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High-salt diets during pregnancy increases renal vascular reactivity due to altered soluble guanylyl cyclase-related pathways in rat offspring☆

Lin Jiang[a,1], Xiaohui Yin[a,1], Axin He[a,1], Lingjun Li[a], Le Bo[a], Xiuwen Zhou[a], Jiaqi Tang[a], Xiuxia Gu[a], Jue Wu[a], Qinqin Gao[a], Juanxiu Lv[a], Caiping Mao[a], Zhice Xu[a,b,*]

[a]Institute for Fetology and Reproductive Medicine Center, First Hospital of Soochow University, Suzhou 215006, China
[b]Center for Prenatal Biology, Loma Linda University, CA 92350, USA

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Abstract

Adverse prenatal factors such as overtake of salt or fat food are potential risks for cardiovascular diseases in offspring. This study tested the hypothesis that prenatal high-salt (HS) diets may influence renal vascular tone and attenuates signaling pathways related to soluble guanylyl cyclase (sGC) or/and large-conductance Ca^{2+}-activated K^+ (BK_{Ca}) channels in the offspring.

Pregnant rats were fed either normal salt (NS) (1% NaCl) or HS (8% NaCl) diet for the whole gestation. Offspring were maintained on NS diets. Renal interlobar arteries in offspring were tested for vascular responses to phenylephrine (Phe), K^+ channels and signal pathways related to sGC.

Phe induced higher vessel tension in interlobar arteries of the HS offspring. Following pretreatment with BK_{Ca} channel inhibitor iberiotoxin, Phe-mediated vasoconstrictions were decreased in HS offspring compared to NS. Phe-mediated constrictions following pretreatment with NO synthase inhibitor *N*(G)-nitro-L-arginine methyl ester or sGC inhibitor 1*H*-1,2,4-oxadiazolo-4,3-quinoxalin-1-one in the HS offspring were less sensitive than NS. The whole-cell K^+ currents and the component of BK_{Ca} channels were not changed in smooth muscle cells from interlobar arteries, whereas the K^+ currents stimulated by sGC activator BAY41-2272 were reduced in the HS offspring. The protein expressions of sGC β1 and β2 in the interlobar arteries of HS offspring were reduced.

The results showed that chronic overintake of salt during pregnancy could increase renal vascular tone in the offspring. The affected signal pathways included down-regulation of sGC function and expression.

Keywords: BK_{Ca} channels; PKG; Prenatal HS; Renal interlobar arteries; sGC

1. Introduction

A modified intrauterine environment such as abnormal maternal nutritional status and fetal exposure to adverse prenatal environments may lead to permanent modifications in individual phenotype called fetal programming [1]. Overintake of salt in adults can contribute to an increased risk for development of cardiovascular diseases, including hypertension [2] and heart or kidney fibrosis [3]. Pregnant women may prefer salty diets due to physiological or pathophysiological changes [4]. Excessive salt intake during pregnancy showed adverse effects on cardiovascular [5] and renal systems [6] in the offspring. Our previous study demonstrated that high-salt (HS) diets during pregnancy could affect local renin-angiotensin system in the fetal and offspring kidney [7]. In addition, recent work demonstrated that the prenatal insult could affect renal development [8]. However, there has been very limited information about whether the function of renal interlobar arteries can be influenced by prenatal HS intake. It is certainly important to address such questions for further understanding of cardiovascular and renal diseases in developmental origins.

The kidney plays an important role in the regulation of body fluid and blood pressure and in the etiology of hypertension [9]. Vascular remodeling, including that occurs in renal interlobar arteries, contributes to hypertension. It is related to structural, functional and mechanical changes that result in increased vascular tone [10,11]. In addition, renal interlobar arterial resistance index serves as a standard of auxiliary diagnosis for renal impairment such as renal artery stenosis [12] and renal vascular thrombosis [13] in clinical works. Therefore, altered interlobar arterial functions are linked to development of renal and cardiovascular diseases.

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* Corresponding author. Institute for Fetology, First Hospital of Soochow University, No. 708, Renmin Road, Suzhou, China. Tel.: +86-512-67781951; fax: +86-512-67780922.
E-mail address: xuzhice@suda.edu.cn (Z. Xu).

