Experimental retinopathy of prematurity: Angiostatic inhibition by nimodipine, ginkgo-biloba, and dipyridamole, and response to different growth factors

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Resumen

PURPOSE. To investigate whether commonly used vasodilating drugs ameliorate angiogenesis in experimental retinopathy of prematurity (ROP), and to study the response of these drugs to different growth factors. METHODS. We used a rat and mouse model of oxygen-induced ischemic retinopathy. Animals were treated with nimodipine, ginkgo-biloba and dipyridamole intraperitoneally starting the day before exposure to room air (day 1). Controls were injected with vehicle solution only. Eyes were processed histopathologically with serial sections and neovascularization was measured by counting the nuclei within the retinal internal limiting membrane, by a masked observer. Retinal and vitreous tissues were assayed by ELISA for VEGF, PDGF and TGFβ2. RESULTS. Nimodipine significantly inhibited the growth of new vessels in rats. The number of nuclei was 310 ± 69 in the control group (n:14) and 121 ± 53 in the treated ones (n:14), ($p<0.0005$). Similar results were found with ginkgo-biloba extracts: 344 ± 53 (n:15) in controls, and 136 ± 29 (n:11) in treated ones ($p<0.0005$), and with dipyridamole: 303 ± 69 (n:13) in controls, and 131 ± 48.5 in treated rats ($p<0.0005$). Results were similar in mice. 186 ± 45 (n:7) nuclei counted in controls against 90 ± 25 (n:6) for dipyridamole treated ($p<0.0005$); and 81 ± 21 for ginkgo-biloba treated animals ($p <0.0005$). A gradual, very significant increase in VEGF values in response to relative hypoxia (room air) contrasted with the significant-inhibition noted both with ginkgo-biloba extracts and dipyridamole. TGFβ2 and PDGF both showed a gradual increase in relative hypoxia at days 2 and 4 of room air (12[removed].

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PALABRAS CLAVE: Angiogenesis. Dipyridamole. Ginkgo-biloba. Neovascularization. Nimodipine.

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