.22); $I^2 = 35\%$

Test for overall effect: Z = 0.11 (P = 0.92)



Analysis 9.1. Comparison 9 Hyaluronic acid versus no hyaluronic acid, Outcome 1 proportion of adhesions at second- look laparoscopy.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 9 Hyaluronic acid versus no hyaluronic acid

Outcome: 1 proportion of adhesions at second- look laparoscopy

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Diamond 1998	119/137	103/108		25.1 %	0.32 [0.12, 0.89]
Johns 2001	12/131	33/134		49.2 %	0.31 [0.15, 0.63]
Lundorff 2001	4/38	6/39		8.8 %	0.65 [0.17, 2.50]
Pellicano 2003	5/18	14/18		16.8 %	0.11 [0.02, 0.50]
Total (95% CI)	**324**	**299**		**100.0 %**	**0.31 [0.19, 0.51]**

Total events: 140 (Treatment), 156 (Control)

Heterogeneity: $Chi^2 = 2.94$, df = 3 (P = 0.40); $I^2 = 0.0\%$

Test for overall effect: Z = 4.60 (P < 0.00001)

Analysis 9.2. Comparison 9 Hyaluronic acid versus no hyaluronic acid, Outcome 2 improvement of adhesion score.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 9 Hyaluronic acid versus no hyaluronic acid

Outcome: 2 improvement of adhesion score

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Johns 2001	18/131	12/134		66.0 %	1.62 [0.75, 3.51]
Lundorff 2001	9/38	7/39		34.0 %	1.42 [0.47, 4.30]
Total (95% CI)	**169**	**173**		**100.0 %**	**1.55 [0.82, 2.92]**
Total events: 27 (Treatment), 19 (Control)					
Heterogeneity: Chi^2 = 0.04, df = 1 (P = 0.85); I^2 =0.0%					
Test for overall effect: Z = 1.36 (P = 0.17)					

Analysis 9.3. Comparison 9 Hyaluronic acid versus no hyaluronic acid, Outcome 3 deterioration of adhesion score.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 9 Hyaluronic acid versus no hyaluronic acid

Outcome: 3 deterioration of adhesion score

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Johns 2001	7/131	20/134		81.0 %	0.32 [0.13, 0.79]
Lundorff 2001	0/38	4/39		19.0 %	0.10 [0.01, 1.97]
Total (95% CI)	**169**	**173**		**100.0 %**	**0.28 [0.12, 0.66]**

Total events: 7 (Treatment), 24 (Control)

Heterogeneity: Chi^2 = 0.54, df = 1 (P = 0.46); I^2 =0.0%

Test for overall effect: Z = 2.93 (P = 0.0033)

Analysis 9.4. Comparison 9 Hyaluronic acid versus no hyaluronic acid, Outcome 4 mean adhesion score.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

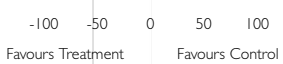
Comparison: 9 Hyaluronic acid versus no hyaluronic acid

Outcome: 4 mean adhesion score

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Diamond 1998	137	0.2 (0.06)	108	0.32 (0.07)		50.4 %	-1.85 [-2.15, -1.55]
Lundorff 2001	38	0.46 (0.01)	39	1.25 (0.01)		49.6 %	-78.21 [-90.90, -65.52]
Total (95% CI)	**175**		**147**			**100.0 %**	**-39.76 [-114.58, 35.07]**

Heterogeneity: Tau^2 = 2894.10; Chi^2 = 139.03, df = 1 (P<0.00001); I^2 =99%

Test for overall effect: Z = 1.04 (P = 0.30)



Analysis 10.1. Comparison 10 SprayGel versus no SprayGel, Outcome 1 proportion of adhesions at second-look laparoscopy.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 10 SprayGel versus no SprayGel

Outcome: 1 proportion of adhesions at second-look laparoscopy

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Mettler 2004	15/22	16/18		100.0 %	0.27 [0.05, 1.50]
Total (95% CI)	**22**	**18**		**100.0 %**	**0.27 [0.05, 1.50]**
Total events: 15 (Treatment), 16 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.50 (P = 0.13)					

