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Extended Abstract

Impact of vasopressin receptors on regulation of immune response in preeclampsia

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Preeclampsia is a common disorder of pregnancy resulting in increased blood pressure and end organ effects. The pathogenesis of preeclampsia is multi-factorial. Arginine vasopressin (AVP) is increased in preeclampsia, and the chronic infusion of AVP throughout gestation has previously been shown to be sufficient to produce a phenotype of preeclampsia in C57BL/6J mice representative of some of the cardiovascular and renal events seen in humans. Alterations in T-helper cell populations and their effector cytokines are also known to occur in preeclampsia. Therefore, we proposed that the increased secretion of AVP may be responsible for the immune changes that occur in preeclampsia. We also hypothesized that known pharmacological AVP antagonist, vaptans, may be able to reverse the effects of AVP infusion. Using our previously published AVP infusion model for preeclampsia, we compared saline controls to mice and their offspring infused with AVP with or without an AVP receptor antagonist vaptan. AVP infusion throughout pregnancy in mice resulted in decreased anti-inflammatory cytokines IL-4 and IL-10 in the maternal kidneys and fetal kidneys, while it increased pro-inflammatory cytokines IFN-ɣ in maternal plasma and IL-17 in the placenta and amniotic fluid. Specifically blocking AVPR-2 increased production of IL-4 and IL-10 in maternal and fetal

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kidneys, increasing the anti-inflammatory response. Interestingly, correction of IL-4 in the placenta required blockade of both AVPR-1a/2 with conivaptan. Proinflammatory marker IL-17 levels in the placenta were corrected by blocking AVPR-1a with relcovaptan, indicating that V1a may be responsible in the placenta for proinflammatory IL-17 production. Overall, the data seem to suggest that AVPR-1a plays a more dominant role in increasing pro-inflammatory markers, while AVPR2 plays more of a role in decreasing anti-inflammatory markers in preeclampsia. These results also support the ability of AVP to induce the immunological changes seen in preeclampsia.

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