

Current Research and Clinical Applications

Acupuncture as an Adjunct Treatment at the Time of Embryo Transfer: A Review of the Current Systematic Reviews

Caroline A Smith PhD
CompleMed, University of Western Sydney, Australia

Assisted reproductive technology (ART) is now an accepted and effective treatment for infertility. During 2004, there were 41 904 ART cycles in Australia, this resulted in 8794 pregnancies and 6792 live deliveries.¹ The relatively low rate of pregnancy success in IVF treatment is largely the consequence of implantation failure, and implantation remains a critical factor in limiting the success with ART. Over the last 10 years, research and improvements to treatment have aimed to increase success rates through the improvement of embryo quality, and improving the uterine environment to assist with embryo implantation.

The use of acupuncture as an adjunct to ART has grown in popularity over recent years, and this has most likely been in response to a number of randomised controlled trials showing an improvement in clinical pregnancies and live births. There are now at least thirteen clinical trials of acupuncture administered prior to egg retrieval and eight trials undertaken to coincide with an embryo transfer.

Many of the clinical trials administered as an adjunct to embryo transfer have used a very similar treatment protocol initially reported by Paulus et al.,² but may have used different design for the control

group. The majority of the randomised controlled trials have reported positive results, whilst others report no statistical difference between study groups. To assist with keeping up to date with the growing evidence from trial data in this area of research, systematic reviews have been published.

A systematic review is a review of the literature that pre-specifies a research question, uses predefined and explicit methods to identify and select the research articles relevant to the question, and applies a pre-established set of criteria to critique the included studies. A meta-analysis includes a pooled statistical analysis of a subset of the included studies that are of a particular study quality and similar design.³ Although systematic reviews are the best tool to summarise the evidence of a specific question, there are limitations to these tools. It is these limitations that explain why two systematic reviews may report different results and conclusions. The search strategy and evaluation criteria are based on subjective decisions and judgments. As Linde, Hammerschlag and Lao point out, changing the criteria for inclusion in the review can change the number of studies included, the use of the statistical methods and, consequently, the results of the meta-analysis.³

What is the evidence from recent systematic reviews of acupuncture as an adjunct to in-vitro fertilisation?

MANHEIMER ET AL.⁴

This systematic review evaluated whether acupuncture improved rates of pregnancy and live births when used as an adjunct treatment to embryo transfer in women undergoing IVF. The authors pre-defined eligible studies as needle acupuncture, randomised controlled trials administered within one day of embryo transfer, compared with sham acupuncture, or no adjunctive treatment, with outcomes of at least one clinical pregnancy, on-going pregnancy, or live birth. Each trial was assessed in a standard way. Most were judged to be satisfactory relating to the risk of bias. The results of the review and meta-analysis were based on seven trials with 1366 women receiving needle acupuncture only. In all the trials women received acupuncture immediately before and after embryo transfer, although two trials included additional treatments at different times during the IVF cycle. The treatment protocol was based on the initial Paulus trial in all but one trial. The methodological assessment described the trials as sound, and the minor concerns were not expected to result in substantial risk of bias.

The review reported on odds ratios for trials using sham and no treatment designs separately and all trials together. Irrespective of the control group design, acupuncture showed a benefit over the control with increasing the pregnancy and live birth rates. Overall, the findings for clinical pregnancy rate were an odds ratio (OR) of 1.65, and 95% confidence interval (CI) of 1.27 to 2.14; for ongoing pregnancy, OR 1.87, and 95%CI 1.4 to 2.49; and for live birth, OR 1.91, and 95%CI 1.39 to 2.64. The authors concluded there is preliminary evidence that needle acupuncture given with embryo transfer improves rates of pregnancy and live births among women undergoing IVF.

EL-TOUKHY ET AL.⁵

A few months ago there was much media interest in a second systematic review published on the effects of acupuncture in IVF. This systematic review included trials of acupuncture conducted during IVF. Their search was comprehensive, resulting in the inclusion of thirteen trials and a total of 2500 women randomised to either acupuncture or a control group. Eight of these trials (1623 women) reported on acupuncture trials conducted around the time of embryo transfer. A meta-analysis of these trials reported no difference in the clinical pregnancy rate (RR 1.23, 95%CI 0.96 to 1.58). There was also no difference in the live birth rate (RR 1.34, 95%CI 0.85 to 2.11). The conclusion from the authors was that the current literature does not provide sufficient evidence that acupuncture administered as an adjunct treatment improves clinical and live birth rates.

CHEONG ET AL.⁶

The Cochrane systematic review on the use of acupuncture as an adjunct to IVF will be published soon. A summary of their forthcoming systematic review has been published in abstract form only following presentation at a conference. A comprehensive search of the English language and Chinese language

literature was undertaken. Thirteen trials met the pre-specified criteria, ten were included and three excluded. They report that acupuncture on the day of embryo transfer improves the clinical pregnancy rate (OR 1.65, 95%CI 1.22 to 2.24) and ongoing pregnancy rate (OR 1.85, 95%CI 1.18 to 2.91). There was no difference in the miscarriage rate compared to controls. They concluded that acupuncture performed on the day of embryo transfer does increase the clinical pregnancy rate of IVF treatment. Further research is required.

