ABSTRACT

Steroid hormones act through two mechanisms. The first is the classical genomic level, which acts at a relatively slow pace from hours to days. The second non-genomic mechanism of steroid activity can influence cellular function during seconds or even milliseconds. During pregnancy both mechanisms take place. Steroid hormones that act non-genomically and influence neuronal excitability are called neuroactive steroids. The aim of this study was to measure the levels of steroid hormones and examine their relationship to the physiology and pathophysiology of pregnancy.

The physiological importance of increased placental progesterone production, lowered production of 5B-pregnanone steroids and increased activity of steroid sulfotransferase with gestational age have been intensely discussed. On the basis of our results, we have proposed an alternative mechanism of maternal progesterone synthesis during pregnancy (progesterone, or the gestagen stabilizing activity of the myometrium = continuation of pregnancy). In contrast to previous results our observations indicate that gestagens arise from precursors in the fetus (from pregnenolone sulfate).

This mechanism is closely connected with the distribution of placental oxido-reductase. Data from this study show an increasing trend in the conversion of 3-oxo-(3β-hydroxy-), 17-oxo, and 20-oxo-steroids to their 3α-hydroxy-, 17β-hydroxy-and 20α-hydroxy metabolites. This indicates that there is a general trend in the fetus toward increased production of active gestagens, and in contrast a lowered production of estrogens and active GABAergic steroids as the term of birth gets closer (likely protecting the fetal CNS from oxidative stress). There has also been an anti-estrogen mechanism by the fetus described. This mechanism is based on increased activity of oxidized forms of 17β-hydroxysteroid dehydrogenase and aldose reductase in the placenta and fetal liver, which protect the fetus from hyper-estrogenization (guarding the fetal CNS by modulating ion channels) induced by increased aromatase activity that occurs as the term of birth gets closer.

In contrast, the ratio of estrogen to gestagens and their GABAergic metabolites increase in the mother. This likely leads to a lowered stabilizing influence of gestagens on the myometrium, which can contribute to inducing contractions of the myometrium and start of labor.