

Acupuncture versus conscious sedation in oocyte retrieval during *in vitro* fertilization in Singapore

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Abstract

Purpose: Acupuncture is a form of pain relief that has been researched extensively with mixed results. To date, there are studies that have compared acupuncture with conscious sedation during oocyte retrieval, yet there remains no consensus as to which is superior. This study aims to compare the analgesic effect of acupuncture with conscious sedation during oocyte retrieval, for patients undergoing *in vitro* fertilization in Singapore.

Patients and methods: We recruited 50 patients for this randomized control trial from the Centre for Assisted Reproduction, Singapore General Hospital from 2015 to 2017. Data was gathered via self administered questionnaire forms for pain and stress scores, and data was analyzed using Graphpad Prism. Categorical variables were analyzed with Chi square test, and ordinal variables were analyzed with Wilcoxon sign rank test.

Results: There were no significant differences detected between the pain scores of both groups, during and after oocyte retrieval. Stress levels were higher in patients undergoing acupuncture only doing the procedure. Both groups also reported high satisfaction rates of the each analgesic method. No pregnancy rate differences were observed between both groups.

Conclusion: Acupuncture, instead of conscious sedation, is a novel way of administering analgesia during oocyte retrieval. It can be an effective form of analgesia in minor surgical procedures such as oocyte retrieval. Further studies would be helpful to determine if acupuncture is a cost effective alternative method of analgesia in our center. The eventual choice of analgesia should always be tailored to each patient after an individualized discussion.

Keywords: Analgesic effect; Patient satisfaction; Pain scores; Pregnancy rate

Abbreviations: OR: Oocyte Retrieval; IVF: In Vitro Fertilization

Introduction

The use of acupuncture originated in the East and has since gained popularity in the West as a form of pain relief. Acupuncture as a form of pain relief in clinical medicine has been researched extensively with mixed results, even with large numbers of randomized control trials to date [1]. However, studies have indeed demonstrated the mechanism of analgesia in acupuncture [2] and the interest in the role of acupuncture in clinical medicine continues to expand. Acupuncture compared with conscious sedation during oocyte retrieval (OR) has been studied in various centers internationally but currently there remains no consensus as to which form of analgesia is superior [3,4]. Singapore is a multicultural nation with a

strong Asian heritage, and the interest in complementary and alternative medicine (CAM) including acupuncture has always been significant. 29% of surveyed residents in Singapore have experienced acupuncture before, and attitudes towards acupuncture are generally welcoming [5]. Since 2005, acupuncture has been allowed in hospitals to complement Western medical treatment. To date, 4 out of 6 acute general hospitals in Singapore offer an acupuncture service for its patients. However, despite the high prevalence of CAM in Singapore, there are currently no local hospitals engaging the use of acupuncture for *in vitro* fertilization (IVF) procedures. Transvaginal oocyte retrieval is a common procedure during IVF and traditionally conscious sedation is used for pain relief. We conducted a randomized control trial in the largest tertiary hospital in Singapore to evaluate the analgesic effect of acupuncture compared to conscious sedation for OR during IVF in a local setting.

Material and Methods

Institutional Review Board approval was completed and 50 patients were successfully recruited for this prospective randomized control trial. Informed and written consent was obtained from study recruits. Patients who were undergoing IVF were recruited from the Centre for Assisted Reproduction in Singapore General Hospital from 2015 to 2017. Institutional review board consent was obtained. Study recruits were only recruited one time for this study, regardless of the number of treatment cycles. Exclusion criteria included patients who were unwilling to accept acupuncture, and patients who in which acupuncture was contraindicated. This included women with a history of bleeding disorders and infectious skin diseases. Study recruits were randomized into 2 groups. Pain scores were assessed using a self-reported questionnaire 1 hour after OR was completed, and patients were asked to rate their pain and stress before, during, and after the procedure. Pain scores were evaluated using the visual analog scale during the questionnaire. Stress scores were rated on a scale of 1 to 10. Other variables included satisfaction approval. Patient satisfaction was patient reported and determined by a “yes” or “no” option, which was then tabulated. The target end point of this study was the end of the oocyte retrieval procedure. Data was analyzed using Graphpad Prism. We analyzed categorical variables using the Chi square test, and ordinal variables were analyzed with Wilcoxon sign rank test.

