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Review

Steroid profiling in pregnancy: A focus on the human fetus

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ABSTRACT

In this review we focused on steroid metabolomics in human fetuses and newborns and its role in the physiology and pathophysiology of human pregnancy and subsequent stages of human life, and on the physiological relevance of steroids influencing the nervous systems with regards to their concentrations in the fetus. Steroid profiling provides valuable data for the diagnostics of diseases related to altered steroidogenesis in the fetal and maternal compartments and placenta. We outlined a potential use of steroid metabolomics for the prediction of reproductive disorders, misbalance of hypothalamic–pituitary–adrenal axis, and impaired insulin sensitivity in subsequent stages of human life. A possible role of steroids exhibiting a non-genomic effect in the development of gestational diabetes and in the neuroprotection via negative modulation of AMPA/kainate receptors was also indicated. Increasing progesterone synthesis and catabolism, declining production of tocolytic 5β-pregnane steroids, and rising activities of steroid sulfotransferases with the approaching term may be of importance in sustaining pregnancy. An increasing trend was demonstrated with advancing gestation toward the production of ketones (and 3β-hydroxyl groups in the case of 3α-hydroxy-steroids) was demonstrated in the fetus on the expense of 3α-hydroxy-, 17β-hydroxy-, and 20α-hydroxy-groups weakening in the sequence C17, C3, and C20. There was higher production of active progestogen but lower production of active estrogen and GABAergic steroids with the approaching term. Rising activities of placental CYP19A1 and oxidative isoforms of HSD17B, and of fetal CYP3A7 with advancing gestation may protect the fetus from hyperestrogenization.

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Contents

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1. Introduction

Steroid metabolomics represents an effective tool in the physiology and pathophysiology of human pregnancy. Besides the diagnostics of numerous fetal, newborn and maternal pathologies, including preterm labor [1,2], there is a growing number of evidence that the multicomponent analysis of steroids in umbilical cord blood at labor may also be effective for predicting endocrine diseases during the lifespan [3–11]. Steroid metabolomics could be of particular importance for the diagnostics and prediction of multifactorial disorders with a polygenic background. The steroid metabolism in pregnancy (Fig. 1) was thoroughly reviewed by Pasqualini [12], the tissue distribution of corresponding enzymes was a subject of our recent review [13] and the physiological importance of sex steroids and corticoids in pregnancy is widely known, while the physiological and pathophysiological relevance of steroids influencing the fetal central and peripheral neuronal system mostly remains an open question. Therefore, we concentrated on steroids exhibiting non-genomic effects as regards their concentrations in fetal body fluids and tissues.

Besides the data found in the literature (including our own), we discuss our current unpublished results (Tables 1–4) obtained from the study group that was described in detail in our recent report [2]. The only modification was the inclusion of 30 additional women with uncomplicated pregnancies. In brief, 80 women (21–41 years of age) at labor from the week 28 to 41 of gestation participated in the study. The women were divided into three groups according to gestational age (GA) at labor. Group A, B, and C contained women