

Role of Progesterone in Stimulated Cycle and Pregnancy

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The beneficial effect of luteal phase support (LPS) after embryo transfer in IVF treatment has unequivocally been accepted as a consequence of a large number of observational studies indicating a luteal phase defect after ovarian stimulation, and interventional trials indicating higher pregnancy rates after LPS.

Various substances (human chorionic gonadotropin (hCG)), progesterone (P), estradiol (E2), gestagen and, more recently, GnRH-agonist), routes of administration, and regimen of administration can be employed. However, because of a lack of larger sized randomised controlled trials, a large number of questions has remained unanswered. So far, no consensus could be reached as regards the optimal (e.g. simplest and safest) route and regimen of administration, the optimal (e.g. most efficient) substance(s), the minimally effective doses of the various substances, and the duration necessary to support the luteal phase.

Recently, we conducted a systematic review with the aim of determining the efficacy of administration of vaginal P as progesterone-in-oil suspension in the form of capsules, suppositories or vaginal cream versus other forms of luteal phase support (including 8 % progesterone polycarbophil vaginal gel, and IM-progesterone oily formulation) after ovarian stimulation for IVF-ET. Overall, the available trials are clinically heterogeneous, and furthermore, sample sizes in the comparison groups are mostly too small to exclude clinically relevant differences with confidence. However, current data from the literature indicate (as a 'best estimate') no statistically significant difference between vaginal P as capsules/suppositories/cream as compared to a wide range of other forms of LPS after IVF.

On the other hand, the current wide-spread practice of P supplementation in early pregnancy is in-fact supported only by weak evidence. However, the 'gold standard' as stated in a large number of text books, is still early pregnancy P supplementation. Although 3 retrospective studies have indicated no benefit of P in early pregnancy, the only available prospective, randomised controlled equivalence trial with 303 patients (150 in one Group and 153 in the other group) comparing 3x200 mg/d vs. no P for 3 weeks after detection of hCG 14 days after ET has indicated a (statistically non-significant) reduction in live birth rate of -3.7% (95 CI – 11.2-3.5%) when no P is given in early pregnancy. Thus, early pregnancy supplementation of P still has to be considered a standard measure, but appropriately designed and powered studies further investigating P withdrawal after detection of hCG 12-14 days after ET are urgently needed.