Analysis 10.2. Comparison 10 SprayGel versus no SprayGel, Outcome 2 improvement of adhesion score.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 10 SprayGel versus no SprayGel

Outcome: 2 improvement of adhesion score

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Mettler 2004	2/18	1/13		100.0 %	1.50 [0.12, 18.54]
Total (95% CI)	**18**	**13**		**100.0 %**	**1.50 [0.12, 18.54]**
Total events: 2 (Treatment), 1 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.32 (P = 0.75)					

Analysis 10.3. Comparison 10 SprayGel versus no SprayGel, Outcome 3 deterioration of adhesion score.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 10 SprayGel versus no SprayGel

Outcome: 3 deterioration of adhesion score

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Mettler 2004	9/18	11/13		100.0 %	0.18 [0.03, 1.06]
Total (95% CI)	**18**	**13**		**100.0 %**	**0.18 [0.03, 1.06]**
Total events: 9 (Treatment), 11 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.89 (P = 0.059)					

Analysis 10.4. Comparison 10 SprayGel versus no SprayGel, Outcome 4 mean adhesion extent (cm2).

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 10 SprayGel versus no SprayGel

Outcome: 4 mean adhesion extent (cm2)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
Johns 2003	14	10.97 (13.61)	14	25.04 (21.02)		100.0 %	-0.77 [-1.54, 0.00]
Total (95% CI)	**14**		**14**			**100.0 %**	**-0.77 [-1.54, 0.00]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.96 (P = 0.050)							
Test for subgroup differences: Not applicable							

Analysis 11.1. Comparison 11 Icodextrin versus no icodextrin, Outcome 1 proportion of adhesions at second look laparoscopy.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 11 Icodextrin versus no icodextrin

Outcome: 1 proportion of adhesions at second look laparoscopy

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
diZerega 2002	18/27	21/26		100.0 %	0.48 [0.13, 1.68]
Total (95% CI)	**27**	**26**		**100.0 %**	**0.48 [0.13, 1.68]**
Total events: 18 (Treatment), 21 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.15 (P = 0.25)					

Analysis 11.2. Comparison 11 Icodextrin versus no icodextrin, Outcome 2 improvement of adhesion score.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 11 Icodextrin versus no icodextrin

Outcome: 2 improvement of adhesion score

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
diZerega 2002	10/27	4/26		100.0 %	3.24 [0.86, 12.12]
Total (95% CI)	**27**	**26**		**100.0 %**	**3.24 [0.86, 12.12]**
Total events: 10 (Treatment), 4 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.74 (P = 0.082)					

Analysis 11.3. Comparison 11 Icodextrin versus no icodextrin, Outcome 3 deterioration of adhesion score.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 11 Icodextrin versus no icodextrin

Outcome: 3 deterioration of adhesion score

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
diZerega 2002	3/27	8/26		100.0 %	0.28 [0.07, 1.21]
Total (95% CI)	**27**	**26**		**100.0 %**	**0.28 [0.07, 1.21]**

Total events: 3 (Treatment), 8 (Control)

Heterogeneity: not applicable

Test for overall effect: Z = 1.70 (P = 0.089)

Analysis 12.1. Comparison 12 Intraperitoneal noxytioline versus no treatment, Outcome 1 clinical pregnancy rate.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 12 Intraperitoneal noxytioline versus no treatment

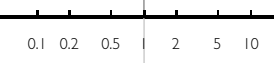
Outcome: 1 clinical pregnancy rate

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Querleu 1989	14/63	19/63		100.0 %	0.66 [0.30, 1.47]
Total (95% CI)	**63**	**63**		**100.0 %**	**0.66 [0.30, 1.47]**

Total events: 14 (Treatment), 19 (Control)

Heterogeneity: not applicable

Test for overall effect: Z = 1.01 (P = 0.31)

