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Alpha1-antitrypsin attenuates renal fibrosis by inhibiting TGF-β1-induced epithelial mesenchymal transition

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Background: Alpha1-antitrypsin (AAT) has anti-inflammatory effect through regulating serine proteinases activity. This study evaluated the inhibitory effects of AAT against the transforming growth factor (TGF)-β1-induced epithelial-to-mesenchymal transition (EMT) in unilateral ureter obstruction (UUO) mice and Madin-Darby canine kidney (MDCK) cells.
Methods: UUO was induced in C57BL/6 mice which were injected intraperitoneally with AAT (80mg/kg) or vehicle on alternate day until day 7. MDCK cells were treated with TGF-β1 (2ng/ml) for 48 hours to induce EMT, and co-treated with AAT (10mg/ml) to inhibit the EMT. Masson's trichrome staining was applied to estimate renal fibrosis area in UUO mice. The expression of α-SMA and E-cadherin in MDCK cells and kidney tissue were evaluated using immunochemistry and immunofluorescence.
Results: Masson's staining revealed that the renal fibrosis area was significantly decreased in AAT-treated-UUO group compared with UUO and vehicle-treated-UUO groups. Increased expressions of α-SMA and decreased expressions of E-cadherin were observed in MDCK cells after TGF-β1 treatment. Co-treatment with TGF-β1 and AAT to MDCK cells significantly attenuated the changes in the expression of α-SMA and E-cadherin. AAT also decreased the phosphorylated Smad-3 expression and the phosphorylated Smad-3/Smad-3 ratio in MDCK cells.
Conclusion: AAT treatment inhibited EMT induced by TGF-β1 in MDCK cells and attenuated renal fibrosis in UUO mice model. It suggested that AAT could inhibit the process of EMT through the suppression of TGF-β/Smad-3 signaling.

Keywords: Alpha1-antitrypsin, epithelial-to-mesenchymal transition, renal fibrosis, transforming growth factor-beta