

# Electro-acupuncture versus conventional analgesia: a comparison of pain levels during oocyte aspiration and patients' experiences of well-being after surgery

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**BACKGROUND:** The primary aims were to compare the pain-relieving effect and post-operative well-being between electro-acupuncture analgesia (EA) and conventional analgesia (CA) comprising opiates. Further aims were to compare time for mobilization, and costs for time and drug consumption. **METHODS:** In all, 160 women undergoing IVF were randomized, according to a computer-generated list, to EA or CA. Well-being was evaluated with the State Trait Anxiety Inventory (STAI). Pain and subjective expectations and experiences were recorded on a visual analogue scale (VAS). Time and drug consumption were recorded. **RESULTS:** Although VAS pain ratings were significantly higher at oocyte aspiration ( $P < 0.0001$ ) and after retrieval ( $P < 0.01$ ) in the EA than in the CA group, they were similar 60 min after surgery. Both groups had similar STAI well-being scores. The EA group was significantly less tired and confused than the CA group after oocyte aspiration. No significant differences in time and costs for drug consumption were noted. **CONCLUSION:** EA cannot generally be recommended as a pain-relieving method at oocyte aspiration but might be an alternative for women desiring a non-pharmacological method. An advantage of EA is less post-operative tiredness and confusion compared with CA.

**Key words:** alfentanil/electro-acupuncture/IVF/oocyte aspiration/pain relief

## Introduction

Oocyte retrieval today is performed by transvaginal ultrasound-guided follicle aspiration. The pain experienced during oocyte aspiration is caused by the passage of the needle through the vaginal wall and by mechanical stimulation of the ovary. The pain is often described as similar to intensive menstrual pain and is probably the most painful component of IVF treatment. Factors that may influence the pain are the number of follicles, the position and mobility of the ovaries, and the woman's capacity to cope with the pain. The procedure is usually quick, and the analgesic method used must be both effective and safe. Today the most commonly used method for pain relief during oocyte aspiration is conventional analgesia together with opiates (Ng *et al.*, 1999, 2001).

Opiates are effective, but negative side effects such as tiredness, confusion and nausea may prolong the period to mobilization and recovery. A paracervical block (PCB), in combination with different sedative pre-medications with or without fast-acting opiates, has been reported to give acceptable pain relief during oocyte aspiration in several

studies (Ng *et al.*, 1999, 2001). At our clinic, conventional analgesia during oocyte aspiration includes sedative pre-medication with oral flunitrazepam (Fluscand 0.5 mg; Pharmachemie BV, The Netherlands), rectal paracetamol (Panodil® 1 g; GlaxoSmithKline, Täby, Sweden), local analgesics (Xylocain® 10 mg/ml; Astra Zeneca, Södertälje, Sweden) administered as a PCB, and i.v. alfentanil (Rapifen® 0.5 mg/ml; Janssen-Cilag AB, Sollentuna, Sweden).

Acupuncture is a potent form of sensory stimulation, which has been introduced into Western medicine to treat different states of pain and disease (Stener-Victorin *et al.*, 2002). Electrical stimulation of the needles, electro-acupuncture (EA), is a pain-relieving method that has been suggested to activate endogenous pain-inhibiting systems such as the spinal/segmental gate mechanism and the endogenous opioid system, including the descending pain inhibitory system (Andersson and Lundberg, 1995; Han, 2003). It has been found to induce pain relief similar to that of fast-acting opiates during oocyte aspiration and to have fewer negative side effects (Stener-Victorin *et al.*, 1999, 2003). EA has also been evaluated in different surgical

procedures and reported to give acceptable pain relief during minor surgery and in post-operative pain (Fanti *et al.*, 2003).

Today, patients ask for non-pharmacological analgesic methods since they wish to avoid the negative side effects of opiates. EA may also be a good alternative for patients who are intolerant of conventional analgesia. Previous studies have investigated the analgesic effect of EA compared with opiates (Stener-Victorin *et al.*, 1999, 2003), but effects on the post-operative well-being of patients have not been evaluated in this context.

From a health economic perspective, it is also important to evaluate costs of new methods.

The primary aims of the present study were to investigate the pain-relieving effect of EA related to oocyte aspiration, and to evaluate post-operative well-being. Further aims were also to investigate time for post-operative mobilization, and costs for treatment concerning time and drug consumption.

## Methods

### Study design

The study was an open, prospective, randomized, single-centre trial performed at the IVF unit of Reproductive Medicine at Sahlgrenska University Hospital in Göteborg. The study compared EA and a PCB