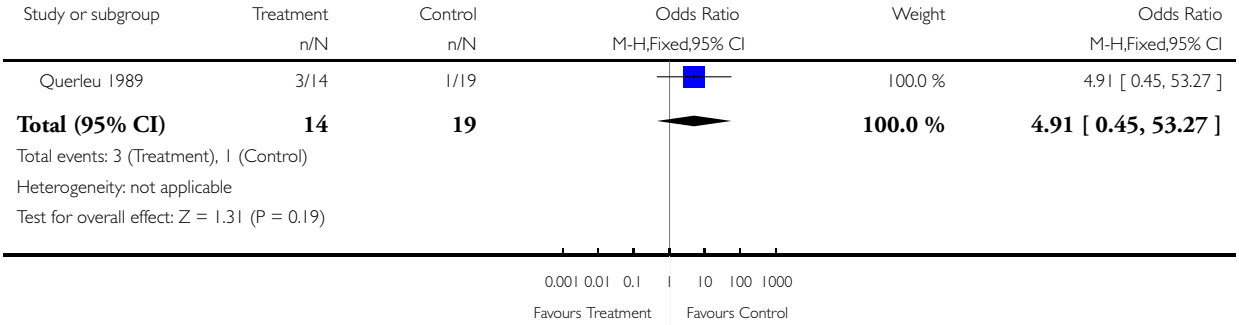


Analysis 12.2. Comparison 12 Intraperitoneal noxytioline versus no treatment, Outcome 2 ectopic pregnancy rate (per pregnancy).

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 12 Intraperitoneal noxytioline versus no treatment

Outcome: 2 ectopic pregnancy rate (per pregnancy)

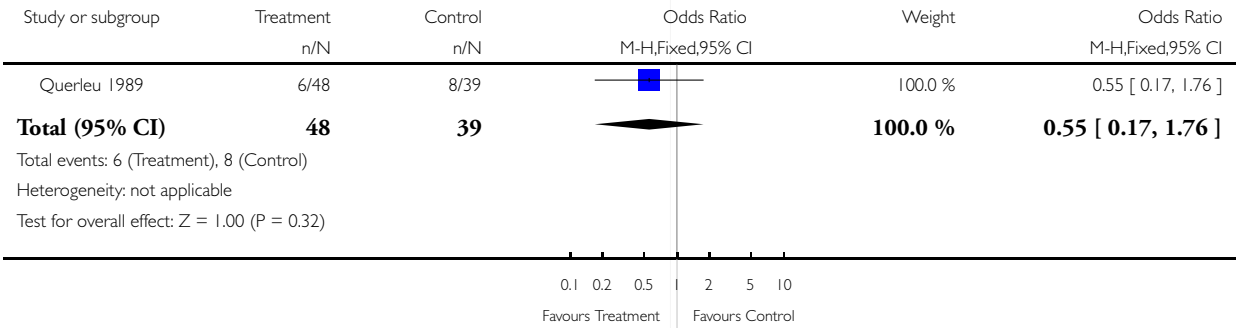


Analysis 12.3. Comparison 12 Intraperitoneal noxytioline versus no treatment, Outcome 3 deterioration of adhesion score.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 12 Intraperitoneal noxytioline versus no treatment

Outcome: 3 deterioration of adhesion score



Analysis 13.1. Comparison 13 Intraperitoneal heparin solution versus no intraperitoneal heparin, Outcome 1 improvement of adhesion score.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 13 Intraperitoneal heparin solution versus no intraperitoneal heparin

Outcome: 1 improvement of adhesion score

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Jansen 1988	15/28	20/35		100.0 %	0.87 [0.32, 2.35]
Total (95% CI)	**28**	**35**		**100.0 %**	**0.87 [0.32, 2.35]**
Total events: 15 (Treatment), 20 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.28 (P = 0.78)					

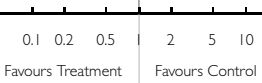
Analysis 13.2. Comparison 13 Intraperitoneal heparin solution versus no intraperitoneal heparin, Outcome 2 deterioration of adhesion score.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 13 Intraperitoneal heparin solution versus no intraperitoneal heparin

Outcome: 2 deterioration of adhesion score

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Jansen 1988	20/44	19/48		100.0 %	1.27 [0.56, 2.91]
Total (95% CI)	**44**	**48**		**100.0 %**	**1.27 [0.56, 2.91]**
Total events: 20 (Treatment), 19 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.57 (P = 0.57)					



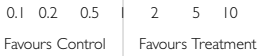
Analysis 14.1. Comparison 14 Systemic promethazine versus no promethazine, Outcome 1 improvement of adhesion score.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 14 Systemic promethazine versus no promethazine

