Subconjunctival carboplatin in fibrin sealant in the treatment of transgenic murine retinoblastoma.

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Abstract:

PURPOSE: To evaluate the efficacy of subconjunctival carboplatin in fibrin sealant in the treatment of transgenic murine retinoblastoma.

DESIGN: Experimental study using LHbeta-Tag transgenic mice in a randomized controlled trial.

PARTICIPANTS AND CONTROLS: Thirty-three 10-week-old LHbeta-Tag transgenic mice: 22 carboplatin-treated animals and 11 control animals.

METHODS: Three groups of 11 mice were treated with a single, 30 microl injection of fibrin sealant in the subconjunctival space of 1 eye; the opposite eye was left untreated as an internal control. Group 1 (low-dose group) received 37.5 mg/ml calculated concentration of carboplatin in fibrin sealant (0.66 mg measured total dose). Group 2 (high-dose group) received 75 mg/ml calculated concentration of carboplatin in fibrin sealant (1.23 mg measured total dose). Group 3 (control group) received fibrin sealant only. Mice were killed on day 22 after treatment. Eyes were serially sectioned, and retinal tumor burden was quantified by histopathologic analysis. For statistical analysis of treatment effects, eyes were divided into 6 groups: low-dose group, sealant-treated eyes; low-dose group, untreated eyes; high-dose group, sealant-treated eyes; high-dose group, untreated eyes; control group, sealant-treated eyes; and control group, untreated eyes.

MAIN OUTCOME MEASURES: Main outcome measure was mean tumor burden per level per eye in each experimental group.

RESULTS: The best therapeutic results were obtained in eyes treated with low-dose carboplatin in fibrin sealant, where no histopathologic evidence of toxicity was observed, and 6 of 11 eyes had zero tumor burden. Tumor burden in the remaining 5 eyes in this group was minimal (4 eyes) or moderate (1 eye) compared with mean control values. Mean tumor burden in this group was significantly smaller than mean tumor burden in untreated eyes from the same mice ($P<0.004$), sealant-treated eyes in the control group ($P<0.004$), and untreated eyes in the control group ($P<0.002$). Although a similar reduction in mean tumor burden was observed in eyes treated with high-dose carboplatin in fibrin sealant, 5 of 10 eyes analyzed in this group also demonstrated histopathologic evidence of severe toxicity.

CONCLUSIONS: Subconjunctival carboplatin in fibrin sealant is effective in the treatment of transgenic murine retinoblastoma. A single injection of low-dose carboplatin in fibrin sealant was sufficient to induce complete or near-complete intraocular tumor regression in 10 of 11 eyes (91%), with no associated histologic evidence of toxicity. These results suggest that subconjunctival carboplatin in fibrin sealant provides sustained release and could have clinical use in the treatment of intraocular retinoblastoma.