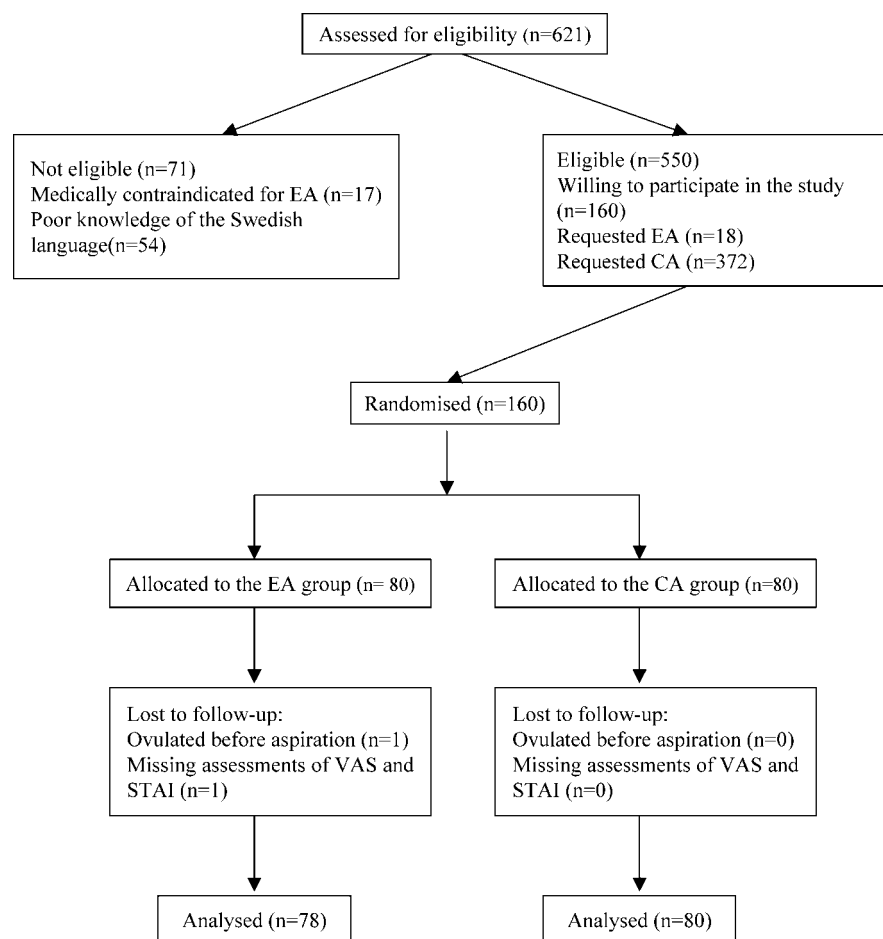
(EA group) with conventional analgesia (i.v. alfentanil) and a PCB (CA group). The CA group was also offered pre-medication (0.5 mg oral flunitrazepam, 1 g rectal paracetamol). The Ethics Committee of Göteborg University approved the study.

### Study group

The study group consisted of women who were undergoing IVF and who consented to be randomized to the EA or the CA group for pain relief during oocyte aspiration. The women were informed about the study ~2 weeks before oocyte aspiration. Inclusion criteria were willingness to participate in the study and knowledge of the Swedish language. Exclusion criteria were earlier participation in the study, epilepsy, a pacemaker, severe nickel allergy, or hepatitis B or C.

A total of 621 women were eligible and 160 were randomized (Figure 1). The women were recruited between March 2002 and October 2003. Each woman enrolled by the physician or the midwife gave her written, informed consent before entering the study. Each woman underwent only one IVF cycle in the study.

Randomization was performed by the study coordinator according to a computerized list and was stratified for the level of anxiety measured by a visual analogue scale (VAS), below or above 22 mm on the VAS, and performed on the day of oocyte aspiration just prior to the pre-operative procedure. The women were randomized into the EA group and the CA group in a 1:1 ratio.



**Figure 1.** Flow chart of patients eligible for the study. EA = electro-acupuncture, CA = conventional analgesia, STAI = state trait anxiety inventory test, VAS = visual analogue scale.

### IVF treatment

All women underwent a stimulation procedure that included down-regulation with a GnRH agonist begun either in the follicular phase or in the luteal phase (1.2 mg per day nasally or 1.0 mg per day as an s.c. injection; Suprecur or Suprefact; Hoechst, Frankfurt, Germany). Downregulation was followed by stimulation with recombinant FSH (Gonal-F, Serono, Geneva, Switzerland or Puregon, Organon, Oss, The Netherlands). Monitoring was performed via vaginal ultrasound scans and serum estradiol measurements. When adequate stimulation was achieved, 10 000 IU of HCG (Profasi, Serono or Pregnyl, Organon) was administered. Fertilization was performed by conventional IVF or by ICSI according to standard techniques. One or two embryos were transferred on day 2 or 3 after oocyte retrieval using a Wallace, a Cook or a Frydman catheter. Luteal support, progesterone, was administered vaginally. Additional embryos were cryopreserved and transferred later. Pregnancy was defined as a positive HCG test in urine on day 19 post-transfer.

### Treatment procedure

EA was administered by four midwives who were educated and trained in the theoretical and practical knowledge of acupuncture and who all had long experience in the IVF unit. No pre-medication was given to the EA group. EA was administered 30–45 min before oocyte aspiration and terminated directly after retrieval. Other midwives not involved in administering EA assisted in the analgesia procedure during oocyte retrieval. The intention was to follow the standard routines at the clinic and avoid any additional benefits of an emotional tie between the midwife and the patient in the EA group compared with the CA group. Acupuncture points and electrical stimulation were the same for all the women in the EA group. The acupuncture points selected were located bilaterally in the abdominal muscles in somatic segments related to the pain area for the uterus and the ovaries (KI 11 and ST 29). Additional points at sites in the muscles below the knee and elbow were selected bilaterally in the arm (LI 10), the hand (LI 4), and just below the knee (ST 36) to extend and prolong the effect of EA stimulation. The point GV 20, on the top of the cranium, was chosen to increase relaxation based on an empirical recommendation in traditional Chinese medicine. The stainless steel needles (Hegu Xeno: Hegu AB, Landsbro, Sweden; size 0.30 × 30 or 50 mm) were inserted intramuscularly to a depth of 15–30 mm. Points ST 36 and GV 20 were stimulated manually every 10th minute by hand to evoke needle sensations and increase activity in the afferent nerves and central pain systems. The points LI 4, LI 10, ST 29 and KI 11 were stimulated electrically. These needles were attached to an electrical stimulator (CEFAR ACUS 4, Cefar, Lund, Sweden) and were electrically stimulated with square-wave pulses (0.18 ms duration) with alternating polarity. The stimulation frequency in the abdomen was high, 80 Hz, while the frequency used in the hands was low, 2 Hz, with burst pulses (a burst length of 0.1 s and a burst frequency of 80 Hz). The high-frequency stimulation intensity induced strong but non-painful paraesthesia with the aim of influencing the spinal cord and activating the gate control system (Stener-Victorin *et al.*, 1999, 2003). The low-frequency stimulation induced non-painful local muscle contractions with the aim of releasing  $\beta$ -endorphins centrally and reducing the sensation of pain.

