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CASE REPORT

# Inadvertent Use of Depot GnRH-agonist Trigger and its Effect on the Luteal Phase: A Case Report

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**Abstract**

The use of short acting GnRH agonist to trigger final oocyte maturation in IVF is a common practice. Its primary advantage is prevention of significant ovarian hyperstimulation syndrome. The effect of a long acting GnRH agonist preparation in that setting is not known. In the current case report, a depot preparation was given accidentally, resulting in prolonged and robust luteal phase activity, with luteolysis achieved only 14 days after administration. In that setting, fresh embryo transfer should be avoided.

## Case Report

To the best of our knowledge, the use of depot GnRH agonist for final oocyte maturation was described only in the context of achieving ovarian suppression before chemotherapy [1]. While it was demonstrated that depot GnRH agonist is effective for final oocyte maturation, the luteal phase endocrine profile in general, and the timing of achieving ovarian suppression in particular, are not known.

We hereby present a case report that confirms that final oocyte maturation can be achieved by depot GnRH agonist administration. We also describe a detailed account of the luteal phase endocrine profile until ovarian suppression ensues.

A 31-year-old patient was evaluated for primary infertility of 5-years duration. Female evaluation was normal except for a hysterosalpingogram (HSG) demonstrating lack of contrast material spillage from the right fallopian tube. Sperm analysis was remarkable for low concentration (2-7 million/ml) and asthenospermia (25%-31% motility), indicating male infertility component. Following 4 cycles of induction of ovulation and intrauterine insemination that failed, the patient underwent IVF treatment.

On day 2 of cycle, estradiol (4 mg daily) was administered for 2 days for scheduling purposes. Subsequently, ovarian stimulation was initiated with daily injections of 150 units of highly purified human menopausal gonadotrophin (Menopur, Ferring, Switzerland). On the sixth stimulation day a GnRH antagonist (0.25 mg Cetrotide, Merck Serono, Germany) was added. A short acting GnRH agonist (0.2 mg Decapeptyl, Ferring) was ordered on the 10$^{th}$ stimulation day for the purpose of final oocyte maturation and ovarian hyperstimulation syndrome (OHSS) prevention as 20 growing follicles (> 12 mm in diameter) were observed in ultrasound. Inadvertently, the patient was administered 2 injections of the very long acting depot GnRH agonist (Decapeptyl CR 3.75 mg Ferring).

Oocyte retrieval performed 36 h after trigger yielded 22 oocytes, of which 20 were mature (MII) oocytes and subjected to Intracytoplasmic Sperm Injection (ICSI). Eighteen normal fertilizations were observed and six cleavage stage embryos were frozen 3 days after retrieval.

To ascertain ovarian suppression for the purpose of planning a thaw cycle, the luteal phase was followed by repeated blood hormones tests as shown in Table 1. Withdrawal bleeding was reported 14 days after oocyte retrieval.

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**Table 1:** Hormone concentrations from oocyte retrieval day +2 onwards.

| Day | 2 | 3 | 6 | 7 | 8 | 9 | 13 |
|---|---|---|---|---|---|---|---|
| Estradiol (pmol/l) | 6,819 | 8,929 | 5,359 | 4,635 | 3,128 | 3,479 | 123 |
| Progesterone (nmol/l) | 135.8 | > 190 | 356 | 273 | 164 | 133 | 2.3 |
| LH (IU/l) | 0.8 | 1.5 | 1 | 1.1 | 0.8 | 2.1 | 0.76 |

Day 0 = oocyte retrieval day.

The use of a single dose of short acting GnRH agonists for final oocyte maturation in the context of OHSS is well-established [2,3]. Based on previous data, complete functional luteolysis appears to be obtained within 5 days after GnRH a trigger [4]. Nevertheless, there could be personal variability as to luteolysis kinetics [5]. In the current case report a depot preparation was given accidentally, resulting in prolonged luteal phase activity, with luteolysis achieved only 14 days after administration. Interestingly, mid-luteal estradiol and progesterone concentrations reflect robust luteotrophic activity, in parallel with low LH levels.

This observed discrepancy between low LH levels and high levels of luteal hormonal activity is intriguing. The possibility that GnRH agonists may support luteal function by acting directly on the corpora lutea was previously described [6,7]. This notion was further tested clinically in a small randomized study suggesting that low doses of GnRH agonist (100 µg of buserelin) exert a stimulatory effect on the corpus luteum [8]. In line with the above reports, this current case report describes, for the first time, the effect of prolonged GnRH agonist activity generated by a high-dose, long acting preparation on the luteal phase, confirming excessive mid-luteal stimulation (pick mid-luteal progesterone was 356 nmol/l). This excessive stimulation clearly justifies the "freeze all" policy (freezing all available embryos, to be later transferred in a thaw cycle), since endogenous hCG production could have exposed the patient to OHSS risk.

In conclusion, inadvertent administration of depot GnRH agonist instead of a short acting preparation facilitates final oocyte maturation; however, excessive mid-luteal stimulation suggests that it is prudent to freeze all embryos.

## References


1. Cavagna M, Dzik A (2011) Depot GnRH-agonist trigger for breast-cancer patient undergoing ovarian stimulation resulted in mature oocytes for cryopreservation: A case report. Reprod Biomed Online 22: 317-319.
2. Devroey P, Polyzos NP, Blockeel C (2011) An OHSS-Free Clinic by segmentation of IVF treatment. Hum Reprod 26: 2593-2597.
3. Humaidan P, Kol S, Papanikolaou EG, Copenhagen GnRH Agonist Triggering Workshop Group (2011) GnRH agonist for triggering of final oocyte maturation: Time for a change of practice? Hum Reprod Update 17: 510-524.
4. Fatemi HM, Polyzos NP, van Vaerenbergh I, Bourgain C, Blockeel C, et al. (2013) Early luteal phase endocrine profile is affected by the mode of triggering final oocyte maturation and the luteal phase support used in recombinant follicle-stimulating hormone-gonadotropin-releasing hormone antagonist in vitro fertilization cycles. Fertil Steril 100: 742-747.
5. Kol S, Breyzman T, Segal L, Humaidan P (2015) 'Luteal coasting' after GnRH agonist trigger - individualized, HCG-based, progesterone-free luteal support in 'high responders': A case series. Reprod Biomed Online 31: 747-751.
6. Tesarik J, Hazout A, Mendoza Tesarik R, Mendoza N, Mendoza C (2006) Beneficial effect of luteal-phase GnRH agonist administration on embryo implantation after ICSI in both GnRH agonist- and antagonist-treated ovarian stimulation cycles. Hum Reprod 21: 2572-2579.
7. Isik AZ, Caglar GS, Sozen E, Akarsu C, Tuncay G, et al. (2009) Single-dose GnRH agonist administration in the luteal phase of GnRH antagonist cycles: A prospective randomized study. Reprod Biomed Online 19: 472-477.
8. Pirard C, Donnez J, Loumaye E (2005) GnRH agonist as novel luteal support: Results of a randomized, parallel group, feasibility study using intranasal administration of buserelin. Hum Reprod 20: 1798-1804.