NOTE

Lack of Release of Human Chorionic Gonadotropin by Gonadotropin-Releasing Hormone

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Synopsis

The effects of either single injection or continuous infusion of synthetic Gn-RH on plasma hCG levels were studied in 5 pregnant women (14-38 week gestation). No definite increase of hCG level was seen in all the cases studied. In view of large dosages of Gn-RH used in this study in comparison with its minimum effective dose for the pituitary gonadotropin release, Gn-RH seems unlikely to play a role in hCG secretion during human pregnancy.

The levels of human chorionic gonadotropin (hCG), in either plasma or urine, are widely believed to show unique changes throughout pregnancy, which increases drastically from 10 to 11 days after ovulation, remains high for the next several weeks, and then declines after 14-15 week gestation. Such changes in hCG level are in marked contrast to the other placental hormones, such as steroids and human chorionic somatomammotropin (hCS), which increase as pregnancy progresses.

Little is, however, known about the mechanism to control hCG secretion from the placenta. The role of Gn-RH is not known in the control mechanism of hCG secretion in contrast to the established role of Gn-RH in gonadotropin secretion from the pituitary.

Concerning the relationships between Gn-RH and placental function, only a few papers have appeared till today. Takagi (1971) reported that a crude hypothalamic extract increased hCG secretion from the cultured placenta, when added to incubation medium. Gibbons et al. (1975) showed that homogenates prepared from fresh human placentas not only caused the release of LH in rats but also was capable to synthesize LH-releasing factors in in vitro incubation with the addition of appropriate precursor amino acids and cofactors.

These studies prompt us to investigate the effects of Gn-RH on hCG secretion in pregnant women.

Materials and Methods

Five normal pregnant women (14-38 week gestation) volunteered for the study and were given Gn-RH (Dai-ichi Pharmaceutical Co.) in either single iv injection or continuous infusion. Plasma hCG level was radioimmunoassayed as described below.

Dosage of Gn-RH:

200 μg of Gn-RH was given to 2 pregnant women by a single injection. 20 to 180 μg/hr of Gn-RH was infused in 3 pregnant women for 1 to 6 hr. In order to determine the proper dosage of Gn-RH infusion, the effect of 2.5, 5, 10, 20 μg/hr infusion on pituitary gonadotropin release was tested in 4 normal cyclic women during the early follicular phase. As shown

Received for publication July 6, 1976.
in Fig. 1, both LH and FSH increased in response to Gn-RH infusion at the dosage of 5 µg/hr or more. Therefore, the pregnant women received Gn-RH infusion around 4 to 36 times the minimum effective dose in non-pregnant women.

**hCG assay:**

A hCG assay kit (CEA-IRE-SORIN, Belgium) was used. Plasma was diluted 100 to 1600 times with phosphate buffer and assayed at several dilutions. The dilution curves were parallel to the standard one, and the value was read from the dilution which met the steepest part of the standard curve.

This assay system crossreacts with pituitary LH. It is, however, believed that concomitant LH does not affect the hCG value assayed, since LH/hCG ratio is around 1/250-1/2500, calculated based on the hCG concentration presented in this paper and LH by the use of LH-β specific radioimmunoassay during pregnancy (Ryes et al., 1976).

**Results**

The changes of plasma hCG level following a single injection are shown in Fig. 2, and those following infusion in Fig. 3. No increase of plasma hCG is recognized in all the cases.

**Discussion**

Although several reports have appeared on the changes of pituitary FSH (Jeppson et al., 1974) and LH (Reys et al., 1976) following Gn-RH injection in pregnant...
women, no comments were made on the effect of Gn-RH on hCG levels.

From the present data, it is strongly suggested that Gn-RH seems unlikely to play a role in hCG secretion during human pregnancy. In addition, radioimmunoassay of Gn-RH in our laboratory failed to reveal detectable activity in the rat placenta, maternal plasma and human amniotic fluid while the rat hypothalamus was shown to have 3.01 ng per hypothalamus by the same assay.

There might be, however, a possibility that a fetal organ and/or placenta produces Gn-RH, and enormous high concentration of Gn-RH is kept in the placenta and stimulates it to secrete hCG. Further studies will be needed to examine the possibility.

Fig. 2. Effect of 200 µg Gn-RH injection on hCG levels in pregnant women.

Fig. 3. Effect of Gn-RH infusion on hCG level in pregnant women. The speed of infusion is indicated in the upper square. In case 1, 100 µg Gn-RH is added, following infusion, with no hCG increase.

References