The CA group received a sedative pre-medication consisting of 0.5 mg of oral flunitrazepam and 1 g of rectal paracetamol prior to the PCB. In the operating theatre, 0.5 mg of alfentanil was administered i.v. before oocyte retrieval was begun.

A PCB consisting of lidocaine (0.5%) was administered to both groups just before oocyte aspiration.

If EA or CA did not result in sufficient pain relief, additional alfentanil or nitrox (AGA, Stenungsund, Sweden) was administered.

A heat therapy pillow was used on the abdomen before, during and after surgery in both groups to increase relaxation and decrease pain (Uvnäs-Moberg *et al.*, 1993).

In accordance with post-operative mobilization procedures, patients were observed for wakefulness and offered breakfast every 30 min.

### Time consumption and costs

Costs for time and drug consumptions in the study were recorded and compared between the EA group and the CA group (Table VI). Costs for time consumption comprised patients' total time at the clinic in minutes, counted in terms of the midwives' salary. The comparison of drug costs between groups was based on total drug consumption, which included pre-medication, peroperative consumption of opiates and post-operative intake of analgesics. Costs for acupuncture and costs for aspiration needles were counted separately.

### State Trait Anxiety Inventory

The State Trait Anxiety Inventory (STAI) (Spielberger, 1983; Gallinelli *et al.*, 2001; Verhaak *et al.*, 2001; Kowalczyk *et al.*, 2003) is a self-report questionnaire comprising two separate 20-item scales measuring state and trait anxiety, termed S-anxiety form Y-1 for state anxiety and T-anxiety form Y-2 for trait anxiety. The S-anxiety form Y-1 scale measures momentarily experienced anxiety. The T-anxiety form Y-2 scale describes general tendencies of an individual to restrain experienced anxiety and is used mainly to evaluate long-term stress. The anxiety scores range from 20 to 80; higher scores indicate higher anxiety. In the present study, a low STAI score indicated a high rated well-being. STAI was assessed on three occasions to measure well-being: (i) before randomization; (ii) 60 min after surgery; and (iii) when the patient had recovered. The definition of recovery used in the study was that the patient had eaten breakfast, had a minimum of subjective pain, felt comfortable and had consented to leave the clinic.

### Visual Analogue Scale

To evaluate subjective pain and subjective experiences, the VAS was used for measurements. The VAS questionnaire contained 29 different variables (Babul *et al.*, 1993; Altman, 1996; DeLoach *et al.*, 1998), each consisting of a 100 mm horizontal line with suitable end-points. The questionnaire was administered on four occasions (Table III): (i) before randomization; (ii) directly after oocyte aspiration; (iii) 60 min after surgery; and (iv) when the patient had recovered. The VAS questions asked on the four occasions had the end-points shown in Table I.

The person who assessed the VAS was blinded to the group to which the patients belonged.

### Sample size calculation

A sample size calculation was made prior to the study based on the following assumption for the primary end-points: if STAI measurements of well-being 60 min after oocyte aspiration had an expected SD of 10.0 in each group, 68 patients would be needed in each group to show a significant difference between groups of 5.0 with a power of 80% and a significance level of 0.05.

To demonstrate equal levels of pain between the groups, directly related to oocyte aspiration and measured with a VAS, the following assumptions were made: given an SD of 18.0 in each group

**Table I.** End-points for the VAS questions

(i) Before randomization
I feel totally calm before the operation—I am very anxious about the operation
I am not afraid of pain at all—I am very afraid of pain
I am not afraid of losing self-control—I am very afraid of losing self-control
I am not afraid of feeling bad afterwards—I am very afraid of feeling bad afterwards
(ii) Directly after oocyte aspiration
I have no pain at the moment—I have unbearable pain
I felt that the operation was not painful—I felt that the operation was unbearably painful
I had good self-control—I had no self-control
I felt that I had participated in the process—I did not feel that I had participated in the process
I have no nausea at the moment—I have unbearable nausea
I am not tired at the moment—I am very tired
I do not feel confused—I feel very confused
I feel totally calm—I am very anxious
I am totally relaxed—I am very tense
(iii) 60 min after surgery
I have no pain at the moment—I have unbearable pain
I have no nausea at the moment—I have unbearable nausea
I am not tired at the moment—I am very tired
I do not feel confused—I am very confused
I feel totally calm—I am very anxious
I am totally relaxed—I am very tense
(iv) When the patient had recovered
I am very satisfied with the operation—I am not satisfied at all
I have no pain at the moment—I have unbearable pain
I have no nausea at the moment—I have unbearable nausea
I am not tired at the moment—I am very tired
I do not feel confused—I am very confused
I feel totally calm—I am very anxious
I am totally relaxed—I am very tense
At this moment I feel fine psychologically—At this moment I feel bad psychologically
At this moment I feel fine physically—At this moment I feel bad physically
The operation was much easier than I expected—The operation was much worse than I expected

concerning pain assessed by VAS directly after oocyte aspiration, 80 patients in each group would be needed to show that the upper limit of the 95% confidence interval (CI) for the difference in means between the groups should not exceed 11.0 with a probability of 0.80.

