Recombinant versus urinary gonadotrophin for ovarian stimulation in assisted reproductive technology cycles. A Cochrane review†

Background
Several systematic reviews compared recombinant gonadotrophin with urinary gonadotrophins (HMG, purified FSH and highly purified FSH) for ovarian hyperstimulation in IVF and ICSI cycles and these reported conflicting results. Each of these reviews used different inclusion and exclusion criteria for trials. Our aim in producing this review was to bring together all randomized studies in this field under common inclusion criteria with consistent and valid statistical methods.

Methods
An extended search was done, including the Cochrane databases, MEDLINE, EMBASE, CINAHL, National Research Register, Current Controlled Trials (up to May 2010).

All randomized controlled trials reporting data comparing clinical outcomes for women undergoing IVF/ICSI cycles and using recombinant FSH in comparison with HMG or highly purified HMG, purified urinary FSH (FSH-P) and highly purified urinary FSH (FSH-HP) for ovarian hyperstimulation in IVF or ICSI cycles were included.

Primary outcome measure was live birth rate and primary safety measure was ovarian hyperstimulation syndrome (OHSS) per randomized woman. Binary outcomes were analysed using odds ratios (ORs) and also reported in absolute terms. Grouped analyses were carried out for all outcomes to explore whether relative effects differed due to key features of the trials.

Results

Trial quality
All 42 trials (a total of 9606 couples) had data on clinical pregnancy; 28 trials had data on live birth and 32 trials had data on OHSS. Most included studies used computer generated randomization with a proper method of allocation concealment. The quality of the trials varied from low to moderate and appeared to be high in some of the larger sponsored trials.

Live birth rate per woman randomized
Comparing rFSH to any of the other gonadotrophins did not result in any evidence of a statistically significant difference in live birth rate (28 trials, 7339 couples, OR 0.97, 95% CI 0.87–1.08; I² of 0%). This suggests that for a group with a 25% live birth rate using urinary gonadotrophins the rate would be between 22.5 and 26.5% using rFSH. Only one urinary gonadotrophin subgroup comparison was significantly different: there were fewer live births after rFSH compared with hMG (11 trials, n = 3197, OR 0.84, 95% CI 0.72–0.99; I² of 0%; (Fig.1). For a live birth rate of 25%, use of rFSH rather than hMG would result in a live birth rate between 19 and 25%.

Safety
There was also no evidence of a difference in the OHSS rate (32 trials, 7740 couples, OR 1.18, 95% CI 0.86–1.61; I² of 0%). This means that for a group with 2% risk of OHSS using urinary gonadotrophins, the risk would be between 1.7 and 3.2% using rFSH.

Conclusions
Differences in clinical effectiveness and safety between the gonadotrophins are small. Clinical choice of gonadotrophin should depend on availability, convenience and costs. We included 42 trials, entailing 9606 couples. Further research on these comparisons is unlikely to identify substantive differences in effectiveness or safety.

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