Modulation of rodent spinal cord radiation tolerance by administration of platelet-derived growth factor.

PURPOSE: To examine the role of platelet-derived growth factor (PDGF) for ameliorating radiation myelopathy of the cervical spinal cord in a rodent model. METHODS AND MATERIALS: After developing the technique for cannulation of the basal cistern, initial animal experiments were conducted to test the feasibility of intrathecal continuous infusion of PDGF in a model of cervical spinal cord irradiation in adult Fisher F-344 rats and to determine the most effective dose level of PDGF. Subsequently, the dose-modification factor was determined in a larger group of rats. Irradiation was given in 2 fractions (16 Gy followed by 14-24 Gy) and animals were examined for the development of paresis. RESULTS: The initial dose-finding experiment revealed significant differences in the incidence of radiation myelopathy (100% in saline-treated control rats, 25% with the most effective dose of PDGF, up to 100% with less effective doses). The most effective dose of PDGF was 0.014 μg per day. Subsequent experiments revealed a median effective dose (ED(50)) of 35.6 Gy (95% confidence interval, 34.7-36.5 Gy) for animals receiving this dose of PDGF in contrast to 33.8 Gy (33.4-34.3 Gy) for the control group (p = 0.003). The dose-modification factor obtained with this dose of PDGF was 1.05. CONCLUSIONS: Intrathecal administration of PDGF concomitant to irradiation of the cervical spinal cord in rats was feasible. Treatment with PDGF significantly increased the
tolerance of the spinal cord. The PDGF experiments should be viewed as a proof of principle that brief therapeutic intervention in the earliest phase of damage induction can reduce late effects in the spinal cord. They form the basis for further studies of growth factor administration in this particular model.