### Statistics

The statistical analysis was made primarily according to intention to treat, i.e. a strict analysis according to randomization group regardless of subsequent protocol violation. In the secondary per protocol analysis, patients were allocated to treatment groups according to the actual treatment given (EA or CA). The primary outcomes were well-being 60 min after surgery and pain related to oocyte aspiration. The secondary outcomes were tiredness and confusion. For descriptive statistics, mean, SD, median and range were used.

Subgroup analyses were performed for three different groups consisting of first cycle patients, patients who were anxious prior to oocyte aspiration and patients who were calm prior to oocyte aspiration. Patients were defined as 'calm' at VAS levels of  $\leq 22$  mm or 'anxious' at VAS levels  $> 22$  mm prior to oocyte aspiration.

Since the number of collected oocytes differed significantly between the groups and might have influenced pain, *P*-values were adjusted for the number of oocytes. Adjustments were made by logistic regression analysis.

Spearman's rank correlation test was used to describe the correlation between two continuous variables; the Mann-Whitney

*U*-test was used for comparisons between continuous variables; Fisher's exact test was used for comparisons between dichotomous variables.

A multivariate analysis with stepwise linear regressions was made on the outcomes; pain and tiredness as the dependent variables. The dependent factors were transformed with Blom's rank method to achieve a normal distribution of variables (Blom, 1958). Independent variables tested were age, number of aspiration, analgesic group, number of oocytes, STAI form Y-1 and form Y-2, VAS I anxiety prior to oocyte aspiration, and fear of pain.

### Results

There were 160 women randomized in the study, 80 to the EA group and 80 to the CA group (Figure 1). Patient characteristics were similar between the groups (Table II).

#### VAS before oocyte aspiration

In total, 29 VAS dimensions of pain, subjective expectations and subjective experiences were measured concerning oocyte aspiration (Table III). Prior to oocyte aspiration, there were no differences between the groups in assessments of anxiety, fear of pain, fear of losing control and fear of feeling bad after the aspiration.

#### VAS after oocyte aspiration

The assessment of momentary pain after retrieval showed that pain was significantly less in the CA group compared with the EA group. The pain related to oocyte aspiration was also significantly less in the CA group. The CA group was significantly more tired and confused directly after retrieval compared with the EA group.

**Table II.** Characteristic variables for randomized patients

Characteristics	EA group ( <i>n</i> = 80)	CA group ( <i>n</i> = 80)	<i>P</i> -value
Age <sup>a</sup>	33.9 ± 3.7, 25.7–39.1	33.2 ± 3.6, 22.6–39.1	0.227
Pregnancy <sup>b</sup>			
Primary infertility	53 (66.2)	53 (66.2)	0.758
Secondary infertility			
One previous pregnancy	19 (23.8)	18 (22.5)	
Two previous pregnancies	6 (7.5)	9 (11.2)	
Four previous pregnancies	2 (2.5)	0 (0.0)	
Parity <sup>b</sup>			0.781
Nulliparous	72 (90.0)	74 (92.5)	
Parous	8 (10.0)	6 (7.5)	
No. of IVF cycles performed, including the current cycle <sup>a</sup>	1.56 ± 0.93, 0–6	1.48 ± 0.93, 1–4	0.587
Not aspirated <sup>b,c</sup>	1 (1.2)	0 (0.0)	
First cycle	48 (60.0)	59 (73.8)	
Second cycle	21 (26.2)	11 (13.8)	
Third cycle	7 (8.8)	3 (3.8)	
≥ Fourth cycle	3 (3.8)	7 (8.8)	
Reason for infertility <sup>b</sup>			0.592
Tubal factor	7 (8.8)	8 (10.0)	
Hormonal factor	7 (8.8)	9 (11.2)	
Endometriosis	4 (5.0)	4 (5.0)	
Male factor	30 (37.5)	33 (41.2)	
Unexplained	27 (33.8)	17 (21.2)	
Mixed (female/male factor)	5 (6.25)	9 (11.2)	

<sup>a</sup>Mean ± SD, range

<sup>b</sup>*n* (%).

<sup>c</sup>The patient ovulated prior to aspiration.

