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Influence of Gestational Diabetes Mellitus on the Activity of Steroid C17-Hydroxylase-C17,20-Lyase in Patients with Intrahepatic Cholestasis of Pregnancy

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Abstract : The incidence of gestational diabetes mellitus (GDM) is higher in women predisposed to developing intrahepatic cholestasis of pregnancy (ICP). Both diseases are associated with altered steroidogenesis when compared with none-ICP controls. However, the effect of GDM on circulating steroids in ICP patients remains unclear. The question remains, whether the levels of circulating steroids differ between ICP patients with and without GDM. In total 10 ICP patients without GDM (ICP+GDM-), 7 ICP patients with GDM (ICP+GDM+), and 15 controls (ICP-GDM-) were monitored during late gestation, at labor, and during three periods postpartum (day 5, week 3, and week 6 postpartum) (Šimják et al., 2018). The relationships between steroid profiles and patients' status were evaluated using the ANOVA model consisting of subject factor, between-subject factors Group (ICP+GDM+, ICP+GDM-, ICP-GDM-), gestational age at the diagnosis of ICP and gestational age at labor, and within-subject factor Stage and ICP × Stage interaction. The levels of the C21 and C19 Δ5 steroids and 5α/β-reduced C19 steroids were highest in ICP+GDM+, while those for the ICP-GDM-, and ICP+GDM- groups were lower. In the C21 Δ4 steroids and their 5α/β-reduced metabolites, the steroid levels were highest in the ICP+GDM-, intermediate in the ICP-GDM- and lowest in the ICP+GDM+ group. This higher concentration in ICP+GDM- group may be of importance as the 5α-pregnane-3α,20α-diol disulfate, is considered as the substance inducing ICP. In general, these data show that the comorbidity with GDM substantially changes the steroidome in ICP patients towards the higher activity of steroid CYP17A1 lyase step in adrenal zona reticularis reduced CYP17A1 hydroxylase step in zona fasciculata. This is consistent with our previously published hypothesis about the critical role of maternal zona reticularis in the pathophysiology of ICP. Our present data also indicate that the comorbidity with GDM might moderate the gravity of the ICP in this way.

Keywords : CYP17A1, GC-MS, gestational diabetes mellitus, intrahepatic cholestasis of pregnancy
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