Why are the findings from these systematic reviews different?

The Cheong systematic review has not been published in full at the time of this journal going to print; therefore, it is difficult to comment on their review and findings.⁶ The following comments will be based on the two earlier systematic reviews.^{4,5}

El-Toukhy and colleagues discuss the difference in their findings compared to the earlier published review.⁴ They suggest the difference in findings and conclusion is due to two reasons. Firstly, an additional study was included in their review.⁷ They also included data from all five arms of the study conducted by Benson, which included laser acupuncture.⁸ Secondly, they comment that the methodological quality of the studies was uneven, that the study interventions differed, points used varied, inclusion criteria varied, differences were noted in the timing of the intervention, and the choice of the sham control differed.

A review of the El-Toukhy review⁵ raises the question whether the Craig trial⁷ should have been excluded from the meta-analysis. It meets the criteria for being included in the systematic review, but the Craig study had very different results from all the other trials,⁷ therefore adding this study to the meta-analysis would increase the heterogeneity, and

potential source of bias. There was also a very high pregnancy rate in the control group of the Craig study,⁷ (much higher than in other trials included in the review) and this may partially explain the lower success rate in the acupuncture group compared with the IVF-only group. The acupuncture intervention in this study was different to other trials in that it was performed off the IVF site and involved a drive to and from the reproductive medicine site which may have involved additional stress to the women.

CONCLUSION

To conclude, new trials are published everyday which can make it hard to keep up to date with the current evidence. However, up-to-date systematic reviews can help practitioners, researchers and policy-makers keep abreast of the evidence in their area. It is not uncommon for different systematic reviews to reach different conclusions, and this is usually explained by different pre-specification of inclusion techniques, and different methods for assessing the quality of the trials and analysing the results. Currently there is no adequate instrument that assesses the quality of an acupuncture intervention in a systematic review. Indeed, inclusion of an instrument would be helpful for acupuncture practitioners and researchers with interpreting the evidence.

The research implications from both systematic reviews highlight the need for further high-quality randomised controlled trials. The clinical implications are that evidence to date suggests that acupuncture administered on the day of embryo transfer is a safe intervention. In the absence of a peer-reviewed published paper of the Craig study,⁷ the evidence from two systematic reviews and meta-analyses^{4,6} is that acupuncture performed on the day of embryo transfer increases clinical and pregnancy rates.

REFERENCES

1. Wang YA, Dean JH, Grayson N, Sullivan EA. Assisted reproduction technology in Australia and New Zealand 2004. Assisted

- reproduction technology series. No. 10. Canberra: Australian Institute of Health and Welfare; 2006.
- Paulus WE, Zhang M, Strehler E, El-Danasouri I, Sterzik K. Influence of acupuncture on the pregnancy rate in patients who undergo assisted reproduction therapy. *Fertil Steril* 2002;77(4):721-4.
 - Linde K, Hammerschlag R, Lao L. Evidence overviews: the role of systematic reviews and meta-analyses. In: MacPherson H, Hammerschlag R, Lewith G, Schnyer R, editors. *Acupuncture research: strategies for establishing an evidence base*. Philadelphia: Churchill Livingstone; 2007. p. 199-217.
 - Manheimer E, Zhang G, Udoff L, Haramati A, Langenberg P, Berman BM, et al. Effects of acupuncture on rates of pregnancy and live birth among women undergoing in vitro fertilisation: systematic review and meta-analysis. *Br Med J* 2008;336(7643):545-9.
 - El-Toukhy T, Sunkara SK, Khairy M, Dyer R, Khalaf Y, Coomarasamy A. A systematic review and meta-analysis of acupuncture in *in vitro* fertilisation. *Br J Obstet Gynaecol* 2008;115(10):1203-13.
 - Cheong Y, et al. Is acupuncture useful in assisted conception? Results of a meta-analysis. Abstract presented at the 24th Annual Conference of the European Society of Human Reproduction and Embryology (ESHRE); 6-9 July 2008; Barcelona, Spain.
 - Craig LB, Criniti AR, Hansen KR, Marshall LA, Soules MR. Acupuncture lowers pregnancy rates when performed before and after embryo transfer. *Fertil Steril* 2007;88(Suppl 1):S40.
 - Benson MR, Elkind-Hirsch KE, Theall A, Fong K, Hogan RB, Scott RT. Impact of acupuncture before and after embryo transfer on the outcome of in vitro fertilization cycles: a prospective single blind randomized study. *Fertile Steril* 2006;86(Suppl 1):S135.
-