**Table III.** Measurements of VAS; mean  $\pm$  SD, median, range, *P*-value and adjusted *P*-value

VAS rating (mm)	Intention to treat			Per protocol		
	EA group ( <i>n</i> = 78) Mean $\pm$ SD, (median, range)	CA group ( <i>n</i> = 80) Mean $\pm$ SD, (median, range)	<i>P</i> ( <i>P</i> adjusted)	EA group ( <i>n</i> = 62) Mean $\pm$ SD, (median, range)	CA group ( <i>n</i> = 42) Mean $\pm$ SD, (median, range)	<i>P</i> ( <i>P</i> adjusted)
VAS I/before randomization						
Anxiety	28.6 $\pm$ 19.8 (24.0, 0–98)	30.4 $\pm$ 21.2 (31.0, 2–83)	0.709	28.5 $\pm$ 21.1 (23.0, 0–98)	29.0 $\pm$ 22.2 (21.5, 1–80)	0.593
Fear	38.0 $\pm$ 18.6 (37.5, 2–92)	34.5 $\pm$ 21.2 (31.0, 2–83)	0.200	37.4 $\pm$ 19.2 (36.0, 0–92)	33.3 $\pm$ 19.7 (28.5, 3–81)	0.250
Self-control	28.5 $\pm$ 19.4 (25.0, 0–78)	34.6 $\pm$ 24.6 (30.5, 0–99)	0.171	29.5 $\pm$ 20.0 (25.0, 0–78)	32.1 $\pm$ 23.1 (29.5, 0–91)	0.656
Condition	26.2 $\pm$ 19.7 (23.0, 0–99)	30.2 $\pm$ 22.2 (28.5, 0–99)	0.269	25.4 $\pm$ 17.6 (23.0, 3–78)	27.5 $\pm$ 20.9 (24.5, 0–87)	0.754
VAS II/directly after oocyte aspiration						
Momentary pain	37.9 $\pm$ 27.1 (34.5, 0–100)	26.9 $\pm$ 21.4 (25.0, 0–93)	0.014 (0.021)	36.5 $\pm$ 26.4 (29.5, 0–95)	26.0 $\pm$ 18.1 (25.5, 0–58)	0.076 (0.086)
Operation pain	48.5 $\pm$ 26.8 (49.0, 0–97)	29.8 $\pm$ 23.4 (25.0, 0–93)	<0.0001 (<0.0001)	43.6 $\pm$ 25.5 (39.5, 1–97)	22.4 $\pm$ 17.2 (19.0, 1–60)	<0.0001 (0.0002)
Self-control	30.6 $\pm$ 25.6 (24.0, 0–88)	20.7 $\pm$ 20.6 (14.5, 0–86)	0.020 (0.016)	23.3 $\pm$ 21.4 (21.0, 0–81)	19.5 $\pm$ 21.8 (11.5, 0–76)	0.053 (0.057)
Participation	25.7 $\pm$ 23.0 (21.0, 0–83)	20.8 $\pm$ 22.6 (10.5, 0–87)	0.145 (0.224)	23.3 $\pm$ 21.4 (20.0, 0–83)	19.5 $\pm$ 21.8 (9.0, 1–87)	0.385 (0.493)
Nausea	15.7 $\pm$ 24.0 (3.0, 0–82)	10.1 $\pm$ 18.8 (2.0, 0–82)	0.456 (0.204)	12.8 $\pm$ 21.2 (2.5, 0–80)	11.5 $\pm$ 21.2 (3.5, 0–92)	0.704 (0.494)
Tiredness	31.3 $\pm$ 26.8 (23.5, 0–95)	41.9 $\pm$ 28.2 (42.0, 0–98)	0.018 (0.007)	26.7 $\pm$ 24.6 (19.5, 0–87)	33.8 $\pm$ 22.8 (34.0, 0–69)	0.100 (0.099)
Confusion	25.7 $\pm$ 28.7 (10.0, 0–96)	40.2 $\pm$ 26.8 (34.5, 0–93)	<0.0001 (0.0005)	20.6 $\pm$ 25.8 (8.0, 0–90)	32.2 $\pm$ 21.0 (28.0, 3–77)	0.0004 (0.008)
Anxiety	17.2 $\pm$ 19.8 (10.0, 0–84)	9.42 $\pm$ 12.8 (7.0, 0–65)	0.347 (0.317)	15.2 $\pm$ 17.5 (7.5, 0–72)	8.6 $\pm$ 11.7 (6.0, 0–65)	0.661 (0.600)
Relaxation	24.3 $\pm$ 21.7 (18.0, 0–89)	18.0 $\pm$ 19.3 (9.5, 0–84)	0.087 (0.116)	21.6 $\pm$ 19.9 (16.0, 0–71)	18.0 $\pm$ 18.4 (9.5, 0–67)	0.562 (0.584)
