Luteal phase support in assisted reproduction cycles

Background
The luteal phase in in vitro fertilization (IVF) cycles is insufficient and therefore supported with either progesterone, hCG or gonadotrophin-releasing hormone (GnRH) agonists. Luteal phase support improves implantation rates and thus pregnancy rates, but the ideal method is still unclear. Progesterone is most frequently used, hCG is known for the risk of ovarian hyperstimulation syndrome (OHSS), but is also widely used. GnRH agonists is a new method for luteal phase support. This is a summary of a meta-analysis published by the Cochrane Library (van der Linden et al., 2011) investigating luteal support in IVF/ICSI.

Methods
The authors searched electronic databases including the Cochrane Library, MEDLINE and EMBASE and conference abstracts in February 2011. Eligible reports were randomized trials of luteal phase support in IVF or ICSI investigating progesterone, hCG or GnRH agonist supplementation. Quasi-randomized trials and trials using frozen transfers or donor oocytes were excluded. Results were presented as risk differences (RDs) with 95% confidence intervals (CIs). In each comparison live birth rate was the primary outcome, secondary outcomes included clinical pregnancy rate, ongoing pregnancy rate, miscarriage rate, OHSS and multiple pregnancy rate per women.

Results
Trials and quality
The original Cochrane review included 69 trials with a total of 16,327 women included. In this Nutshell summary we only discuss the clinically most relevant findings. We included 10 studies in this report, with a total of 2,455 women. Seven studies had an unclear risk of bias. Two studies had a low risk of bias, although neither study reported blinding. One study reported more participants recruited than analysed, but did not report reasons.

Live birth rate
One study (156 women) compared progesterone with placebo and found significantly more live births when progesterone was used (RD: 11%, 95% CI: 2–19).

Three studies investigated progesterone + GnRH agonist versus progesterone alone (figure). One study (154 women) with a single dose of GnRH agonist in GnRH antagonist cycles found significantly more live births in the progesterone + GnRH agonist group (RD: 19%, 95% CI: 5–32). Two studies (301 women) investigated progesterone + multiple dose GnRH agonist versus progesterone alone in agonist cycles and also showed a significant result in favour of progesterone + GnRH agonist, RD: 18%, 95% CI: 8–28). The pooled RD for live birth rate including all three trials was 18% (95% CI: 10–26).

OHSS rate
OHSS rates were higher with hCG than with placebo or no treatment (RD: 11%, 95% CI: 6–17), and with hCG compared with progesterone (RD: 4%, 95% CI: 0–9). OHSS rates were also higher with hCG and progesterone compared with progesterone alone (RD: 5%, 95% CI: 2–9%). The last finding is based on three studies with outlying results, and should be interpreted with caution.

Conclusion
In this updated Cochrane review, the live birth rate was significantly higher with progesterone for luteal phase support in IVF/ICSI cycles. Co-treatments did not improve outcomes, except for GnRH agonists. We found no evidence favouring a specific route, dosage or duration of progesterone.

hCG alone or as a supplement to progesterone was associated with a higher risk of OHSS and should therefore be avoided.

Reference

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