The story of spontaneously hypertensive rat (SHR): A Review

Dear Editor

Spontaneously hypertensive rat (SHR) is considered a good animal model of human essential or primary hypertension, and has been extensively used to study cardiovascular disease. Like in human beings, the hypertensive response starts with advancing age in this strain of rats and the cause of the rising blood pressure remains unknown. Judging by the number of publications, SHR rat is the ost studied model of hypertension [1]. The SHR strain was obtained during the 1960s by Okamoto and colleagues, by selective breeding of Wistar-Kyoto (WKY) rats with high blood pressure and therefore in all the studies the normotensive WKY rats are employed as controls for SHR [2]. Rise in blood pressure begins around 5-6 weeks of age and the systolic pressures may reach values between 180 and 200 mmHg in the adult. Starting between 40 and 50 weeks, SHR develops characteristics of cardiovascular disease, like hypertrophy of heart and blood vessels [3]. Some of these may develop still higher blood pressure and die of stroke. This sub-group is designated as SHR-SP (stroke prone). As in the case of human hypertension, the kidney is the first suspect in the pathophysiology of high blood pressure of SHR rat. Renal transplantation from the SHR to a normotensive Wistar rat increases blood pressure of the recipient. Conversely, transferring a Wistar kidney to SHR normalizes blood pressure in the hypertensive recipient [4]. Even if the transplantation takes place at a young age before the onset of hypertension in the donors, benefits are seen [5], indicating a primary role for the kidney in the development of hypertension in SHR. Interestingly the kidneys of SHR show some kind of adaptive or compensatory changes. For example, kidneys transplanted from SHR to a hypertensive recipient retain their structural features better than kidneys transplanted from normotensive rats [6], demonstrating an adaptation to high blood pressure. Calcification of vasculature that sometimes occurs in humans, has been demonstrated in the smooth muscle cells of SHR, Osterix (a transcription factor for osteogenesis), and alkaline phosphatase (ALP) (a marker of vascular calcification) were significantly increased in aortic smooth muscle cells from SHR compared to similar cells from WKY [7]. However the most interesting aspect of SHR, is the derangement of calcium metabolism! Reduction in active transport of calcium by the intestine [8] and excess loss through urine [9] may lead to hypocalcemia. Circulating level of 1,25 DHCC is reduced due to a reduction in synthesis of the active metabolite of vitamin D by the kidney in SHR [10]. Correction of hypocalcemia by feeding high calcium diet or administration of vitamin D is accompanied by reduction in blood pressure. Feeding low calcium diet leads to increase in hypertensive response [11-12]. What is the link between calcium and hypertension? Does such link exist in humans? These questions remain to be answered.

References

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