



## POTENTIAL OF IGANIDIPINE EYE DROP, A NEW WATER-SOLUBLE DIHYDROPYRIDINE-DERIVATIVE $Ca^{2+}$ -ANTAGONIST

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**Purpose:** To evaluate the potential of topical iganidipine, a new water-soluble dihydropyridine-derivative  $Ca^{2+}$ -antagonist, to exert pharmacological activity in the posterior retina.

**Method:** Iganidipine was intravenously injected or its ophthalmic solution (0.03%) was unilaterally instilled in pigmented rabbits and effects on intravitreously injected ET-1 induced retinal artery constriction were studied. Seven days after intravitreous injection of various doses of iganidipine together with NMDA or kainic acid (KA), rat eyes were processed for the inner plexiform layer (IPL) thickness measurement or counting of the number of retinal ganglion cells in rats where Dil had been injected into the superior colliculi in both sides. Müller cells from rats were cultured and after 4-time passages various concentrations of iganidipine were added. mRNA and protein were extracted 6 hours after the application and the levels of mRNA and protein of BDNF and CNTF were determined using RT-PCR, real-time PCR and western-blot analysis.

**Result:** Twice-daily 20-day iganidipine instillation significantly suppressed intravitreous ET-1 (2.5 or 0.5 ng) induced retinal artery constriction only in the ipsilateral eye, while intravenous iganidipine giving a free plasma concentration of about  $10^{-8}$  M suppressed intravitreous ET-1 (0.5 ng) induced retinal artery constriction to a similar degree as twice-daily 20-day instillation. At a dose giving final intravitreous concentration of about  $10^{-8}$  M or higher, iganidipine significantly suppressed KA-induced damage of RGCs. Iganidipine up-regulated BDNF and CNTF production by Müller cells at a concentration of  $10^{-8}$  M or higher.

**Conclusion:** In pigmented rabbits, topically instilled 0.03% iganidipine reached the ipsilateral posterior retina by local penetration at a concentration of about  $10^{-8}$  M. At this level, iganidipine could exert vasodilating or neuroprotective activity, or up-regulate BDNF and CNTF production by Müller cells.