VAS III/60 min post-operatively						
Momentary pain	26.1 $\pm$ 24.3 (15.0, 0–93)	23.5 $\pm$ 19.8 (14.0, 0–74)	0.648 (0.605)	22.9 $\pm$ 22.0 (12.5, 0–90)	19.8 $\pm$ 15.8 (11.0, 0–50)	0.861 (0.492)
Nausea	9.7 $\pm$ 17.3 (1.0, 0–79)	9.1 $\pm$ 14.8 (2.0, 0–55)	0.370 (0.729)	7.2 $\pm$ 15.7 (1.0, 0–50)	10.4 $\pm$ 15.6 (2.0, 0–53)	0.266 (0.21)
Tiredness	24.5 $\pm$ 20.5 (11.5, 0–93)	29.2 $\pm$ 21.9 (15.0, 0–91)	0.250 (0.296)	22.7 $\pm$ 18.9 (10.5, 0–93)	25.6 $\pm$ 18.9 (11.0, 1–61)	0.390 (0.476)
Confusion	15.8 $\pm$ 21.6 (3.0, 0–76)	20.1 $\pm$ 20.7 (7.0, 0–75)	0.016 (0.453)	11.9 $\pm$ 17.4 (2.5, 0–65)	13.6 $\pm$ 15.1 (4.0, 1–44)	0.057 (0.607)
Anxiety	12.0 $\pm$ 19.6 (3.0, 0–71)	9.4 $\pm$ 12.8 (3.0, 0–45)	0.885 (0.523)	7.2 $\pm$ 14.0 (3.0, 0–71)	8.6 $\pm$ 11.7 (3.0, 0–44)	0.489 (0.950)
Relaxation	15.3 $\pm$ 20.2 (4.5, 0–82)	11.1 $\pm$ 12.8 (3.0, 0–50)	0.336 (0.135)	11.1 $\pm$ 15.6 (4.0, 0–73)	10.2 $\pm$ 11.0 (2.5, 0–33)	0.687 (0.590)
VAS IV/at recovery						
Satisfaction	15.3 $\pm$ 16.3 (9.0, 0–70)	9.8 $\pm$ 12.6 (5.0, 0–65)	0.017 (0.039)	14.6 $\pm$ 16.6 (8.0, 0–70)	8.8 $\pm$ 10.2 (5.0, 0–38)	0.092 (0.111)
Momentary pain	18.2 $\pm$ 18.5 (13.0, 0–72)	17.3 $\pm$ 17.1 (10.5, 0–72)	0.988 (0.888)	15.7 $\pm$ 17.2 (9.5, 0–68)	13.4 $\pm$ 12.3 (9.0, 0–49)	0.887 (0.837)
Nausea	4.6 $\pm$ 8.8 (1.0, 0–42)	6.5 $\pm$ 13.0 (1.0, 0–61)	0.492 (0.197)	3.3 $\pm$ 6.6 (1.0, 0–42)	6.4 $\pm$ 13.6 (1.0, 0–61)	0.348 (0.048)
Tiredness	19.5 $\pm$ 24.5 (7.5, 0–93)	19.5 $\pm$ 21.6 (11.0, 0–88)	0.600 (0.730)	15.8 $\pm$ 22.1 (5.0, 0–93)	15.4 $\pm$ 19.5 (6.0, 0–75)	0.673 (0.694)
Confusion	12.2 $\pm$ 19.6 (2.0, 0–76)	11.3 $\pm$ 15.1 (5.0, 0–65)	0.085 (0.865)	9.7 $\pm$ 17.1 (2.0, 0–74)	9.7 $\pm$ 12.9 (4.0, 0–46)	0.050 (0.909)
Anxiety	6.5 $\pm$ 8.7 (3.0, 0–47)	7.2 $\pm$ 11.1 (3.0, 0–60)	0.948 (0.478)	5.1 $\pm$ 6.8 (2.0, 0–33)	5.6 $\pm$ 7.5 (2.5, 0–30)	0.693 (0.334)
Relaxation	8.6 $\pm$ 11.0 (4.0, 0–63)	8.1 $\pm$ 13.3 (3.0, 0–64)	0.467 (0.882)	7.2 $\pm$ 8.4 (3.0, 0–32)	7.4 $\pm$ 12.5 (2.0, 0–64)	0.687 (0.484)
Psychological	8.3 $\pm$ 12.9 (4.0, 0–87)	9.2 $\pm$ 14.0 (3.0, 0–79)	0.957 (0.598)	7.2 $\pm$ 9.7 (3.0, 0–46)	7.4 $\pm$ 13.5 (2.0, 0–79)	0.766 (0.805)
Physiological	16.2 $\pm$ 16.8 (10.5, 0–77)	14.2 $\pm$ 16.5 (9.0, 0–68)	0.281 (0.854)	16.1 $\pm$ 17.8 (9.5, 0–77)	11.7 $\pm$ 14.1 (6.0, 0–61)	0.276 (0.520)
Expectations	40.5 $\pm$ 27.2 (46.0, 0–100)	22.7 $\pm$ 25.7 (8.5, 0–98)	<0.0001 (0.0002)	38.5 $\pm$ 27.6 (46.0, 0–100)	17.4 $\pm$ 20.8 (3.5, 0–86)	<0.001 (0.0003)