Analgesic protocol

Acupuncture was performed by a single, experienced and licensed traditional Chinese medicine physician recruited from the pain service in Singapore General Hospital. Study recruits were also given the option of additional conscious sedation should pain relief be inadequate, and they were informed of this option prior to the recruitment into the study. Acupuncture needles were inserted 15-25mm into acupuncture points located on the abdomen, back, and hands. The needles were then connected to an electrical stimulator which provided an electrical pulse stimulation that was titrated. The intensity was gradually increased to a level just below the patient’s self-reported pain threshold. The patient’s comfort and vital signs were monitored continuously during the oocyte retrieval procedure in both groups. The acupuncture was conducted throughout the oocyte retrieval procedure, and the acupuncture needles were removed after oocyte retrieval was completed. Patients who were unable to tolerate the pain during oocyte retrieval despite the acupuncture were given conscious sedation, following an identical drug regime outlined in the conscious sedation group.

Patients who received conscious sedation were given intravenous pethidine 40 mg and intravenous midazolam 4 mg 10 min before the start of the oocyte retrieval procedure, with a maximum dose of 50mg pethidine and 5mg midazolam.

Results

The mean age was 34.2 years; with a range from 18-39, with an average BMI of 24 (18-39). (Table 1) All 4 major races in Singapore were represented, although the majority was Chinese (86%). (Table 2) No patients undergoing acupuncture requested for additional conscious sedation during the procedure. No patients also suffered from any complications from acupuncture or conscious sedation. No patients dropped out of this study, and all study recruits were successfully followed up to the targeted study end point.

Patients who underwent acupuncture reported significantly higher mean pain scores only before the procedure, at 1.58, compared to patients who underwent conscious sedation, for which the reported mean score was 0.38 ($p=0.013$).

The mean pain scores during and post procedure showed no significant differences. The mean pain score reported during OR in patients undergoing sedation was 2.04 compared to 3.29 in patients who underwent acupuncture, which was not statistically significant. Similarly when we compared pain scores after OR, patients who underwent sedation reported a slightly lower mean pain score of 1.21, compared to 1.67 in patients who underwent acupuncture, however no statistical difference detected (Table 3).

We also compared self-reported stress levels among both groups. We found that patients who were undergoing acupuncture had higher levels of stress only during the procedure (3.17 vs 0.83, $p=0.005$). Post procedure, the mean stress levels of patients undergoing acupuncture then dropped to 0.38, comparable to the mean stress score of 0.13 in patients who had undergone sedation (Table 4).

Both groups surveyed showed high satisfaction rates that did not have a significant difference ($p=0.552$). Overall, 92% ($n=23$) of patients who underwent acupuncture claimed that they were satisfied with the level of analgesia for the oocyte procedure, while 96% ($n=24$) of patients who underwent conscious sedation were found to be satisfied (Table 5).

Table 1: Mean age and BMI.

| | Acupuncture | Sedation |
|----------|-------------|----------|
| Mean Age | 34.2 | 34.1 |
| Mean BMI | 25 | 23 |

Table 2: Racial demographics.

| Race | Acupuncture (n=25) | Percentage | Sedation (n=25) | Percentage |
|---------|--------------------|------------|-----------------|------------|
| Chinese | 20 | 80% | 23 | 92% |
| Malay | 2 | 8% | 2 | 8% |
| Indian | 2 | 8% | 0 | 0% |
| Others | 1 | 4% | 0 | 0% |

Table 3: Comparison of mean pain scores.

