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허혈-재관류 손상모델에서의 Substance P가 신손상에 미치는 영향

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Substance P Inhibits Kidney Damage and Fibrosis in Long-term Unilateral Ischemia-reperfusion Injury

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Background: Role of Bone marrow, a reservoir for endothelial precursor cells (EPCs) and mesenchymal stem cells (MSCs), in kidney regeneration is still obscure. Recently substance-P (SP), an injury-inducible messenger to mobilize bone marrow stem cells, has been suggested to be a novel target of regenerative medicine. We investigated the long-term effects of the SP on kidney exposed to IRI.

Methods: Unilateral renal ischemia-reperfusion injury (IRI) model was established in C57BL/6 mice and 5 ng/kg/day SP or saline was administered twice a week for 5 weeks after the surgery. Renal function was monitored, and histological changes and fibrosis in the kidney were evaluated in both three weeks and five weeks. TGF- β 1 and α -SMA expressions, markers of renal fibrosis were determined by Western blot. The mobilization and homing of EPC in peripheral blood and renal tissues were also assessed by FACS.

Results: Renal IRI increased SP levels in peripheral blood. Mobilized EPCs and MSCs in peripheral blood showed peak at 1 day after IRI, followed by subsequently decreased at 3 and 5 days. Administration of SP maintained the peripheral mobilization of EPCs to 5 days. In addition, homing of EPC in renal tissue was also significantly increased of SP treated group. Tubular injury scores of the SP group were significantly lower than those of the saline group at both 3 and 5 weeks. Interstitial fibrosis was also consistent with the result of tubular damage as there was significantly lower degree of interstitial fibrosis in SP group at 5 weeks. Intrarenal TGF- β 1 and α -SMA expressions in SP treated group were significantly lower than those in saline treated group.

Conclusion: Our data show that long-term administration of SP ameliorates kidney damage and fibrosis after ischemic reperfusion injury and suggest the possible role of SP and bone marrow derived stem cells in kidney regeneration.

Key Words: 물질P, 혈관전구세포, 허혈-재관류 손상

Substance P, EPC, Ischemia reperfusion injury