Effect of Beraprost Sodium, a PGI₂ Analogue, on Proliferation of Cultured Rat Glomerular Mesangial Cells

Y.	Yuchi	Makita
K.	Keiko	Sekizuka
L.N.	Li Ning	Wang
M.	Mitsumine	Fukui
Y.	Yasuhiko	Tomino

Division of Nephrology, Department of Medicine, Juntendo University School of Medicine, Tokyo, Japan

Dr. Yasuhiko Tomino, Division of Nephrology, Department of Medicine, Juntendo University School of Medicine, Tokyo 113 (Japan)

Dear Sir,

A study of the effect of beraprost sodium (BPS) on proliferation of cultured rat glomerular mesangial cells is described. Prosta-cyclin (PGI₂) synthesized from arachidonic acid by cyclo-oxygenase is a potent relaxant of vascular smooth muscle and a anti-aggregatory agent [1]. BPS, a stable analogue of PGI₂, has a long biological half-life and is orally effective in inhibiting the aggregation of platelets [2]. Recently, Wang et al. [3] reported that BPS might improve albumin-uria and glomerular filtration rate (GFR) due to its vasodilating effects in the early phase of streptozotocin (STZ)-induced diabetic rats. Sakai et al. [4] examined the cyto-protective effect of BPS in cultured human endothelial cells from the umbilical vein. They showed an effect of BPS on proliferation of endothelial cells and speculated contribution to an increase in cyclic AMP (cAMP) level in endothelial cells treated with BPS. Davison et al. [5] reported a pro-liferative effect of dibutyryl cAMP in human dermal microvessel endothelial cells, but not in human umbilical cord vein endothelial cells. This effect appeared at a concentration of 5×10^{-4} M, but at not more than 1×10^{-3} M or less than 1×10^{-4} M [5]. However, the effect of BPS on glomerular mesangial cells has remained unclear. In this study, rat glomerular mesangial cells were cultured with 0.5% fetal calf serum (FCS) in RPMI 1640 for 48 h. The cells were incubated with 200 mg/dl or 500 mg/dl of glucose and 0-30 μ mol/l of BPS in RPMI 1640 containing 10% FCS for 18 h. Thereafter, proliferation of the glomerular mesangial cells was determined by the 5-bromo-2'-deoxy-uridine labelling and detection kit III. Proliferation of glomerular mesangial cells was suppressed after incubation with high-glucose medium without BPS treatment. In high-glucose medium, the proliferation of the mesangial cells under the incubation with low dose BPS (0.1-0.3 μ g/l) was significantly greater than that without BPS ($p < 0.05$). On the other hand, the proliferation of the mesangial cells under incubation with high-dose BPS (10-30 μ g/l) was significantly lower than that without BPS in the same medium ($p < 0.05$). These findings suggest that the low-dose BPS might improve the suppression of mesangial cell proliferation in the high-glucose medium. It

is postulated that BPS might influence the viability of the mesangial cells under the high-glucose conditions.

References

Akiba T, Miyazaki M, Toda N: Vasodilator actions of TRK-100, a new prostaglandin I₂ analogue. *Br J Pharmacol* 1986;89:703-711. Sim AK, McCraw AP, Cleland ME, Nishio S, Septh O: Effect of a stable prostacyclin analogue on platelet function and experimentally-induced thrombosis in the microcirculation. *Arzneimittel Forsch* 1985;35:1816-1818. Wang LN, Tang Z, Shou I, Fukui M, Tomino Y: Effects of the PGI₂ analogue, beraprost sodium (BPS), on glomerular prostanoid synthesis in STZ-induced diabetic rats. In press. Sakai A, Yajima M, Nishio S: Cytoprotective effect of TRK-100, a prostacyclin analogue, against chemical injuries in cultured human vascular endothelial cells. *Life Sci* 1990;47: 711-719. Davison PM, Karasek MA: Human dermal microvascular endothelial cells in vitro: Effect of cyclic AMP on cellular morphology and proliferation rate. *J Cell Physiol* 1981;106:253-258.

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