The Mann–Whitney U-test was used to compare differences in the VAS ratings between the EA group and the CA group.

**VAS 60 min after oocyte aspiration**

Sixty minutes after oocyte aspiration, no significant differences in pain ratings between the two groups were noted. The CA group was still significantly more confused 60 min after oocyte aspiration compared with the EA group.

**VAS at recovery**

At recovery, the EA group rated oocyte aspiration as significantly more painful than expected. At the same time point, women in the CA group reported that they were significantly more satisfied with oocyte aspiration compared with the EA group. At recovery, no significant differences in tiredness and confusion between the groups were found.

Adjustments for the number of oocytes did not alter the results for any of the pain assessments.

The results from the three subgroup analyses, including first cycle patients, anxious patients prior to oocyte aspiration, and calm patients prior to oocyte aspiration, were similar to those for the total study group (data not shown).

The analgesic groups and STAI form Y-1 were found in the regression analyses (Tables IV and V) to be independently correlated with pain during oocyte aspiration. Age, number of oocytes and analgesic groups were independently correlated with tiredness.

No differences between groups were found in consumption of total time at the clinic or in time needed for mobilization (Table VI). The CA group had significantly higher costs for

**Table IV.** Factors analysed for univariate correlations with pain and tiredness

Variable	Pain during oocyte retrieval ( <i>n</i> = 158)		Tiredness directly after oocyte retrieval ( <i>n</i> = 158)	
	CC	<i>P</i> -value	CC	<i>P</i> -value
Age	-0.0009	0.991	-0.316	<0.0001
No. of eggs	0.135	0.090	0.122	0.127
No. of aspirations	0.092	0.248	-0.006	0.941
STAI/form Y-1	0.201	0.012	0.145	0.069
STAI/form Y-2	0.174	0.030	0.103	0.201
VAS/anxiety	0.165	0.038	-0.025	0.752
VAS/fear for pain	0.125	0.120	-0.007	0.928
Analgesic group				
EA group	48.5 ± 26.8 <sup>a</sup>	<0.0001	31.3 ± 26.8 <sup>a</sup>	0.018
CA group	26.9 ± 21.4 <sup>a</sup>		41.9 ± 28.2 <sup>a</sup>	

<sup>a</sup>Mean ± SD.

CC = correlation coefficient; STAI = State Trait Anxiety Inventory Test; VAS = visual analogue scale.

**Table V.** Variables independently predictive of pain and tiredness

Variable	Pain during oocyte retrieval ( <i>n</i> = 158)	Tiredness directly after oocyte retrieval ( <i>n</i> = 158)
	<i>P</i> -value	<i>P</i> -value
Age	NS	0.001
STAI/form Y-1	0.015	NS
No. of oocytes	NS	0.044
Analgesic group	<0.0001	0.021

STAI = state trait anxiety inventory test.

**Table VI.** Time consumed (minutes; mean, SD, range)<sup>a</sup> and costs (Euro; mean, SD, range)<sup>b</sup> for time and drugs

Time and costs	EA group ( <i>n</i> = 79)	CA group ( <i>n</i> = 80)	<i>P</i> -value
Time required for aspiration <sup>a</sup>	12.1 ± 5.8, 4–37	9.9 ± 4.7, 3–27	0.009
Time for mobilization <sup>a</sup>	104.6 ± 36.1, 28.0–250.0	102.5 ± 28.9, 52.0–176.0	0.980
Total time at the clinic <sup>a</sup>	225.3 ± 46.0, 151.0–420.0	220.7 ± 37.1, 149.0–317.0	0.874
Costs for time consumption <sup>b</sup>	85.6 ± 17.5, 57.4–159.6	83.9 ± 14.1, 56.6–120.5	0.499
Drug cost <sup>b</sup>	5.4 ± 1.0, 4.8–9.2	6.6 ± 0.9, 6.3–10.3	<0.0001
Acupuncture cost <sup>b</sup>	0.7 ± 0.0, 0.7–0.7		
Costs for aspiration needle <sup>b</sup>	33.7 ± 1.3, 33.0–36.3	34.0 ± 1.5, 33.0–36.3	0.178
Total cost <sup>b</sup>	125.3 ± 17.9, 95.9–202.5	125.0 ± 14.3, 97.1–160.8	0.718

EA = electro-acupuncture; CA = conventional analgesia.

drug consumption compared with the EA group (Table VI). Additional alfentanil was administered during the oocyte aspiration significantly more often in the CA group, to 29 women (36.2%), than in the EA group, to 16 women (20.0%) (Table VII). Nitrox was given to six women (7.5%) in the EA group and to four women (5.0%) in the CA group. No differences in total costs were found between the groups.

Few patients in either groups experienced complications from the retrieval such as low blood pressure and vaginal bleeding; all recovered during the day of the operation. There were no differences in pregnancy rate between the groups (Table VII).

**Well-being**

No significant differences in well-being between the two groups as measured with the STAI were noted at any occasion (Table VIII).

**Time consumption and time costs**

The mean time (minutes) for oocyte retrieval (Table V) was 12.1 ± 5.8 and 9.9 ± 4.7 in the EA and CA groups

**Table VII.** Treatment and outcome variables

Variable	EA group ( <i>n</i> = 79)	CA group ( <i>n</i> = 80)	<i>P</i> -value
No. of follicles <sup>a,c</sup>	15.8 ± 9.4, 0–50	13.4 ± 8.6, 2–40	0.042
No. of oocytes retrieved <sup>a,c</sup>	12.5 ± 6.7, 0–28	10.5 ± 6.4, 2–33	0.029
Additional alfentanil peroperatively <sup>b</sup>	16 (20.0)	29 (36.2)	0.003
Needles used for aspiration <sup>b</sup>			0.269
Single lumen needle	64 (80.0)	57 (71.3)	
Flush needle	16 (20.0)	23 (28.8)	
Embryo transfer <sup>b</sup>	68 (85.0)	63 (78.6)	0.412
Pregnancy per cycle <sup>b</sup>	23 (28.8)	26 (32.5)	0.731
Pregnancy per transfer <sup>b</sup>	23 (33.8)	26 (41.3)	0.470

<sup>a</sup>Mean ± SD, range

<sup>b</sup>*n* (%).

<sup>c</sup>*n* = 80 in the EA group; one patient was lost to follow-up due to ovulation prior to oocyte aspiration.

