Stimulation of the Kallikrein-Kinin System by Pregnancy May Help Restore Renal Vasodilator Response to Glycine in Dahl Salt-Sensitive Rats

To the Editor:

We would like to contribute to the discussion of possible mechanisms involved in the pregnancy-induced restoration of the renal vasodilator response to glycine in Dahl salt-sensitive rats reported by Whitescarver and Heesch1 in the December issue of Hypertension. We want to call attention to the role of renal kinins, postulated as mediators of amino acid–induced hyperperfusion and hyperfiltration by Jaffa and collaborators.2 They have demonstrated in rats that the effects of amino acid infusion on glomerular filtration rate, renal plasma flow, and renal vascular resistance are associated with an increased production of kinins. The changes in glomerular hemodynamics induced by the amino acid load could be blunted by bradykinin antagonists and by infusion of aprotinin, a tissue kallikrein inhibitor, which prevented the increase of urinary kinins.

Urinary kallikrein activity, an expression of renal synthesis, is consistently elevated during normotensive human pregnancy. We have reported increased urinary kallikrein activity at the early stages of pregnancy in humans (before week 16) and in Sprague-Dawley rats (from days 4 to 21).3 In Sprague-Dawley rats, both of which increase during sodium deprivation to levels similar to those of Dahl salt-resistant rats under a normal sodium intake.4 In this animal model, the stimulatory effect of gestation on urinary kallikrein has not been described, but in another hypertensive model with decreased urinary kallikrein, the one-kidney, one clip model, the enzyme increases markedly to values similar to those of pregnant control rats.6 Additional evidence of the capacity of gestation to stimulate the kallikrein-kinin system is the increased kallikrein content in the uterus of the early pregnant rat, which is selectively localized in the implantation node.7,8 We believe that this enhanced vasodilator system participates in the implantation reaction, in of bradykinin effects are nitric oxide and prostaglandins.9 This suggests that the vasodilator response to glycine load by a direct effect of kinins and/or through kinin-enhanced local synthesis of nitric oxide and prostaglandins.

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References


Response

Ors Valdés, Salas, and Vio propose an interesting mechanism for the restoration of the glycine-induced hyperfiltration and hyperemia found during pregnancy in Dahl salt-sensitive rats, which we reported in the December issue of Hypertension.1 We agree that, similar to other animal models of hypertension, it is feasible that the deficient renal kallikrein-kinin system in Dahl salt-sensitive rats is stimulated by pregnancy. This in turn could contribute to the restored renal vasodilator response to glycine load, possibly through kinin-enhanced local synthesis of nitric oxide and prostaglandins.

In a subsequent study, part of which has been published in abstract form, we have examined the interaction of renal nitric oxide and angiotensin II (Ang II) during glycine infusion in Dahl rats. Blockade of nitric oxide production with N°-nitro-L-arginine methyl ester resulted in severe renal vasoconstriction in Dahl salt-sensitive rats. Blockade of Ang II with saralasin restored the glycine-induced hyperfiltration and hyperemia in virgin Dahl salt-sensitive animals, similar to the effects of pregnancy. We used a postsynaptic Ang II receptor antagonist rather than a converting enzyme inhibitor in these experiments to avoid the increase in kinins associated with converting enzyme blockade. Because inhibition of Ang II restored the renal vasodilator response to glycine, this would indicate increased Ang II vasoconstrictor effects in the salt-sensitive strain. Recent reports indicate that an inability to increase nitric oxide levels with increased salt intake may contribute to hypertension in Dahl salt-sensitive rats.2 In addition, pregnancy is associated with increased...
Letters to the Editor

nitric oxide production in other rat strains. We propose that a pregnancy-induced increase in renal nitric oxide opposes the action of Ang II in the kidneys of the Dahl salt-sensitive rat, thus restoring a normal renal response to glycine infusion. Although we did not directly evaluate the role of renal kinins in our experiments, the work of Dr Valdés and colleagues suggests that increased renal kinins during pregnancy could contribute to the increased vasodilation by increasing nitric oxide.

Shirley A. Whitescarver
Cheryl M. Heesch
Department of Physiology
The Ohio State University
Columbus, Ohio

References
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G Valdés, S P Salas and C P Vio

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