Pregnancy-specific $\beta_1$-glycoprotein (SP1) after In Vitro Fertilization and Embryo Transfer

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Summary. Recent reports indicate that SP1, a “pregnancy-specific $\beta_1$-glycoprotein”, can be used as a biological marker for very early pregnancy and occult abortion. In this investigation, SP1 serum concentrations were measured in the luteal phase of 48 menstrual cycles stimulated for in-vitro fertilization (IVF) and embryo transfer (ET). All patients received hMG for ovarian stimulation. Ovulation was induced by $\beta$-hCG and also administered to support the luteal phase. In the 8 pregnancies arising after ET, SP1 (< 0.5 ng/ml) was not detected before 13 to 19 days after laparoscopy. In contrast, the pregnancy-dependent $\beta$-hCG increase was detectable earlier than SP1 despite the administration of hCG given for luteal support. However, low SP1 readings (0.5–1.1 μg/ml) as early as 3 days after laparoscopy were observed in 11 cycles without a positive sign of $\beta$-hCG production. Our results suggest that SP1 determinations cannot be used as a marker for occult abortion; also, positive SP1 readings without increase $\beta$-hCG, especially during the early luteal phase after ET, have to be interpreted with caution.

Key words: Pregnancy-specific $\beta_1$-glycoprotein (SP1) – Early pregnancy – In vitro fertilization and embryo transfer

Introduction

In vitro fertilization (IVF) and several infertility treatments use $\beta$-hCG for the induction of ovulation and in order to support the luteal phase. Depending on the $\beta$-hCG dose administered, the early detection of pregnancy and/or occult abortion by this gonadotropin cannot be performed within 8–10 days after $\beta$-hCG injection (Braunstein et al. 1973; Jones et al. 1983). However, to screen the therapeutic efforts, it is important to detect occult abortions as well as

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biochemical pregnancies. SP1 is one of the modern placental proteins and is supposed to be pregnancy-specific (Bohn 1971; Bischof 1984). It is immunologically different from hCG and the pituitary gonadotropins. According to Horne et al. (1976) it is produced by the syncytiotrophoblast and subsequently released into the maternal serum in rising concentrations from early pregnancy until delivery (Tamsen et al. 1984).

The development of highly sensitive enzyme immunoassays (Brenner 1978) allowed the detection of SP1 in serum within 13–20 days of ovulation (Eiermann et al. 1981; Tatra and Kemeter 1983). Recently, SP1 increase in early pregnancy has been reported to occur about the same time as the first positive β-hCG reading (Ahmed and Klopper 1983). Thus, SP1 seems to be an additional biochemical marker for the detection of very early pregnancy. In this study we investigated the possibility whether SP1 can be used as a marker for very early pregnancy and/or occult abortion in patients undergoing the therapy of IVF and ET.

**Patients and Methods**

We examined 48 menstrual cycles of 20 healthy patients of age 21 to 38 years who were undergoing IVF and ET treatment due to irreversible tubal disease. One to 3 cycles per patient were studied. Human menopausal gonadotropin (hMG; Pergonal 75 IU FSH/LH, Serono Interlabo S.A., Carouge-Geneva) was used for ovarian stimulation. 150 IU hMG were applied daily, starting on the 3rd day of the respective cycle. Later on the hMG dose was individualized according to the ovarian response. The hMG treatment was stopped when 17β-estradiol (E2) levels reached 1 nmol/l or more, and at least 2 follicles of 1.7 cm diameter or larger were found. For ovulation induction 10,000 units of hCG (Profarsi, Serono Interlabo S.A.) were administered and laparoscopy was performed after 34–36 h of hCG injection.

For SP1 measurement venipunctures were performed in 48 cycles on days 3, 5, 8 and 10; an additional blood sample was taken in 37 cycles on day 13. In addition, β-hCG of the luteal phase was assayed in all ET leading to pregnancies and in 12 cycles in which IVF and ET therapy failed. β-hCG and SP1 were measured in early pregnancies that were diagnosed by β-hCG level exceeding 40 U/l on day 18 in order to avoid overlap with the injected hCG.

SP1 was determined by enzyme immunoassay using the Enzygnost-SP1 kit (Behring AG, Marburg, FRG). The detection limit of our assay was 0.5 ng/ml. Interassay variation was 12.5% at a range of 20 ng/ml. – β-hCG was assayed by RIA (Clinical Assays, Cambridge, MA, U.S.A.). The detection limit was 5 U/l, the interassay variation was 7.8% at a range of 95 U/l. Serum samples were frozen at −24°C until assayed.

**Results**

SP1 values exceeding the detection limit of 0.5 ng/ml were found in 20 of 48 menstrual cycles investigated. These cycles which exhibited positive SP1 values (> 0.5 ng/ml) were divided into 3 groups.

The first group consisted of 8 patients who revealed an early pregnancy as follows: 3 normal pregnancies after IVF/ET treatment, 1 pregnancy was leading to an anembryonic sac, and 1 yielded an extrauterine pregnancy. Furthermore, a first trimester abortion and 2 embryo losses within 25 days after laparoscopy were observed. The SP1- and hCG concentrations obtained in these cycles are