

An Algorithm Combining Ultrasound Monitoring and Urinary Luteinizing Hormone Testing: A Novel Approach for Intrauterine Insemination Timing

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Abstract

Objective: Intrauterine insemination (IUI) is a commonly used treatment for infertility. Optimal timing of insemination is achieved either by ultrasound monitoring of follicular growth followed by the administration of human chorionic gonadotropin (hCG) or by the detection of a luteinizing hormone (LH) surge through urinary LH testing (uLH). However, in cycles where follicular growth is monitored, there is a possibility of a premature LH rise which may affect the outcome of treatment. The objective of the current study was to determine the frequency of spontaneous LH surges in ultrasound-monitored IUI cycles.

Methods: One hundred IUI cycles were followed for this prospective cohort study. In combination with ultrasound monitoring, uLH testing was performed twice daily. A serum LH test was performed in the case of an inconclusive uLH test result. IUI was performed either on the day after a positive LH test or, if the diameter of the dominant follicle reached 18 mm and the LH test was still negative, 36 hours after ovulation triggering by administration of hCG.

Results: Of the 87 analyzed cycles, 19 (21.8%) exhibited a premature LH surge as detected by urine testing. Eleven further cycles had an inconclusive urine result, and in six of these (6.9% of cycles) the result was confirmed positive by serum LH testing, giving a total of 25 cycles (28.7%) experiencing a premature LH surge.

Conclusion: A considerable proportion of patients undergoing ultrasound-monitored IUI cycle had a spontaneous LH surge before ovulation triggering was scheduled. This could affect pregnancy rates following IUI.

Key Words: Insemination; ovulation prediction, luteinizing hormone, pregnancy rate

Competing Interests: None declared.

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Résumé

Objectif : L'insémination intra-utérine (IIU) est un traitement couramment utilisé contre l'infertilité. La chronologie optimale de l'insémination est déterminée par la mise en œuvre d'un monitoring échographique de la croissance folliculaire, suivi de l'administration de gonadotrophine chorionique (hCG), ou par la détection d'une poussée d'hormone lutéinisante (LH) au moyen d'un dépistage urinaire visant la LH (uLH). Cependant, au sein des cycles dans le cadre desquels la croissance folliculaire fait l'objet d'un monitoring, une hausse prématurée de la LH peut en venir à se manifester, ce qui pourrait affecter l'issue du traitement. La présente étude avait pour objectif de déterminer la fréquence des poussées spontanées de LH dans le cadre de cycles d'IIU faisant l'objet d'un monitoring échographique.

Méthodes : Cent cycles d'IIU ont fait l'objet d'un suivi aux fins de la présente étude de cohorte prospective. Conjointement avec le monitoring échographique, un dépistage uLH a été mené deux fois par jour. Un dépistage sérique de la LH a été mené en présence de résultats peu concluants à l'issue du dépistage uLH. L'IIU a été menée le jour suivant l'obtention d'un dépistage positif de la LH ou, lorsque le diamètre du follicule dominant atteignait 18 mm et que le dépistage de la LH s'avérait toujours négatif, 36 heures à la suite du déclenchement de l'ovulation par administration de hCG.

Résultats : Parmi les 87 cycles analysés, 19 (21,8 %) ont connu une poussée prématurée de LH détectée par dépistage urinaire. Onze autres cycles ont obtenu des résultats peu concluants à la suite du dépistage urinaire : dans six de ces cycles (6,9 % des cycles), le résultat a été confirmé comme étant positif au moyen d'un dépistage sérique de la LH. Ainsi, un total de 25 cycles (28,7 %) ont connu une poussée prématurée de LH.

Conclusion : Une proportion considérable des patientes qui se sont soumises à un cycle d'IIU faisant l'objet d'un monitoring échographique ont connu une poussée spontanée de LH avant qu'un déclenchement de l'ovulation ne soit planifié. Cela pourrait affecter les taux de grossesse à la suite de l'IIU.

