Human tissue Kallikrein 1 rescues erectile function in rats with hyperhomocysteinaemia by protecting endothelial function and inhibiting fibrosis

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Introduction

To investigate the detailed mechanism of erectile dysfunction (ED) induced by hyperhomocysteinaemia (HHcy) in rats and determine whether Human Tissue Kallikrein 1 (hKLK1) might improve it, as we have proved the protective role of hKLK1 on erectile function in aged rats.

Methods

We established a rat model of HHcy through dietary-rich methionine (Met) in male Sprague-Dawley (SD) rats. Male wild-type SD rats (WTR) and transgenic rats harboring the hKLK1 gene (TGR) were fed to 10 weeks of age. Then 24 WTRs were divided into control (n=8), the low-dose (4% Met, n=8), and the high-dose (7% Met, n=8). Another 8 age-matched TGRs with the high-dose formed the TGR+7%Met group. 30 days later, erectile function, level of total homocysteinaemia (tHcy), oxidative stress, endothelial function, cavernous nerve function and fibrosis of all groups were determined.

Results

1. hKLK1 in the TGR+7%Met group could greatly decrease the tHcy levels and improve ED induced by HHcy in rats.
2. hKLK1 could inhibit oxidative stress of rats HHcy.
3. For the endothelial function, hKLK1 could preserve the endothelial cell-cell junction.
4. hKLK1 could enhance endothelial regeneration and activated the Akt/eNOS signaling pathway.
5. For the fibrosis, hKLK1 could preserve normal corpus cavernosum structure.
6. hKLK1 could preserve normal muscle content through inhibiting apoptosis and promoting autophagy on corpus cavernosum smooth muscle cells.

Conclusion

hKLK1 might effectively improve ED induced by HHcy in rats by protecting endothelial function, promoting cavernous nerve function and inhibiting fibrosis, which suggested hKLK1 might be a potential treatment method for ED.