**Table VIII.** Well-being measured with the STAI (points; mean  $\pm$  SD), *P*-value and adjusted *P*-value

Well-being	Intention to treat				Per protocol			
	EA group ( <i>n</i> = 78)	CA group ( <i>n</i> = 80)	<i>P</i> -value	Adjusted <i>P</i> -value	EA group ( <i>n</i> = 63)	CA group ( <i>n</i> = 42)	<i>P</i> -value	Adjusted <i>P</i> -value
Prior to randomization								
STAI I/State I	34.8 $\pm$ 8.4	34.3 $\pm$ 8.5	0.506	0.829	34.1 $\pm$ 8.4	32.9 $\pm$ 7.5	0.428	0.531
STAI I/Trait I	34.0 $\pm$ 7.7	33.3 $\pm$ 7.6	0.585	0.759	33.2 $\pm$ 7.3	31.8 $\pm$ 7.0	0.297	0.363
60 min post-operatively								
STAI II/State II	28.9 $\pm$ 8.4	27.6 $\pm$ 6.6	0.463	0.480	27.2 $\pm$ 6.0	26.2 $\pm$ 5.2	0.435	0.697
STAI II/Trait II	32.3 $\pm$ 8.1	32.0 $\pm$ 8.0	0.848	0.854	31.0 $\pm$ 7.3	30.5 $\pm$ 7.1	0.711	0.965
At recovery								
STAI III/State III	26.8 $\pm$ 5.6	28.6 $\pm$ 7.8	0.564	0.337	26.4 $\pm$ 5.3	25.9 $\pm$ 5.1	0.604	0.939
STAI III/Trait III	30.7 $\pm$ 8.1	33.0 $\pm$ 8.1	0.208	0.438	30.5 $\pm$ 7.3	30.4 $\pm$ 6.9	0.942	0.725

STAI = State Trait Anxiety Inventory Test.

respectively ( $P = 0.009$ ). Despite the difference in oocyte aspiration time, the time for mobilization and the total time at the clinic were similar between groups. Drug costs were significantly lower for the EA group ( $P < 0.0001$ ). When comparing the total costs (Table VI) for time and drug consumption between the EA group and the CA group, no differences were found.

## Discussion

In the present study, women in the EA group reported significantly more pain during oocyte aspiration and directly after oocyte retrieval compared with the CA group. Women in the CA group also reported that they were significantly more satisfied with oocyte aspiration compared with the EA group. Despite these circumstances, 50% of the women in the EA group said that they would be willing to use EA again for pain relief. No significant differences were found in pain ratings 60 min after oocyte aspiration. Well-being comparing the EA and the CA group was similar despite significant differences in pain ratings between the groups. The findings of more pain in the EA group were unexpected in view of previous studies with similar EA protocols that found no differences in pain relief between EA and CA (Stener-Victorin *et al.*, 1999, 2003). However, another recent study with a similar CA protocol including pre-medication (Humaidan and Stener-Victorin, 2004) reported more pain in the EA group compared with the CA group.

In the present study, 25 women in the CA group refrained from pre-medication. Therefore, an analysis to compare reported pain levels between the women who used pre-medication and those who did not in the CA group was made. No difference in reported pain was found ( $P = 0.483$ ). In comparisons with the EA group, the two pre-medication subgroups still reported significantly lower levels of pain.

One factor that might influence pain ratings is that the questions related to pain in the present study were not the same as those used in earlier studies, which might make comparisons between studies difficult (Stener-Victorin *et al.*, 1999, 2003; Humaidan and Stener-Victorin, 2004).

Another possible explanation for the significantly higher pain reported by the EA group in the present study might be

that the study group was less homogenous. Since results from previous studies found similar pain-relieving effects between EA and opiates, it might have been easier in the present study for the medical staff to recruit women whose attitudes towards non-pharmacological methods varied more and was less positive than in previous studies.

An interesting observation was that the women randomized to EA sometimes resisted additional alfentanil despite insufficient pain relief from EA. When asked about it afterwards, the women could not give an explanation. Many women emphasized that they had invaluable support in coping with the pain from the medical team. Patient motivation and support from the medical team seem to be very important components of pain relief.

It is known that the pain-relieving effect of EA can be lowered if patients feel emotionally unsafe and uncomfortable with the method (Harro *et al.*, 1993; Widerström-Noga *et al.*, 1998; Cohen *et al.*, 1999).

The EA group reported significantly lower levels of tiredness and confusion after oocyte aspiration and were significantly less confused during the first 60 min after oocyte retrieval. These findings were expected. The women in the EA group expressed satisfaction with less tiredness and confusion compared with the CA group.

No significant differences in time for mobilization or in total costs between the EA and the CA groups were noted. Humaidan and Stener-Victorin (2004) reported that hospitalization time was significantly shorter and costs were significantly lower in the EA group.

In the present study, the EA group used significantly less additional alfentanil during surgery compared with the CA group. The use of less additional alfentanil is in line with the findings of previous studies (Stener-Victorin *et al.*, 2003; Humaidan and Stener-Victorin, 2004). A reduction in the use of opiate medication during oocyte aspiration may be desirable, as alfentanil is found in the follicular fluid shortly after i.v. administration (Soussis *et al.*, 1995). Furthermore, recent studies evaluating the analgesic effect of EA during colonoscopy have confirmed that EA analgesia decreases the consumption of additional drugs during and after surgery (Wang *et al.*, 1997). It has also been confirmed that when additional drugs are administered in combination with EA,

lower doses of opiates provide sufficient pain relief (Wang *et al.*, 1997; Fanti *et al.*, 2003).

No differences in any clinical IVF outcome parameters between the two groups were found. No negative side effects were reported, which is in line with the results of previous studies made under similar conditions (Wang *et al.* 1997, Fanti *et al.* 2003).

In conclusion, EA cannot generally be recommended as a pain-relieving method at oocyte retrieval but might still be an analgesic alternative for women who wish to try a non-pharmacological method. Women in the EA group were less tired and confused after oocyte aspiration, and 50% of the women in the EA group reported that they were willing to use EA again as an analgesic method. Since pain varies from individual to individual, it is important to individualize the analgesic procedure.

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