[1] Jiang, Yin and He contributed equally to this work.

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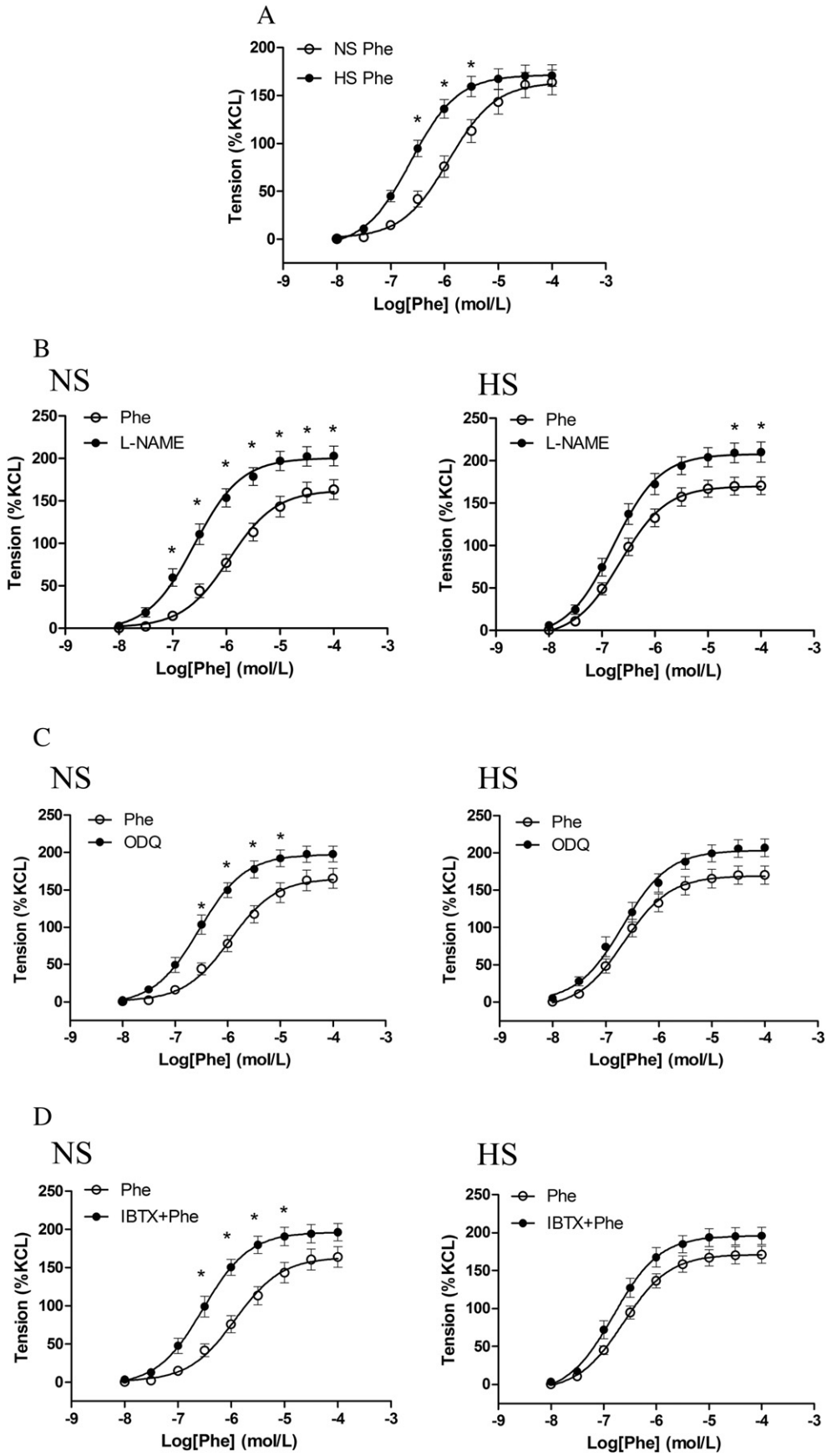
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