Epidural Perfusion Cooling Protects Against Spinal Cord Ischemia in Rabbits

An Evaluation of Cholinergic Function

ŽELMIRA MALATOVÁ,∗1 IVAN VANICKÝ,1 JÁN GÁLIK,1 AND M. MARŠALA2

1Institute of Neurobiology, Slovak Academy of Sciences, Soltesovej 6, 040 01 Kosice, Slovak Republic; and 2Department of Anesthesiology, University of California, San Diego, La Jolla, CA

Received January 31, 1994; Revised July 15, 1994 and November 28, 1994; Accepted December 9, 1994

ABSTRACT

The protective effect of regional epidural spinal cord cooling was evaluated in a rabbit spinal cord ischemia model. Hypothermia was performed by the continual perfusion of 2–4°C cold saline in the epidural space around the ischemic lumbar segments, 4 min before and during ischemia. The spinal cord was deeply hypothermic (21°C) throughout the whole ischemic period. Ischemia was induced by the occlusion of the abdominal aorta for 40 min under normothermic or hypothermic conditions. Recovery of motor and sensory functions, spinal cord-evoked potentials, and motor-evoked potentials were then evaluated up to 24 h postischemia. After this period, choline acetyltransferase (ChAT) and acetylcholinesterase (AChE) activities were measured, in particular, zones of the lumbar spinal cord. AChE was also investigated histochemically.

Animals in the normothermic group displayed fully developed spastic paraplegia with near complete loss of spinal somatosensory and motor-evoked potentials. AChE histochemistry showed extensive necrotic changes affecting lumbosacral gray matter. These changes corresponding with the pronounced losses of ChAT and AChE activities indicated irreversible injury of the spinal cord. In contrast, after

*Author to whom all correspondence and reprint requests should be addressed.
hypothermic ischemia, animals survived without any sign of neurological impairment with almost full recovery of the spinal cord-evoked potentials. ChAT and AChE activities in the gray matter showed near control values corresponding with histochemical analysis of fully preserved gray matter. Hypothermia under the present experimental conditions efficiently protected the spinal cord against ischemic injury.

**Index Entries:** Spinal cord; ischemia; paraplegia; hypothermia; choline acetyltransferase; acetylcholinesterase.

**INTRODUCTION**

Transient spinal cord ischemia and its resulting neurological deficit represents a serious complication after thoracoabdominal aneurysm repair (Szilagyi et al., 1978). Depending on the completeness and duration of the ischemic period, neurological deficit initially can be expressed as a transient loss of motor and sensory function and after longer ischemic intervals as a spastic/ﬂaccid paraplegia. Corresponding with the degree of neurological deficit, histopathological analysis shows selective damage of small inhibitory interneurons localized in the central gray matter or the development of extensive gray matter necrosis and lower motor neuron lesion (DeGirolami and Zivin, 1982; Maršala et al., 1991). Electrophysiological and histochemical analyses in the animals with such a degree of histopathological changes show the subtotal loss of spinal somatosensory evoked potentials (SSEP) and a significant reduction of the cholinergic enzyme activity in the lumbar gray matter, respectively (Malatová et al. 1989; Malatová and Maršala, 1993; Vanický et al., 1993).

Although the precise mechanism leading to the neuronal degeneration after ischemia is not completely understood, several biochemical variables seem to be well defined. Among these changes, the release of excitatory amino acids (Simpson et al., 1990; Martiniak et al., 1991; Maršala et al., 1994), prostaglandins (Jacobs et al., 1987; Shoami et al., 1986), tissue lactic acidosis (LeMay et al., 1987), postischemic hyperoxia, and the corresponding oxygen free radical production (Halat et al., 1989) appear to be involved.

Several pharmacological treatment studies interacting with proposed pathobiochemical cascade were reported however, none has been shown to provide definitive protection against a prolonged period of spinal ischemia (Kirschner et al., 1989). Recently, it has been reported that even a mild degree of cerebral hypothermia provides powerful protection against global cerebral ischemia (Busto et al., 1989; Moller et al., 1989; Baldwin et al., 1991). Comparable effects against experimental ischemic spinal cord injury were reported (Vacanti and Ames, 1984; Robertson et al., 1986; Colon et al., 1987). In our laboratory, a similar protective effect of moderate spinal