Acupuncture and **in vitro** fertilization: updated meta-analysis

Sir,

We updated our previously published meta-analysis (El-Toukhy et al., 2008), following the recent publication of another randomized controlled study of acupuncture in IVF at the time of embryo transfer (So et al., 2009). Our updated meta-analysis showed no improvement in clinical pregnancy rates with acupuncture at the time of embryo transfer (Fig. 1). A restricted meta-analysis using high quality studies that employed sham acupuncture in the control group also failed to show improvement in live birth rates (Fig. 2).

Despite 14 randomized trials of acupuncture in IVF, some of which are of high quality and nearly 3000 women recruited into these studies, acupuncture has not been shown to improve IVF outcome. Many published studies on the role of acupuncture in IVF recommend that further well designed and sufficiently powered randomized trials to evaluate the impact of acupuncture at the time of embryo transfer on IVF outcome are carried out (Cheong et al., 2008; Pinborg et al., 2008). However, based on current evidence, this recommendation is difficult to justify.

If further research into the effects of acupuncture as an adjunct to IVF treatment is to be carried out, small studies are unlikely to provide a definitive answer. There are currently five ongoing randomized controlled trials of acupuncture and IVF with a sample size ranging from 100 to 600 women (metaRegister of Controlled Trials; Pinborg et al., 2008). It is unclear what these studies will offer over and above the existing studies. For current practice, we believe that women should be advised that there is no evidence that receiving acupuncture during IVF treatment (whether at the time of oocyte collection or embryo transfer) improves IVF outcome.

References


![Figure 1](https://example.com/figure1.png)

**Figure 1** Meta-analysis of the studies evaluating the effect of acupuncture administered around the time of embryo transfer on the clinical pregnancy rate in women undergoing IVF.
Influence of activating and inhibitory killer immunoglobulin-like receptors on predisposition to recurrent miscarriages

Sir,

We read with interest the paper from Faridi et al. (2009) ‘Influence of activating and inhibitory killer immunoglobulin-like receptors on predisposition to recurrent miscarriages’ published recently in Human Reproduction.

This is one of many recent papers on this topic which have presented frustratingly conflicting results and conclusions. There have been reports of a lack of association of recurrent miscarriage with maternal KIR repertoire (Witt et al., 2004), a lack of inhibitory receptors (Varla-Leftheriota, 2005), a lack of activating receptors (Hiby et al., 2008; Hong et al., 2008) or related to an increase in the frequency of activating KIR (Wang et al., 2007).

Of concern is the disparity in the findings in these studies with no consensus and increasing confusion. The reasons for this are likely to be as follows.

(i) The studies all have small numbers of patients that have used different selection criteria. To determine any influence of the highly polymorphic KIR genes in a heterogeneous condition such as recurrent miscarriage, it is essential to strictly define the affected group. Only women with three or more first trimester miscarriages and no live births should be included. Investigations ruling out other possible causes should be undertaken (e.g. anti-phospholipid antibodies, thyroid disease, uterine anomalies etc.).

(ii) The controls should be matched with regard to age and ethnicity and should all have had a normal first pregnancy with no history of preeclampsia or fetal growth restriction.

(iii) There are large numbers of KIR haplotypes that differ in both gene content and allelic polymorphism at individual KIR loci. These have been categorized as KIR A or KIR B haplotypes based on the presence/absence of particular KIR genes, and it is essential that they are defined in the same way. A current working definition provided by the IPD KIR database being as follows; Group B haplotypes are characterized by one or more of the following genes: KIR2DL2, KIR2DL5, KIR2DS1, KIR2DS2, KIR2DS3, KIR2DS5 and KIR3DS1. Conversely, Group A haplotypes are characterized by the absence of all these genes. The distinction between Group A and B haplotypes is a useful one, having potential biological and medical significance.

(iv) Studies of populations worldwide have established that KIR gene frequencies and KIR genotype occurrence vary markedly among different ethnic groups (Middleton et al., 2008; Single et al., 2008).

In view of the above considerations, there are several possible explanations for why this paper on recurrent miscarriage has conflicting findings. The patients and controls were carefully selected on the basis of their clinical characteristics but consisted of four different caste groups divided into 12 different populations. It is known that the KIR gene frequencies differ quite considerably in some of these groups, and this may have skewed their findings (Rajalingam et al., 2002; Kulkarni et al., 2008). Even though the authors have tried to match numerically the controls and affected women as closely as possible with such small numbers, bias is still likely to be introduced.