Outcome: 1 improvement of adhesion score

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Jansen 1990a	20/36	27/39		100.0 %	0.56 [0.22, 1.43]
Total (95% CI)	**36**	**39**		**100.0 %**	**0.56 [0.22, 1.43]**
Total events: 20 (Treatment), 27 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.22 (P = 0.22)					



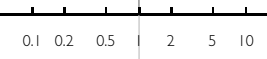
Analysis 14.2. Comparison 14 Systemic promethazine versus no promethazine, Outcome 2 deterioration of adhesion score.

Review: Fluid and pharmacological agents for adhesion prevention after gynaecological surgery

Comparison: 14 Systemic promethazine versus no promethazine

Outcome: 2 deterioration of adhesion score

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Jansen 1990a	13/47	18/46		100.0 %	0.59 [0.25, 1.42]
Total (95% CI)	**47**	**46**		**100.0 %**	**0.59 [0.25, 1.42]**
Total events: 13 (Treatment), 18 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.17 (P = 0.24)					



ADDITIONAL TABLES

Table 1. Risk of bias assessment of included studies

Study	Allocation concealment	Randomisation method	Blinding	ITT analysis	Power calculation
Adhesion SG 1983	Yes	True	Yes	No	No
Diamond 1998	Yes	True	Yes	No	No
diZerega 2002	Yes	True	Yes	No	No
Jansen 1985	Yes	True	Yes	No	Yes
Jansen 1988	Yes	True	Yes	No	Yes
Jansen 1990a	No	True	No	No	Yes
Jansen 1990b	No	True	No	No	Yes
Johns 2001	No	True	Yes	No	No
Johns 2003	Yes	True	Yes	Yes	No
Larsson 1985	No	True	Yes	No	No
Lundorff 2001	No	True	Yes	No	No
Mettler 2004	Yes	True	Yes	Yes	No
Pellicano 2003	Yes	True	Yes	Yes	No
Querleu 1989	No	Method not stated	No	No	Yes
Rock 1984	Yes	True	No	No	No
Rosenberg 1984	Yes	True	Yes	No	No

WHAT'S NEW

Last assessed as up-to-date: 12 January 2006.

Date	Event	Description
9 February 2011	Review declared as stable	This review is going to merge into the review: Ahmad G, Duffy JMN, Farquhar C, Vail A, Vanderkerchove P, Watson A, Wiseman D. Barrier agents for adhesion prevention after gynaecological surgery. Cochrane Database of Systematic Reviews

(*Continued*)

		2008, Issue 2. Art. No.: CD000475. DOI: 10.1002/14651858.CD000475.pub2

HISTORY

Protocol first published: Issue 1, 1998

Review first published: Issue 4, 1998

Date	Event	Description
7 November 2008	Amended	Converted to new review format.
13 January 2006	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

MEM: contact author and the primary reviewer of this update.

AW: senior co-author and contact reviewer for the original review.

PV: co-author of the original review

RL: co-author of the original review

DECLARATIONS OF INTEREST

Watson A has received lecture fees from Gynecare and Shire. Gynecare is the manufacturer of Intergel. The same author has received consultancy fees from NL laboratories, the manufacturer of Adept.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- Yorkshire Regional Health Authority Research & Development Unit, UK.

NOTES

This review is going to merge into the review: Ahmad G, Duffy JMN, Farquhar C, Vail A, Vanderkerchove P, Watson A, Wiseman D. Barrier agents for adhesion prevention after gynaecological surgery. Cochrane Database of Systematic Reviews 2008, Issue 2. Art. No.: CD000475. DOI: 10.1002/14651858.CD000475.pub2.

INDEX TERMS

Medical Subject Headings (MeSH)

Anticoagulants [*therapeutic use]; Glucocorticoids [*therapeutic use]; Gynecologic Surgical Procedures [*adverse effects]; Infertility, Female [prevention & control]; Plasma Substitutes [*therapeutic use]; Randomized Controlled Trials as Topic; Rehydration Solutions [*therapeutic use]; Tissue Adhesions [prevention & control]

MeSH check words

Female; Humans