THE ROLE OF NITRIC OXIDE IN NUCLEUS PULPOSUS-INDUCED NERVE ROOT INJURY

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Introduction: Nerve root dysfunction and sciatic pain in disc herniation is considered to be caused not only by mechanical compression, but also related to the presence of nucleus pulposus (NP) in the epidural space. Autologous NP has previously been shown to induce endoneural edema and to decrease nerve conduction velocity in spinal nerve roots in experimental disc herniation models and inflammatory mediators have been suggested to be involved in these mechanisms. Nitric oxide (NO), a potent inflammatory mediator, is implicated in vasoregulation, neurotransmission and neuropathic pain. The enzyme nitric oxide synthase mediates the production of NO.

Three series of experiments were performed in rat and pig disc herniation models to investigate 1) nitric oxide synthase (NOS) activity in spinal in nerve roots after autologous nucleus pulposus (NP) exposure and 2) to evaluate the effects of systemic treatment with aminoguanidine (AG), a nitric oxide synthase inhibitor, on vascular permeability and nerve conduction velocity.

Methods: Series I: NOS activity in rat nerve roots (n=5) exposed to autologous NP were compared to nerve roots (n=5) from sham operated animals.

Series II: S2 and S3 nerve roots in the pig were exposed unilaterally for autologous NP. In the AG group (n=7), aminoguanidine (200 mg/kg in 50 ml NaCl) was injected intravenously immediately before NP application. The control group (n=8) received the same amount of NaCl. The animals were kept anaesthetized for 2 hours, subsequently perfused. Nerve conduction velocity (NCV) was measured over the exposed area after seven days. The Mann-Whitney test was used for comparisons between the groups.

Series III: In nucleus pulposus exposed pig spinal nerve roots the edema after systemic AG administration was less severe than without AG-treatment (Figure 2).

Results: Series I: In a disc herniation model in the rat calcium-independent NOS-activity was measurable in NP-exposed nerve roots compared to no detectable calcium-independent NOS-activity in nerve roots from sham-operated animals (a), reflecting increased inducible nitric oxide synthase (iNOS) activity. Calcium-dependant NOS-activity (b), reflecting endothelial and neuronal nitric oxide synthase (eNOS and nNOS) was comparable in the two groups. (Figure 1)

Discussion: The results from the present study demonstrate that nucleus pulposus increases iNOS-activity in spinal nerve roots and that nitric oxide synthase inhibition reduces nucleus pulposus-induced edema and prevents reduction of nerve conduction velocity. In the present study, systemic AG treatment reduced spinal nerve root edema comparable to the effects of methylprednisolon in a previous study. The spinal nerve conduction velocity for AG treated animals (71±18 m/s) was comparable to a previously published control series where retroperitoneal fat was applied on spinal nerve roots (76 ± 11 m/s) indicating that AG blocks the negative effect of NP on NCV.

These observations extend previous data about the importance of inflammatory mediators in the pathophysiology of disc herniation and nerve root injury. Furthermore, the results suggest that nitric oxide is involved in the pathophysiological effects of nucleus pulposus in disc herniation. The exact role of NO in relation to other inflammatory mediators and to mechanical compression in nerve root pain warrants further investigations.

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