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Titel des Beitrags: Vascular endothelial growth factor gene therapy improves nerve regeneration in a model of obstetric brachial plexus palsy.

Abstract: The treatment of obstetric brachial plexus palsy has been limited to conservative therapies and surgical reconstruction of peripheral nerves. In addition to the damage of the brachial plexus itself, it also leads to a loss of the corresponding motoneurons in the spinal cord, which raises the need for supportive strategies that take the participation of the central nervous system into account. Based on the protective and regenerative effects of VEGF on neural tissue, our aim was to analyse the effect on nerve regeneration by adenoviral gene transfer of vascular endothelial growth factor (VEGF) in postpartum nerve injury of the brachial plexus in rats. In the present study, we induced a selective crush injury to the left spinal roots C5 and C6 in 18 rats within 24 hours after birth and examined the effect of VEGF-gene therapy on nerve regeneration. For gene transduction an adenoviral vector encoding for VEGF165 (AdCMV.VEGF165) was used. In a period of 11 weeks, starting 3 weeks post-operatively, functional regeneration was assessed weekly by behavioural analysis and force measurement of the upper limb. Morphometric evaluation was carried out 8 months post-operatively and consisted of a histological examination of the deltoid muscle and the brachial plexus according to defined criteria of degeneration. In addition, atrophy of the deltoid muscle was evaluated by weight determination comparing the
left with the right side. VEGF expression in the brachial plexus was quantified by an enzyme-linked immunosorbent assay (ELISA). Furthermore the motoneurons of the spinal cord segment C5 were counted comparing the left with the right side. On the functional level, VEGF-treated animals showed faster nerve regeneration. It was found less degeneration and smaller mass reduction of the deltoid muscle in VEGF-treated animals. We observed significantly less degeneration of the brachial plexus and a greater number of surviving motoneurons (P< 0.05) in the VEGF group. The results of this study confirmed the positive effect of VEGF-gene therapy on regeneration and survival of nerve cells. We could demonstrate a significant improvement on the motor-functional as well as on the histomorphological level. However, increased vascularization of the nerve tissue caused by VEGF does not seem to be the major reason for these effects. The clinical use of adenoviral VEGF-gene therapy in the newborn cannot be justified so far.