Static urine osmolality with elevated first trimester urine copeptin in human preeclampsia

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Keywords: Osmolality, copeptin, arginine vasopressin, preeclampsia

We have previously shown that maternal plasma copeptin (CPP), as a marker of vasopressin, is highly predictive of preeclampsia (PE) in the first trimester and remains elevated throughout pregnancy. Furthermore, in maternal urine samples we demonstrated that CPP was also significantly elevated in the first trimester in women who later developed PE. Because a urine dipstick test could be easily used in the clinic, we sought to validate this finding in a new and expanded cohort of samples and to determine whether these changes persist throughout pregnancy. In addition, to begin to address the mechanism for this difference, we also assessed urine osmolality to further probe renal function. In a case-control study (IRB# 2015038355), banked maternal urine samples and clinical data from each trimester from women who developed PE (N=117) and controls (N=593) were obtained from the University of Iowa Maternal Fetal Tissue Bank (MFTB) (IRB# 200910784). CPP concentrations were measured by

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ELISA. Osmolality was determined by freezing point depression. Differences between groups were detected by Chi square, Student’s T Test, or ANOVA as appropriate. Using a validation cohort and a different ELISA (USCN vs Phoenix Pharmaceuticals), we validated our earlier findings. We again find a significant increase in the concentration of urine CPP in the first trimester in women who developed preeclampsia compared to women who did not (0.304 ± 0.03 vs 0.223 ± 0.01 pg/ml, P=0.03). No significant differences in copeptin were observed in urine CPP in the 2nd and 3rd trimesters from PE and control women (2nd tri: 0.205 ± 0.04 vs 0.213 ± 0.02; 3rd tri: 0.290 ± 0.03 vs 0.336 ± 0.02 pg/ml P>0.05 in 2nd and 3rd trimesters). In this cohort, we did not detect differences in urine osmolality between preeclamptics and controls in any trimester (1st tri: 606.09 ± 50.16 vs 604.28 ± 16.72; 2nd tri 582.10 ± 36.30 vs 596.96 ± 16.98; 3rd tri: 479.63 ± 58.81 vs 583.75 ± 19.61 mOsm/kg H2O). We conclude that (i) PE is associated with increased maternal urinary CPP in the 1st trimester; (ii) this increase does not correlate with expected increases in urine osmolality. Future work will focus on understanding the mechanisms involved in the elevation in urinary CPP such as early immunologic changes or renal concentrating responses.

Presented at “Complicated Maternal Fetal Medicine Cases,” the University of Iowa Carver College of Medicine Ob/Gyn Postgraduate Conference, 2 November 2018, Hilton Garden Inn, Iowa City, Iowa.