

PROGESTERONE

Use

Several trials are currently studying the prophylactic use of this natural hormone in women with a previous history of preterm labour, or found, during mid-pregnancy screening, to have an unusually short cervix.

Pharmacology

The chemical structure of progesterone, a natural hormone produced by the ovary's corpus luteum, was first determined in 1934. It was synthesised artificially soon after that and used, intermittently, for many years in the treatment of various menstrual disorders despite very little objective evidence of benefit. It has also been in intermittent use, ever since 1960, to reduce the risk of miscarriage. While there was no evidence that it does manage to reduce the general miscarriage rate in a Cochrane review of 14 small trials in 2003, there did seem to be a case for mounting a further trial in women who had already suffered at least three miscarriages. Indeed a systematic review undertaken in 1990 did suggest that it might also have a role in reducing the risk of preterm labour in women with a strong prior history of this problem, and interest in this approach to the prevention of recurrent preterm labour has increased significantly in the last ten years.

Considerable interest was generated by some small trials suggesting that use reduced the risk of preterm birth in women who have already experienced preterm birth, but larger trials failed to replicate these findings. However, in a trial that involved the mid-pregnancy screening of an unselected population of women (Fonseca *et al.*, 2007) prophylaxis in the 1.7% with a very short cervix (≤ 15 mm) almost halved delivery before 34 weeks. Retrospective review in another recent trial (DeFranco *et al.*, 2007) found that prophylaxis had also been effective in the subgroup (46/659) with a mid-trimester cervical length of less than 28 mm.

Warnings about exposure to any progestogen in early pregnancy were issued in the 1960s after reports appeared saying that this could cause masculinisation of the female fetus, but it seems, in retrospect, that most cases were caused by exposure to norethisterone rather than progesterone. There would seem to be a three-fold increase in the risk of second- or third-degree hypospadias in boys after first trimester use, but later use does not seem to be associated with any general excess of congenital abnormality. The only study of intrauterine use as a contraceptive during breast feeding found no evidence that this interfered with lactation.

Prophylaxis

Vaginal capsules: The nightly insertion of a 200 mg progesterone capsule into the vagina from the 24th to the 34th week of pregnancy nearly halved the risk of preterm birth in women found to have a short cervix on mid pregnancy screening in one recent trial. The current OPTIMA trial is also testing a 200 mg pessary.

IM prophylaxis: 250 mg depot injections of hydroxyprogesterone caproate given IM once a week from the 20th to the 36th week of pregnancy reduced the risk of recurrent preterm delivery in one small trial.

Supply and administration

Vaginal capsules: Capsules containing 200 mg of micronized progesterone (Utrogestan[®]) made by Besins International in Belgium were used in the trial reported by Fonseca in 2007.

Vaginal gel: Vaginal applicators delivering a gel containing 90 mg of progesterone (Prochieve[®]) made by Columbia Laboratories, NJ, USA, were used in the trial reported by O'Brien and by DeFranco in 2007.

IM prophylaxis: 17 α -hydroxyprogesterone caproate (also known as hydroxyprogesterone hexanoate [BANM]) is the analogue of the natural hormone that was used in the studies by Meis in 2003 and Facchinetti in 2007. 250 mg ampoules made up in castor oil, with benzyl benzoate as a preservative, are manufactured by Schering Health Care Ltd, and could be imported into the UK from Germany on request.

References

See also the relevant Cochrane reviews ©

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