

Fetal thyroid-stimulating hormone response to maternal administration of thyrotropin-releasing hormone

J.G. Thorpe-Beeston, MD,^a K.H. Nicolaidis, MD,^a R.J.M. Snijders, MSc,^b J. Butler, MA,^b
and A.M. McGregor, MD^c

London, England

Thyroid-stimulating hormone was measured in fetal blood samples obtained by cordocentesis before and after blood transfusion in Rh-affected pregnancies at 25 to 37 weeks' gestation. In eight of 26 study subjects thyrotropin-releasing hormone was given to the mothers immediately after the pretransfusion samples were obtained. In this group the fetal thyroid-stimulating hormone concentrations in the posttransfusion samples were significantly higher than those before the transfusion. (AM J OBSTET GYNECOL 1991;164:1244-5.)

Key words: Thyroid function, cordocentesis, respiratory distress syndrome

Animal studies have shown improvement in fetal pulmonary maturation after the maternal administration of thyrotropin-releasing hormone.¹ In human beings, intravenous injection of thyrotropin-releasing hormone to pregnant women within 3 hours before delivery at term was associated with increased thyroid-stimulating hormone concentrations in cord blood at delivery.^{2,3} The aim of this study was to investigate whether maternal thyrotropin-releasing hormone, administered at earlier gestations, could also stimulate the fetal pituitary.

Patients and methods

Serum thyroid-stimulating hormone was measured by radioimmunoassay in maternal and umbilical venous blood samples⁴ obtained immediately before and after fetal blood transfusion by cordocentesis,⁵ in 26 red blood cell isoimmunized pregnancies at 25 to 37 weeks' gestation. In eight patients, immediately after obtaining the pretransfusion fetal blood sample, thyrotropin-releasing hormone (200 µg) was given intravenously to the mothers.

Results

In the eight patients who were given thyrotropin-releasing hormone, gestation (mean = 32, SD = 2 weeks), fetal hemoglobin increase as a result of the transfusion (mean = 6.5, SD = 1.2 gm/dl), expansion

of the fetoplacental blood volume⁵ (mean = 70, SD = 24%), and rate of transfusion (mean = 8.7, SD = 2.9 ml/min) were not significantly different from the corresponding values in the 18 patients who were not given thyrotropin-releasing hormone (mean = 30, SD = 3 weeks, $t = -1.87$; mean = 6.6, SD = 2.4 gm/dl, $t = -0.03$; mean = 97, SD = 63%, $t = 1.12$; mean = 10.8, SD = 3.9 ml/min, $t = 2.28$, respectively).

In the group that received thyrotropin-releasing hormone, the mean thyroid-stimulating hormone concentration in the posttransfusion samples was significantly higher than that before the transfusion both in maternal (Fig. 1; mean difference = 7.687 mU/L, $t = 6.04$, $p < 0.001$) and fetal blood (Fig. 1; mean difference = 41.929 mU/L, $t = 6.27$, $p < 0.01$). The percentage increase in fetal thyroid-stimulating hormone concentration was significantly related to the time interval between the administration of thyrotropin-releasing hormone and the collection of the posttransfusion samples (Fig. 1; $r = 0.832$, $n = 8$, $p < 0.05$), but not to gestation at transfusion ($r = 0.092$), the change in fetal hemoglobin concentration ($r = 0.03$), the rate of transfusion ($r = 0.228$), or expansion of the fetoplacental blood volume ($r = 0.427$). In the control group there were no significant differences between the pretransfusion and posttransfusion thyroid-stimulating hormone concentrations in either the fetal (mean difference = 1.317, $t = 1.03$) or maternal blood (mean differences = 0.13, $t = 1.11$).

Comment

Fetal blood transfusion does not change the fetal thyroid-stimulating hormone concentration. However, maternal administration of thyrotropin-releasing hormone is associated with a rapid increase in fetal thyroid-stimulating hormone. Because the magnitude of the

From the Harris Birthright Research Centre for Fetal Medicine^a and the Departments of Clinical Biochemistry^b and Medicine,^c King's College School of Medicine and Dentistry.

Received for publication August 15, 1990; revised November 12, 1990; accepted November 27, 1990.

Reprint requests: K. H. Nicolaidis, MD, King's College School of Medicine and Dentistry, Denmark Hill, London, United Kingdom SE5 8RX.

