Sex-specific differences in hypothalamus-pituitary-adrenal axis activity in newborns with very low birth weight

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Introduction

Male preterm infants are at increased risk of neonatal mortality when compared to their female counterparts. The mechanisms explaining this male disadvantage are not fully elucidated yet.

Objectives

To compare glucocorticoid metabolite excretion in urine obtained at day 10 between male and female infants born with a very low birth weight (VLBW, i.e., <1,500 g). We hypothesized that male preterm infants have impaired adrenocortical function.

Methods

Subjects: 36 infants (18 boys) born at a gestational age (GA) of 27.5±1.6 weeks with a birth weight of 1,028± 265 g

Study procedures: Over a 4-hr period, urine was collected. Glucocorticoid metabolites were measured using gas chromatography-mass spectrometry.

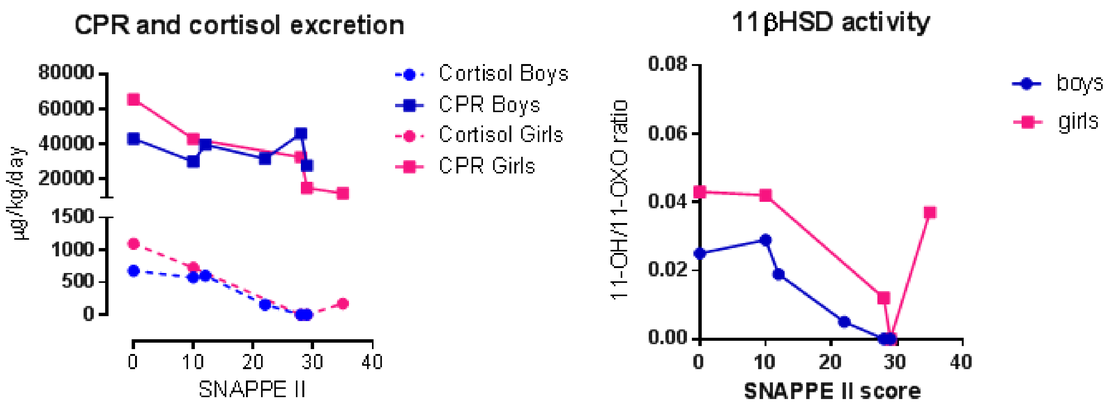
Outcome measures:
(1) sum of all glucocorticoid metabolites, as an index of the cortisol production rate (CPR)
(2) cortisol excretion
(3) ratio of 11-OH/11-OXO metabolites, as an estimate of 11β-HSD activity

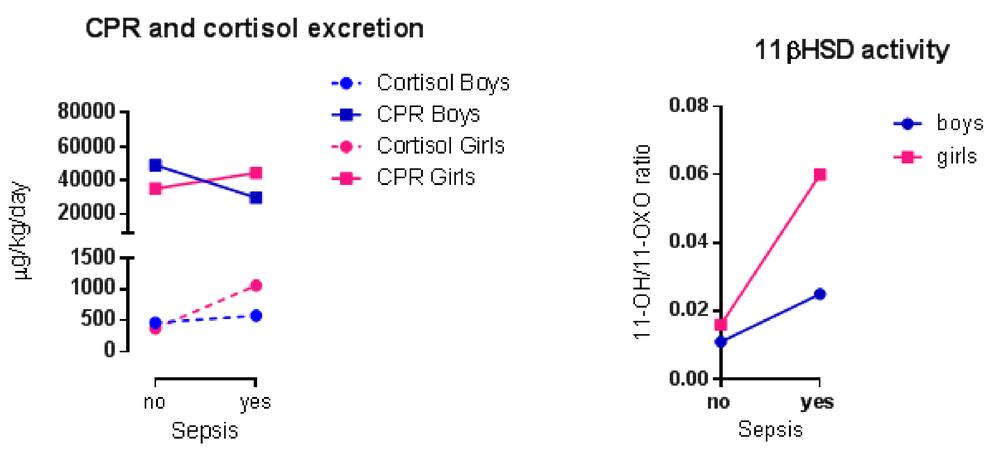
Analysis: Differences between boys and girls, including interaction with SNAPPE II (Score of Neonatal Acute Physiology Perinatal Extension-II) and sepsis, were assessed by linear regression analysis. Analyses were adjusted for GA

Results

Boys and girls did not differ in perinatal characteristics, including GA, birth weight, illnesses and nutrition.

The graphs below present sex-specific glucocorticoid metabolite excretion in relation to SNAPPE II score or sepsis. No significant sex-specific differences were found for CPR, cortisol excretion or 11β-HSD activity.





However, interaction between sex and SNAPPE II on 11β-HSD activity was observed (P = 0.04), with the interconversion favouring cortisone in boys with lower SNAPPE II. Furthermore, a tendency towards an interaction between sex and sepsis on CPR and 11β-HSD activity was observed (P= 0.09 and P= 0.10, respectively). As compared to girls with sepsis, boys with sepsis tended to have a lower CPR and a 11β-HSD activity in favour of cortisone.

Conclusion

This study provides some evidence for sex-specific differences in adrenocortical function of newborns with very low birth weight. These patterns might contribute to sex-specific differences in neonatal mortality. Future research is necessary to explore sex-specific characteristics in steroid metabolism and its influencing factors in infants with VLBW.

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