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Phosphodiesterase V Inhibitor Attenuates the Fibrotic Gene Expression of Human Renal Fibroblast derived from Kidney Biopsy Tissue

Manas Ranjan Behera, Mohit Rai, Mantabya Singh, Anupma Kaul, Narayan Prasad, Vikash Agarwal, Durga Prasanna Misra
Department of Internal Medicine-Nephrology, Sanjay Gandhi Postgraduate Institute of Medical Sciences , India

Objectives : 1. To evaluate the effect of PDE5 inhibitors on TGFβ1 induced profibrotic genes (Col1a1, Col1a2, ASMA1, FN1, CTGF, and TIMP1) expression at mRNA level. 2. To Evaluate the Effect of PDE5 inhibitors on TGFβ1 induced expression of anti-fibrotic gene (MMP2) at mRNA level.
Methods : This is a pilot study to evaluate the efficacy of PDE5i on TGFβ1 induced fibrosis on fibroblasts derived from kidney biopsy specimen of CKD patients. Renal fibroblasts were cultured. The fibroblasts cells were treated with PDE5i inhibitor (tadalafil) (at different doses of 1µm, 5µm, 10µm and 15µm), both before and after stimulation with transforming growth factor beta-1 (TGF-b1) (at doses of 5ng/ml, 10ng/ml, 15ng/ml and 20ng/ml). Gene expression was studied by real-time polymerase chain reaction (RT-PCR) for messenger ribonucleic acid (mRNA) of pro-fibrotic genes Col1a1, Col1a2, FN1, CTGF, ASMA, TIMP1, and anti-fibrotic MMP2.
Results : Our results shows that TGFβ significantly increased the expression of profibrotic gene (Col1a1, Col1a2, ASMA, CTGF, FN and TIMP1) at concentration of 10 ng/ml in the fibroblast cells derived from kidney biopsy specimen. Treatment of fibroblast cells with Tadalafil (PDE5 inhibitor) significantly decreased the pro-fibrotic gene mRNA expression (Col1a1, Col1a2, ASMA, CTGF, FN and TIMP1) with increased anti-fibrotic gene expression (MMP2) at the dose of 5µm and 10 µm concentration in the fibroblast cells (Figure 1).
Conclusions : Till date PDE5i not used to retard progression of CKD. We found that, PDE5i reduces the fibrosis in this in vitro study. Hence, this drug may be proposed as a potential therapy for retard progression of CKD.

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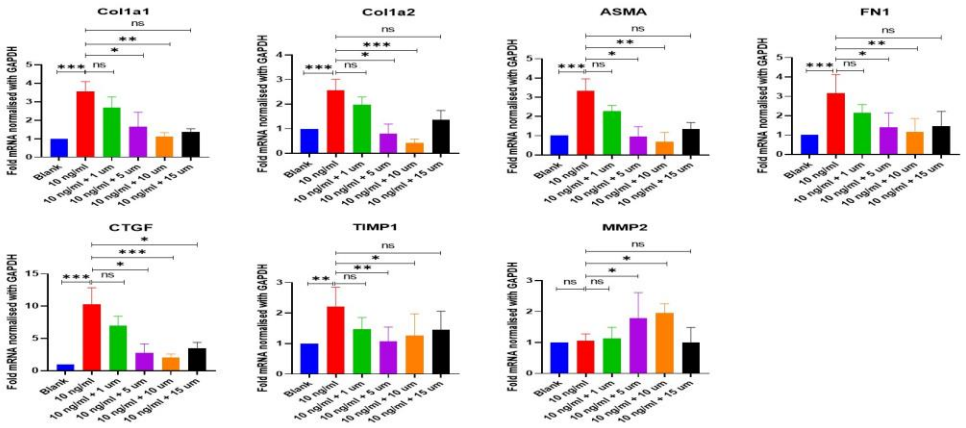

Figure1: Effect of PDE5 inhibitor on fibroblasts cells stimulated with TGF-β.