

IgA 신병증의 동물 모델인 HIGA 마우스에서 지방유래 줄기세포의 전신투여가 신장 기능에 미치는 효과에 대한 연구

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The Effect of Systemic Administration of Adipose-derived Stem Cells on Renal Function in HIGA Mice

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Background: Previous studies suggest that T cell dysregulation is important in the pathogenesis of IgA nephropathy. However, the role of Th1/Th2 system in IgA nephropathy remains unclear. Adipose-derived stem cells (ASCs) have immune-modulating effects and are an emerging therapeutic modality in various diseases. In this study, we performed animal experiments to investigate the therapeutic effect of ASCs in HIGA mice, the animal model of IgA nephropathy.

Material and Method: Sixty female HIGA mice were divided into 6 groups. To evaluate the effects of ASCs at different stages of IgAN, ASCs were isolated from mice before and after the disease onset. Each group received different treatments (Group 1: control DMEM injection, Group 2: preonset ASC, Group 3: postonset ASC, Group 4: human ASC, Group 5: Steroid, prednisolone 5mg/kg via gavage, Group 6: Steroid and postonset ASC). We injected 5,000,000 cells/kg of ASC through tail vein every 2 weeks for 3 months. After 3 months treatment, we observed the functional and morphologic changes in the kidney. We also analyzed the changes in the Th1 and Th2 balance.

Result: Serum creatinine levels were decreased in the human ASC, steroid and combination treatment groups. The amounts of 24 hour proteinuria were significantly decreased in all treatment groups. In addition, mesangial proliferation and glomerulosclerosis index were also decreased in all treatment groups. In accordance with these changes, renal expression of pro-fibrotic molecules including TGF β 1, type IV collagen, MCP-1 and PAI-1 was decreased in the treatment groups. Renal expression of Th1 cytokines such as TNF- α and IFN- γ was significantly decreased in all treatment groups and that of Th2 cytokines such as IL-4 and IL-10 was increased in pre-onset ASC, steroid and combination treatment groups. In splenic T cells, there were no significant changes in the level of Th1 and Th2 cytokines, but the ratio of IFN- γ positive T cells over IL-4 positive T cells was significantly decreased in the steroid and combination treatment groups.

Conclusion: ASC treatment showed a beneficial effect both functionally and structurally in the animal model of IgA nephropathy. This effect was probably mediated by the immune-modulating effect of ASC. Further studies will be needed to clarify the clinical application of ASC in the treatment of human IgA nephropathy

Key Words: IgA 신증, 지방유래 줄기세포, HIGA 마우스

IgA nephropathy, Adipose-derived stem cell, HIGA mice