Obesity Accelerates the Deterioration of Renal Function in Developmental Programming of Hypertension. Role of Angiotensin II and Oxidative Stress

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Numerous studies have shown gender-dependent differences in the deterioration of renal function in models of developmental programming of hypertension (DPH). It is also known that obesity is associated to changes in renal function and that both angiotensin II (Ang II) and oxidative stress are involved in the renal alterations that occur in obesity and in animals with DPH. The main objectives were to examine whether the increment of arterial pressure (AP) and the deterioration of renal function are accelerated as a consequence of obesity in SD rats with DPH; whether these changes are gender-dependent; and to evaluate the role of Ang II and oxidative stress in these AP and renal function changes. A high fat diet (60%) was given during the first 4 months of age and DPH was induced by an AT receptor antagonist during nephrogenic period (ARAnp). Systolic AP (mmHg) was greater (P<0.05) in ARAnp-obese rats (167 ± 3 in ♂; 146 ± 4 in ♀) than in ARAnp (155 ± 3 in ♂; 137 ± 3 in ♀); obese (147 ± 2 in ♂; 137 ± 2 in ♀) or control (127 ± 1 in ♂; 119 ± 2 in ♀) rats. Three days administration of candesartan (7 mg/kg/day) led to a decrease in AP that was greater (P<0.05) in ARAnp-obese rats (55 ± 3 in ♂; 45 ± 4 in ♀) than in ARAnp (40 ± 3 in ♂; 37 ± 4 in ♀); obese (38 ± 4 in ♂; 27 ± 4 in ♀) or control (12 ± 2 in ♂; 14 ± 3 in ♀) rats. The acute Ang II infusion (30 ng/kg/min) induced an increase in renal vascular resistance (mmHg/ml/min/gr kw) that was also greater in ARAnp-obese rats (217 ± 45% in ♂; 145 ± 38% in ♀) than in ARAnp (103 ± 9% in ♂; 97 ± 8% in ♀); obese (106 ± 14% in ♂; 106 ± 17 in ♀) or control (51 ± 7% in ♂; 51 ± 10% in ♀) rats. The response to candesartan or Ang II infusion in ARAnp-obese rats was gender-dependent and may be explained by an enhanced oxidative stress. The expression of P67phox in the renal cortex was greater (P<0.05) in ARAnp-obese rats (3,00 ± 0,05 in ♂; 2,60 ± 0,04 in ♀) than in ARAnp (1,16 ± 0,04 in ♂; 1,66 ± 0,03 in ♀); obese (0,94 ± 0,06 in ♂; 1,02 ± 0,02 in ♀) or control (1,00 ± 0,02 in ♂; 1,02 ± 0,023 in ♀) rats. The results of this study suggest that obesity at an early age enhances the hypertension and accelerates the deterioration of renal function that occurs when cardiovascular disease is programmed during the perinatal period. It is also shown that Ang II and oxidative stress seems to play an important role in these AP and renal function changes.

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