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A Study to Determine Whether Serum Follicle-Stimulating Hormone Can Be a Marker for Ovarian Hyperresponse to Follicle-Maturing Drugs for *in vitro* Fertilization

Key Words

Multiple follicles
High estradiol
In vitro fertilization
Follicle-stimulating hormone
Gonadotropins

Abstract

The study presented herein evaluated whether 26 of 122 consecutive women who tend to hyper-respond (serum estradiol >4,000 pg/ml or >30 follicles) following controlled ovarian hyperstimulation for *in vitro* fertilization have higher serum FSH levels at certain critical stages during the follicular phase. Baseline day-2 serum FSH and blood levels taken on days 5 and 6 of human menopausal gonadotropin therapy were not different in the hyper-responders from those responding normally. The only significant difference in serum FSH was seen on the day of human chorionic gonadotropin where it was actually lower in the hyper-responders. Thus, there does not appear to be a critical serum FSH level which would dictate a decrease in gonadotropins to prevent hyper-response.

Introduction

The population at risk for ovarian hyperstimulation following *in vitro* fertilization have been previously defined by Navot et al. [1] and Asch et al. [2], based on estradiol (E₂) levels (>4,000 pg/ml) and the number of eggs retrieved (>30).

Many ovarian hyperstimulation regimens are fixed protocols. The finding of some hormonal marker that can provide a clue that hyper-response is likely would be extremely helpful since the gonadotropin dosage could possibly be reduced.

In vitro fertilization cycles are typically monitored by serum E₂ levels and ultrasound for follicular size and number and sometimes by serum progesterone and LH but most centers do not use serum FSH for monitoring.

FSH is the hormone considered responsible for recruitment of follicles. Dropping FSH levels from the mid-follicular phase to ovulation are considered the main reason for atresia of all other follicles but the dominant follicle. The study presented herein measured serum FSH levels, including baseline (before gonadotropin therapy) and 3 additional times after gonadotropins were started to see whether the level of FSH could predict those who eventually fit the criteria for risk of ovarian hyperstimulation syndrome (OHSS).

The objective of this study was to compare the early, mid and late follicular serum FSH levels between patients with an increased risk for OHSS to those with a normal risk. If differences were found, serum FSH could possibly be used as a clinical marker for patients at an increased risk of OHSS.

that, since the FSH in the blood of the hMG-treated women was probably derived from injected hormones and differences in serum E₂ were found 1 day earlier than the divergence of FSH profiles, the differences in metabolism of the exogenously administered FSH are involved primarily in determining differing gonadal reactions [4].

However, another explanation for differing responses to the same dose of gonadotropins may be the intrinsic sensitivity of the ovaries to LH and FSH. Our data, using a much greater number of patients in the study than used by Ben-Rafael et al. [4], are more consistent with this hypothesis.

It should be noted, however, that the study presented herein and that of Ben-Rafael et al. [4] actually compared

different events: we evaluated responders with an increased risk of OHSS to responders with a normal risk of OHSS, and they compared low responders to high (normal) responders [4]. Thus, the possibility does exist that poor response could be related to excessive metabolic clearance of FSH resulting in a lower number of recruited follicles.

However, the measurement of early follicular phase serum FSH does not seem warranted to help prevent severe ovarian hyperstimulation by reducing the gonadotropin dosage according to a critically high serum FSH level.

References

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