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Adenovirus-mediated delivery of CGRP ameliorates diabetic neuropathy in mice

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Objective: Calcitonin gene-related peptide (CGRP) is a principal neurotransmitters in nerve system. Our previous studies have demonstrated CGRP is involved in inhibiting oxidative stress in Schwann cells stimulated with high glucose. In this study, we investigated the therapeutic effects of CGRP gene transfer on neuropathy in streptozotocin(STZ)-induced diabetic mice.

Methods: To construct an adenovirus expression vector expressing CGRP, Ad-CGRP was cloned using Gateway technology. STZ was intraperitoneally injected into 18 male C57BL/6J mice and then the mice were randomly divided into three groups.Ad-CGRPwas administered intramuscularly into the mice once a week. Control mice received either adenovirus expressing LacZ or vehicle only. In addition, six age- and sex-matched non-diabetic mice were assigned as normal controls and receivedvehicle. Four weeks after administration, the mice were sacrificed and the mRNA level of CGRP in muscles were examined (RT-PCR) to confirm CGRP overexpression. Hot plate test and assessments of the motor nerve conduction velocity were performed. Sciatic nerve blood flowwas also determined with laser doppler.

Results: The recombinant adenovirus vectors containing mice CGRP were generated. CGRP levels in muscles were enhanced in Ad-CGRP group. CGRP gene transfer increased motor nerve conduction velocity and sciatic nerve blood flow, as well as reduced the latency of hot plate test in diabetic mice.The Ad-controlhad no effect on mice.

Conclusion: This study suggests that CGRP gene transfer may have the therapeutic potential for the management of diabetic neuropathy.

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