Altered Osmotic Control Supports Hypothalamic Dysfunction in the Etiology of Preeclampsia

Mengda Liu1, Taryn E. Nishimura2, Alyssa T. Ray2, Jeremy A. Sandgren3, Sabrina M. Scroggins PhD2, Donna A. Santillian PhD2, Mark K. Santillan MD, Ph.D2,3, Justin L. Grobe PhD2,3,4

Secondary Student Training Program1, Department of Obstetrics and Gynecology2, Molecular and Cellular Biology3, Department of Pharmacology4, University of Iowa

BACKGROUND

• Recently, our group has demonstrated that arginine vasopressin (AVP) secretion is elevated as early as six weeks gestation in the pregnancy-associated cardiovascular disorder, preeclampsia.

• We have also established that AVP infusion throughout mouse pregnancy leads to symptoms of preeclampsia.

• These two discoveries lead us to the hypothesis that AVP is an early predictor for the development of preeclampsia.

• However, why AVP secretion is elevated remains a mystery.

• AVP is primarily regulated by increased plasma osmolality and acts to decrease it. Therefore, it is important to determine whether patients affected by preeclampsia have increased plasma osmolality.

HYPOTHESIS

Plasma osmolality is increased in patients affected by preeclampsia.

Figure 1: BASIC AVP PHYSIOLOGY

Figure 2: AVP infusion as a novel clinically relevant model of preeclampsia

Our group recently demonstrated that vasopressin (AVP) is upregulated in preeclamptic women as early as the 6th week of pregnancy. We also showed that AVP infusion throughout pregnancy models preeclampsia by causing proteinuria, acute kidney injury, intrauterine growth restriction, and elevated blood pressure.

Figure 3: MATERNAL CHARACTERISTICS

Mothers do not differ in any characteristics, but do have expected trends for increases in chronic hypertension, DM, BMI, and systolic blood pressures (SBP). Significance = p<0.05.

Figure 4: PREGNANCY CHARACTERISTICS

Pregnancy characteristics do not differ except in gestational age and birthweight in the preeclampsia cohort. This is expected based on the disease.

Figure 5: Plasma copeptin is increased in preeclampsia in both the first and second trimester.

As expected based on our past studies, copeptin (measured by ELISA) was elevated in the first and second trimesters in the preeclampsia patients. *P<0.05

Figure 6: Plasma osmolality is decreased in the first trimester of patients with preeclampsia

Contrary to our hypothesis, plasma osmolality (measured by osmometer) was decreased in the first and second trimesters in patients affected by preeclampsia. *P<0.05

Figure 7: LOGISTIC REGRESSION

These data demonstrate that 1st trimester plasma osmolality is a good predictor for the development of preeclampsia. Significance = p<0.05.

CONCLUSIONS

• Osmolality is decreased in the first trimester of pregnancy in women affected by preeclampsia.

• As expected, copeptin levels were also increased in the first and second trimesters of pregnancies affected by preeclampsia. This means that AVP secretion was elevated in these patients.

• These data suggest that sensitivity to AVP in the kidney is intact and that elevation in AVP are not due to osmotic stimuli. Thus, some other stimulus is causing increased secretion of AVP.

REFERENCES:


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