6/1/27002

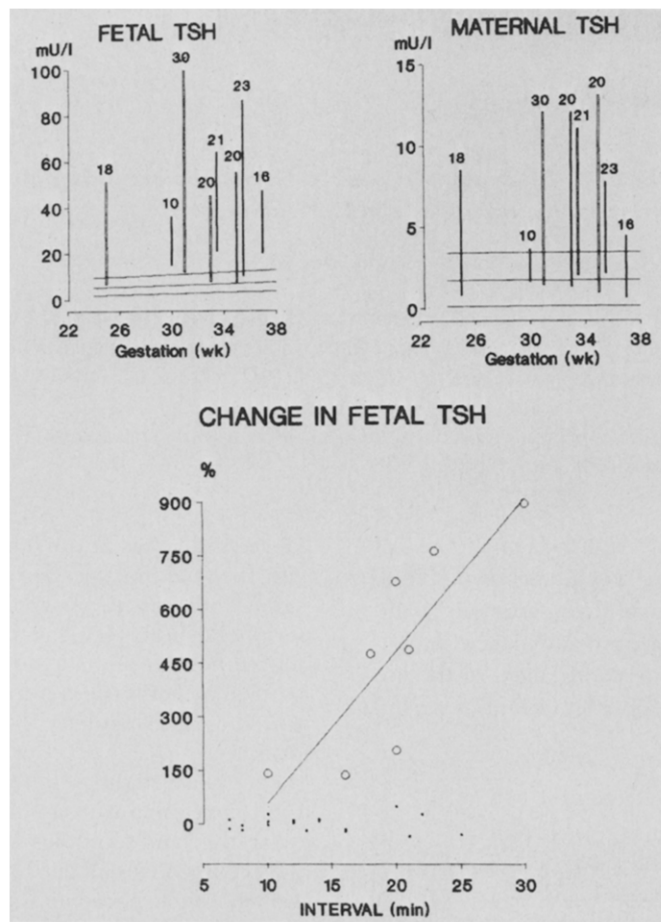


Fig. 1. Increase in fetal and maternal blood concentration of thyroid-stimulating hormone (mU/L) within 10 to 30 minutes from administration of thyrotropin-releasing hormone (actual time interval given above thyroid-stimulating hormone response in each case), plotted on appropriate reference range (mean, 5th, and 95th percentiles) for gestation (*top*). Change in fetal thyroid-stimulating hormone is significantly related to time interval from administration of thyrotropin-releasing hormone to mother (o); in control fetuses (.) there was no significant difference between pretransfusion and posttransfusion thyroid-stimulating hormone concentrations.

fetal response is similar to that reported in fetuses undergoing thyrotropin-releasing hormone stimulation at term,^{2,3} the data of the present study suggest that fetal pituitary responsiveness is established from at least 25 weeks' gestation. Furthermore, the fetal response to thyrotropin-releasing hormone is much greater than the maternal response, and this increased sensitivity may be a consequence of reduced negative feedback on the pituitary because the fetal thyroid hormone concentration is lower than that in postnatal life.¹

Further study is necessary to investigate the reproducibility of these findings in normal pregnancies and to define the possible effect of the increased fetal thyroid-stimulating hormone on the fetal thyroid gland, the time course of this response, and whether maternal thyrotropin-releasing hormone, unlike corticosteroids, can enhance fetal lung maturation from as early as 25 weeks' gestation.

REFERENCES

1. Rooney SA, Marino PA, Gobran LI, Gross I, Warshaw JB. Thyrotropin-releasing hormone increases the amount of surfactant in lung lavage from fetal rabbits. *Pediatr Res* 1979;13:623-5.
2. Roti E, Gnudi A, Braverman LE, et al. Human cord blood concentrations of thyrotropin, thyroglobulin, and iodothyronines after maternal administration of thyrotropin-releasing hormone. *J Clin Endocrinol Metabol* 1981;53:813-7.
3. Moya F, Mena P, Heusser F, et al. Response of the maternal, fetal, and neonatal pituitary-thyroid axis to thyrotropin-releasing hormone. *Pediatr Res* 1986;20:982-6.
4. Thorpe-Beeston JG, Nicolaides KH, Felton CV, et al. Maturation of the fetal thyroid and increasing thyroid-stimulating hormone. *N Engl J Med* 1991;324:532-6.
5. Nicolaides KH, Soothill PW, Rodeck CH, Clewell W. Rh disease: intravascular fetal blood transfusion by cordocentesis. *Fetal Ther* 1986;1:185-92.