

1, 25-dihydroxyvitamin D₃ decreases adriamycin-induced podocyte apoptosis and loss

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Abstract :

Background: Selective proteinuria is frequently observed in glomerular diseases characterized by podocyte injury. Although, 1,25-dihydroxyvitamin D₃ [1,25(OH)₂D₃] has potential therapeutic effects on chronic kidney diseases through decreasing podocyte loss, the mechanism underlying the beneficial effects of 1,25(OH)₂D₃ on podocytes remains still unknown. The present study tested the hypothesis that 1,25(OH)₂D₃ directly reduced podocyte apoptosis and loss.

Methods: Sprague-Dawley (SD) rats were randomly assigned into three groups: Adriamycin (ADR) group (n=15), ADR+1,25-(OH)₂D₃ group (n=16), and control group (n=16). Rats in ADR+1,25-(OH)₂D₃ group were treated with 1,25(OH)₂D₃ for 8 weeks. The number of podocytes and foot process width (FPW) were detected by transmission electron microscopy. The number of apoptotic podocytes per glomerulus and that of apoptotic nuclei and caspase-3 activity in cultured podocytes were determined by TUNEL staining. The average number of podocytes per glomerulus was quantified by immunohistochemistry. Expressions of p-Smad2/3, p-Smad1/5/8, Fas, Fas-Associated protein with Death Domain (FADD), Bax, and Bcl-2 proteins were examined by Western blot assay.

Results: Compared with control group, proteinuria, FPW, apoptotic podocytes, caspase-3 activity, the protein expressions of p-Smad2/3, Fas, FADD, and Bax were significantly increased, podocyte density, p-Smad1/5/8 and Bcl-2 expression were decreased in ADR group. 1,25(OH)₂D₃ significantly reduced proteinuria, FPW, caspase-3 activity, expressions of p-Smad2/3, Fas, FADD, and Bax and apoptosis of podocytes, but increased serum albumin, number of viable podocytes, p-Smad1/5/8 and Bcl-2 expression in ADR treated rats.

Conclusion: ADR-induced podocyte apoptosis was associated with the imbalance of p-Smad2/3, p-Smad1/5/8 the activity of caspase-3 and aberrant expressions of, Fas, FADD, Bax and Bcl-2. The beneficial effects of 1,25(OH)₂D₃ on podocytes may be attributable to inhibit podocyte apoptosis and the amelioration of podocytopenia.

Key Word :

1, 25-dihydroxyvitamin D₃, podocyte, proteinuria