Efficacy of auto-crosslinked hyaluronan gel for adhesion prevention in laparoscopy and hysteroscopy: a systematic review and meta-analysis of randomized controlled trials

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CRD summary
The review concluded that auto-crosslinked hyaluronan gel significantly reduced the number of intraperitoneal adhesions after laparoscopic myomectomy and intrauterine adhesions after hysteroscopic surgery. The review was generally well conducted, but the limited evidence base and potential for missed studies means the authors’ conclusions should be considered tentative.

Authors’ objectives
To assess the efficacy of auto-crosslinked hyaluronan gel for postoperative adhesion prevention following endoscopic gynaecological surgery.

Searching
MEDLINE, EMBASE and The Cochrane Library were searched for relevant studies from inception to October 2010 without restrictions. Search terms were reported. The reference lists of retrieved studies and reviews were also searched, and requests for additional studies were made from the authors of relevant studies.

Study selection
Randomised controlled trials (RCTs) that investigated the use of auto-crosslinked hyaluronan gel to prevent postoperative intraperitoneal or intrauterine adhesion formation in women who underwent gynaecological surgery were eligible for the review. The outcome of interest was incidence of postoperative adhesions at blind second look in women who underwent surgery with application of auto-crosslinked hyaluronan gel, compared with women who underwent surgery alone. Reviews and abstracts were excluded.

Three of the included studies performed hysteroscopy and two studies performed laparoscopic myomectomy. All studies used the same hyaluronan gel, Hyalobarrier. The mean age of participants ranged from 29 to 37 years, where reported. The adhesions score, where reported, was either based on the American Fertility Society classification or the Operative Laparoscopy Study Group classification. Timing of the second look after surgery ranged from 60 days to 98 days.

Two reviewers independently selected studies for the review.

Assessment of study quality
Studies were assessed for quality using the Jadad scale. Criteria included adequate randomisation, blinding, and an adequate description of withdrawals and drop-outs. Studies were considered high quality if the overall Jadad score was at least three points.

Three reviewers independently assessed studies for quality, with inconsistencies resolved through discussion and consensus.

Data extraction
Data were extracted on the incidence of postoperative adhesions to enable calculation of odds ratios (ORs), with corresponding 95% confidence intervals (CIs). Where continuous data were presented graphically, the data were not considered in meta-analyses.

Three reviewers independently extracted data for the review.

Methods of synthesis
Effect sizes, with 95% confidence intervals, were pooled in meta-analyses using a fixed-effect model unless statistical heterogeneity was identified; in which case a random-effects model was used. Adverse effects were assessed.
narratively. Heterogeneity was assessed with $\chi^2$ (with a value of $P<0.1$ being considered significant). Publication bias was assessed by the Duval and Tweedie trim and fill method.

**Results of the review**
Five randomised controlled trials (RCTs) (335 women) were included in the review. All studies had an overall Jadad score of 3 or greater.

Compared to controls who had surgery alone, surgery plus auto-crosslinked hyaluronan gel was associated with a significant reduction in the incidence of postoperative adhesions after laparoscopic myomectomy (OR 0.24, 95% CI 0.10 to 0.63; two studies) and after hysteroscopic surgery (OR 0.41, 95% CI 0.22 to 0.77; three studies). There was no evidence of significant heterogeneity between groups. The analysis of publication bias indicated minimal risk of bias.

In the two laparoscopic myomectomy trials, six adverse events were reported; three in the gel groups and three in the surgery only groups. No adverse events were reported in the three trials using hysteroscopy.

**Authors’ conclusions**
Auto-crosslinked hyaluronan gel significantly reduced the number of intraperitoneal adhesions after laparoscopic myomectomy and intrauterine adhesions after hysteroscopic surgery.

**CRD commentary**
The review addressed a clear research question, supported by appropriate inclusion criteria. Relevant sources were searched for studies without language or publication restriction. Although no specific attempts were made to find unpublished studies, some attempt was made to investigate publication bias. This analysis reported minimal publication bias, but there were too few studies to adequately assess this formally. Appropriate methods were used to select studies, extract data and assess studies for quality, which minimised the chance of reviewer error or bias. A valid tool was used for quality assessment. The included studies were few in number and had small sample sizes, but they were all considered high quality. Synthesis of studies and assessment of heterogeneity were appropriate. The review was generally well conducted, but the limited evidence base and potential for missed studies means the authors’ conclusions should be considered tentative.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that further RCTs were needed that assessed the use of auto-crosslinked hyaluronan gel in the prevention of postoperative adhesions in patients who underwent different laparoscopic intra-abdominal surgical procedures, gynaecological, urologic and general surgery.

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