| Symptoms | Acupuncture | Sedation | p values |
|----------------------------|-------------|----------|----------|
| Mean pain scores before OR | 1.58 | 0.38 | 0.013 * |
| Mean pain scores during OR | 3.29 | 2.04 | 0.139 |
| Mean pain scores after OR | 1.67 | 1.21 | 0.411 |

*p values significant

Table 4: Comparison of mean stress scores.

| Symptoms reported | Acupuncture | Sedation | p values |
|------------------------------|-------------|----------|----------|
| Mean stress scores before OR | 3.08 | 1 | 0.383 |
| Mean stress scores during OR | 3.17 | 0.83 | 0.005 * |
| Mean stress scores after OR | 0.38 | 0.13 | 0.625 |

*p values significant

Table 5: Comparison of number of satisfied patients.

| | Acupuncture (n=25) | Sedation (n=25) |
|----------------------------------|--------------------|-----------------|
| Number of satisfied patients | 23 | 24 |
| Number of patients not satisfied | 2 | 1 |

Discussion

In our experience, the most significant levels of pain are suffered during oocyte retrieval itself, and this may continue on even after the procedure has been completed. Therefore, although people undergoing acupuncture had higher pain scores before the procedure, the overall low levels reported were reassuring.

Given that the pain scores between both groups during and post procedure were not found to be statistically different, acupuncture did provide effective analgesia that was non-inferior to conscious sedation, to our patients during the most painful parts of the procedure. Therefore, both groups reported equally high satisfaction outcomes.

It is known that the perception of pain is influenced by many factors including stress and anxiety [6]. Overall, the patients who underwent acupuncture had increased stress levels in this study, most significantly, during the procedure itself. As expected, this may have been due to the anxiety and fear in experiencing a novel form of treatment, as it was not possible to blind the patients from the treatment randomized to them. All study participants were reassured that acupuncture was conducted by a licensed practitioner, and that they were free to request for additional analgesia should they feel the need to. Although the reported stress levels were not absolutely high, they may have inadvertently increased the pain scores in patients who underwent acupuncture. However, the absolute increment in mean pain scores for patients undergoing acupuncture compared to sedation was overall minor.

The largest limitation in this study would be the small sample size, which limits the power of this study. The recruitment of patients was limited by resources. As a single acupuncture physician was recruited for this study, we were not able to recruit large numbers of patients in this study within the study time frame.

Further analysis with a larger sample size would also be useful, in order to promote acupuncture as a viable alternative for other minor surgical procedures besides oocyte retrieval.

Limitations include the presence of reporting bias as it was not possible to achieve double-blindness for this study. We also acknowledge that patients who underwent conscious sedation were more likely to have recall bias due to the sedation and amnesic effects of the sedation drugs used. We also attempted to maintain the consistency of the acupuncture and paracervical block technique used, by keeping to a single acupuncturist and a single physician for all patients; however, this may not be reproducible outside of this trial. Other factors such as age, and racial differences were also not accounted for in this study. Pregnancy outcomes were also subject to a number of confounders that were not accounted for, such as the type of infertility, and number of embryos transferred.

Acupuncture is a relatively safe procedure with a low risk of complications, the most common being bleeding and pain [7]. Serious adverse events such as infection are reportedly rare [8]. The good safety profile of acupuncture is a benefit in encouraging the uptake of this novel technique. Potential drawbacks of acupuncture include longer treatment times, and the need for more trained personnel, and more studies would be helpful in order to assess the cost effectiveness of this method in our center.

Conclusion

This is the first time in Singapore we have introduced an alternative anesthetic method to conscious sedation for OR during IVF. We are

heartened by the high levels of satisfaction with this novel technique. We would encourage larger studies to be undertaken to evaluate if acupuncture is a cost effective method in our center, so that we would be able to promote it as an effective analgesic method that may be used in various other minor surgical procedures. The eventual choice of analgesia should be tailored to each patient, and we recommend an individualized discussion.

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