INTRODUCTION

Intrauterine insemination, generally in combination with ovarian stimulation, is a commonly used option for mild male factor, cervical factor, and unexplained infertility.¹ Various factors are known to affect the outcome in IUI cycles, including the cause of the infertility, the woman's age, the sperm quality, and the ovarian stimulation protocol.²⁻⁴ Accurate timing of insemination is one of the most important variables that can affect the success of an IUI cycle.⁵ As the oocyte fertilization window is very short, correct timing is essential, and insemination should coincide, as much as possible, with ovulation.⁶

Two methods are generally employed to ensure accurate timing for insemination: (1) monitoring follicular growth through serial ultrasound measurements, followed by the administration of human chorionic gonadotropin with IUI 36 hours afterwards; or (2) detection of the luteinizing hormone surge by uLH testing with IUI on the next day. No clear advantage of one method over the other has been reported in terms of pregnancy rates.⁷⁻⁹

However, in cycles in which follicular growth is monitored, a spontaneous premature LH rise before hCG administration is a possibility,^{10,11} and this can occur even before the dominant follicle reaches a mean diameter of 18 mm.¹² Ovulation will usually occur within 24 hours after an LH surge,¹³ and therefore IUI performed 36 hours after hCG administration in these cycles could be too late.

The objective of the current study was to determine the frequency of spontaneous LH surge, as measured by uLH testing, in serial ultrasound-monitored IUI cycles, with the aim of optimizing the timing of insemination using a novel IUI monitoring protocol.

MATERIALS AND METHODS

A pilot prospective cohort study was conducted at the OVO fertility clinic in Montreal, Quebec, from July to October 2009. Patients undergoing ultrasound monitoring of follicular growth for IUI treatment cycles, with either no stimulation or mild ovarian stimulation with clomiphene citrate (100 mg daily from day 3 to day 7) or letrozole

(5 mg daily from day 3 to day 7) were eligible for inclusion in the study. The use and the type of mild ovarian stimulation were determined by the patient's treating physician at their preceding consultation. Patients with polycystic ovary syndrome or any type of anovulation were excluded. Those receiving gonadotropins, metformin, 17- β estradiol, or progesterone at any point in their cycle were also excluded.

Because the study was designed as a pilot study to answer a descriptive statistical question, i.e., the frequency of spontaneous LH surge in 100 ultrasound-monitored IUI cycles, a sample size calculation was not performed.

Patients were approached on the day of their first ultrasound examination, which was scheduled according to the standard method at the clinic (length of the shortest menstrual cycle minus 16 days). If they agreed to participate in the study and provided informed consent, they were given a uLH kit (Conceive, Pendopharm, Pharmascience Inc., Montreal QC) consisting of seven ovulation test sticks and one pregnancy test. All ultrasound examinations were performed in the morning by reproductive endocrinology and infertility specialists using a 7.5 MHz transvaginal probe with Voluson ultrasound machine (General Electric, Baie D'Urfé QC). If, after routine transvaginal ultrasound monitoring, the mean diameter of the dominant follicle measured ≤ 13 mm, another ultrasound was scheduled according to the standard protocol of the clinic (2 days later). If on the second ultrasound the follicle measured 14 to 17 mm, patients were instructed to begin uLH testing twice daily (at 0700 and 1900) until a positive test result was seen or recombinant hCG was administered. Patients with follicles of 18 mm diameter or more were asked to perform a uLH test at 1900 on the same day. The administration of hCG was performed in the evening of the day when the dominant follicle reached 18 mm mean diameter and the uLH test remained negative. IUI was performed on the day following a positive uLH result, or 36 hours after hCG administration. If the patient was unable to interpret the result of a uLH test (inconclusive uLH result), she was asked to come to the clinic for a serum LH test (Microparticle enzyme immunoassay, AxSYM LH test, Abbott Laboratories, Saint-Laurent QC). A serum LH value of 8 IU/L or more was considered positive and, in these cycles, IUI was scheduled for the next day. In the case of a negative serum LH test, the patient was instructed to continue uLH testing (Figure 1).

Gradient density centrifugation was used for sperm preparation and a CCD standard IUI catheter (CCD International, Paris, France) was used for IUI. No luteal phase support was given.

ABBREVIATIONS

hCG	human chorionic gonadotropin
IUI	intrauterine insemination
LH	luteinizing hormone
uLH	urinary luteinizing hormone

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