The pain-relieving effect of electro-acupuncture and conventional medical analgesic methods during oocyte retrieval: a systematic review of randomized controlled trials

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CRD summary
This review assessed pain relief from acupuncture and other conscious sedation methods used in assisted reproduction therapy. The author concluded that no method was found to be superior for pain relief during oocyte removal, and clinical pregnancy rates appeared similar between interventions. Limitations in the search and study selection process may have introduced bias into the review.

Authors' objectives
To compare the effects of different methods of conscious sedation on pain relief and pregnancy rates in couples undergoing assisted reproduction techniques.

Searching
MEDLINE was searched from 1990 to 2004; the search terms were reported. In addition, the bibliographies of relevant papers were checked. Only published articles were included in the review.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Different methods of conscious sedation were eligible: electro-acupuncture (EA) with a paracervical block (PCB); different combinations of intravenous sedatives (midazolam, fentanyl, diazepam, pethidine and alfentanil); different combinations of intramuscular sedatives (midazolam or promethazine); PCB alone; or PCB in combination with sedatives. The included studies assessed various treatments which were categorised as: intravenous versus intramuscular sedatives; patient versus physician administration; PCB versus placebo or no treatment; comparisons of two types or doses of drugs used for PCB; intravenous sedation and PCB versus placebo and PCB; EA and PCB versus intravenous sedation and PCB; EA and PCB versus PCB with intravenous sedation and diazepam.

Participants included in the review
Studies of patients undergoing oocyte retrieval whilst conscious and without needing an anaesthesiologist were eligible. The mean age of the included women ranged from 30.6 to 35.1 years.

Outcomes assessed in the review
Pain and clinical pregnancy rate per in vitro fertilisation (IVF) cycle were the outcomes specified by the inclusion criteria. The primary outcome was pain during oocyte retrieval. The secondary outcome of the review was the clinical pregnancy rate per IVF cycle started. The review also assessed abdominal pain after oocyte retrieval. Most of the studies used a visual analogue scale (VAS) to record pain but two used 4- or 5-point scales.

How were decisions on the relevance of primary studies made?
One reviewer selected studies for the review.

Assessment of study quality
Study validity was assessed using eight criteria: randomisation, allocation concealment, blinding, use of a cointervention, completeness of follow-up, sample size calculation, use of a crossover design, and differentiation of patients and cycles. Quality scores could range from 3 (worst) to 21 (best). The author stated that the reviewer process
was completed independently, but no further details were provided.

**Data extraction**
The author stated that the reviewer process was completed independently, but no further details were provided. Means and standard deviations of the average and maximum pain intensity during oocyte removal and of abdominal pain 1 to 2 hours after removal were extracted where possible. The numbers of clinical pregnancies were used to calculate odds ratios (ORs).

**Methods of synthesis**
How were the studies combined?
For studies that were judged to be sufficiently similar, weighted mean differences (WMDs) and pooled ORs were calculated using fixed-effects models.

How were differences between studies investigated?
Statistical heterogeneity was assessed using a chi-squared test.

**Results of the review**
Twelve RCTs (n=1,646) were included.

Most of the trials were of moderate to high quality, with nine scoring 12 or more out of a maximum of 21 (scores ranged from 6 to 16).

The studies assessed different combinations of sedation methods. Only three studies that compared EA plus PCB (using lidocain) with intravenous alfentanil (with and without diazepam) were considered similar enough for pooling. These showed a significant reduction in average pain during oocyte removal which favoured the alfentanil group (WMD 5.08, 95% CI: 2.18, 7.99; heterogeneity p=0.25). Alfentanil was also associated with a significant reduction in abdominal pain 1 to 2 hours after the procedure (WMD 6.03, 95% CI: 2.22, 9.85; heterogeneity p=0.018), but there was no significant difference between interventions for maximum pain (WMD -1.91, 95% CI: -3.92, 0.09; heterogeneity p=0.025). In terms of pregnancy rates, there was no significant difference between the EA and alfentanil groups (OR 0.99, 95% CI: 0.71, 1.37; heterogeneity p=0.21).

The results from other studies were reported in the 'Discussion' section of the paper.

One study (n=51 in each treatment arm) compared three different strengths of lignocaine (0.5%, 1.0% and 1.5%) for PCB and reported no increased improvement in maximum pain intensity during oocyte removal when using higher concentrations of lidocain.

**Authors' conclusions**
No method was found to be superior to another and no consensus on which method was best for pain relief during oocyte removal could be reached; clinical pregnancy rates were found to be similar. Low doses of lignocaine can be recommended in PCB and EA without premedication.

**CRD commentary**
This review addressed a clear research question and specified inclusion criteria for the study design, interventions and outcomes. The search was fairly limited as it only involved searches of MEDLINE and bibliographies, and only published studies were included in the review. This means that other relevant unpublished studies might have been missed. The quality assessment and data extraction appear to have been performed independently, but not the study selection, which, as the author discussed, increases the risk of bias. Study quality was assessed using relevant questions for RCTs and full results were presented for each study.

Only three studies were considered similar enough to be combined in a meta-analysis, the methods of which appear
reliable. However, a number of other studies used similar pain outcome measures and it was unclear why these were not also included in meta-analyses. There was little discussion of the results of studies assessing interventions other than EA, and the presentation of their results made it difficult to assess which interventions were beneficial. The meta-analysis provided conflicting results depending on whether average or maximum pain was used as the outcome, and the author highlighted the limitations of using VASs to measure pain. The author's conclusion, that no consensus could be made about which method was best for pain relief, appears reliable, although the limited search strategy and study selection by one person increases the risk of bias. However, the recommendation about lignocaine is not supported by the results presented.

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

**Practice:** The author stated that low doses of lignocaine can be recommended for pain relief in PCB, as well as EA without premedication. Conscious sedation is appropriate in patients who are willing and cooperative. As pain is subjective, the optimal method of conscious sedation should be made on an individual basis.

**Research:** The author stated that further research is needed to identify the impact and significance of different needle locations and stimulation frequencies in EA. There is also a need to examine the effects of method of analgesia on IVF outcomes. Only RCTs should be conducted in future, using standardised outcome measures, measuring pain during oocyte removal, and using newer methods of pain assessment.

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