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Acute thermal nerve root injury

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Summary. Bone cement is sometimes used for vertebral body reconstruction following tumor removal. During such procedures, the polymerization of the methyl-metacrylate in the bone cement generates heat. Such temperature increase might cause damage to the nerve roots within the spinal canal. In the present study, pig cauda equina nerve roots were subjected to controlled temperature increases by means of a heat-generating probe. A temperature of 40°C applied for 5 min did not cause any changes in nerve root function. However, 70°C resulted in a complete block of nerve root function within 5 min. Histological nerve fiber damage was seen after exposure to 60°C and 70°C. The present study provides basic knowledge of heat-resistance properties of spinal nerve roots that might be directly applicable as guidelines for safety margins during surgical spine reconstruction procedures using bone cement.

Key words: Temperature – Bone cement – Tumor – Nerve root – Cauda equina – Spine

The surgical excision of primary or metastatic vertebral tumors always results in some loss of vertebral bone. This bone volume defect is frequently replaced with bone cement. However, the dramatic increase in heat during polymerization of the cement has raised the question of potential heat injury to the adjacent nervous structures [9, 11]. In the present study a controlled, experimental model was applied to define critical temperature thresholds for inducing heat injury in spinal nerve roots.

Materials and methods

A total of 20 pigs, body weight 25–30 kg, were anesthetized with 20 mg/kg body weight of Ketalar (ketamine 50 mg/ml, Parke-Davis, Morris Plains, N.J.) i.m. and 35 mg/kg body weight of Pentothal (thiopental sodium, Abbott, Laboratories, Chicago, Ill.) i.v. The pigs were ventilated on a respirator Anesthesia was maintained by an i.v. bolus of 100 mg/kg bodyweight of chloralose (a)-D(+)-gluco-chloralose (Merck, Darmstadt, Germany) and by a continuous supply of 30 mg/kg chloralose per h. A laminectomy from the fifth sacral to the fourth coccygeal vertebra was performed. The preparation was covered with Spongostane (Ferrosan, Denmark) to maintain temperature and moisture. Local tissue temperature was continuously monitored and maintained at 37.5–38.0°C by means of a heating lamp.

Heat injury

A specially designed probe was used to induce heating of the cauda equina (Fig. 1). The area of the probe in contact with the cauda equina was 5.0 × 10.0 mm. Since the pig cauda equina is 5 mm wide, a 10-mm-long segment of the total cauda equina was exposed to the heat. The probe is hollow and can be connected to a water circulation. The water was heated by an automatically adjusting heater/pump device for laboratory use. The temperature of the water is efficiently transmitted to the surface facing the cauda equina, and it was monitored via a hermistor in direct contact with the probe (Fig. 1). When the probe had reached the desired temperature and the neurophysiologic recordings had reached baseline (see below), the probe was gently held in close contact with the cauda equina, with only minimum contact force, for 5 min. After this procedure, the heated segment of the cauda equina, like the non-heated segments, was covered with Spongostane to maintain body temperature and humidity.

Neurophysiologic assessment

The cauda equina was stimulated by two E2 subdermal platinum needle electrodes (Grass Instrument Co., Quincy, Mass.), which were connected to a Grass SD9 stimulator (Grass Instrument Co.) and gently placed intermittently on the spongostane covering the cauda equina 10 mm cranial and 10 mm caudal to the segment of the cauda equina selected for heating. The stimulation sites were marked by placing a 5-mm-long ligature on the top of the spongostane. An EMG was registered by two subdermal platinum needle electrodes, which were inserted into the paraspinal muscles in the tail approximately 10 mm apart. The EMG was visualized using a Macintosh IIci computer provided with Superscope software and MacADIOS II A/D converter (GW Instruments, Sommerville, Mass.) together with a Grass P18 preamplifier (Grass Instrument

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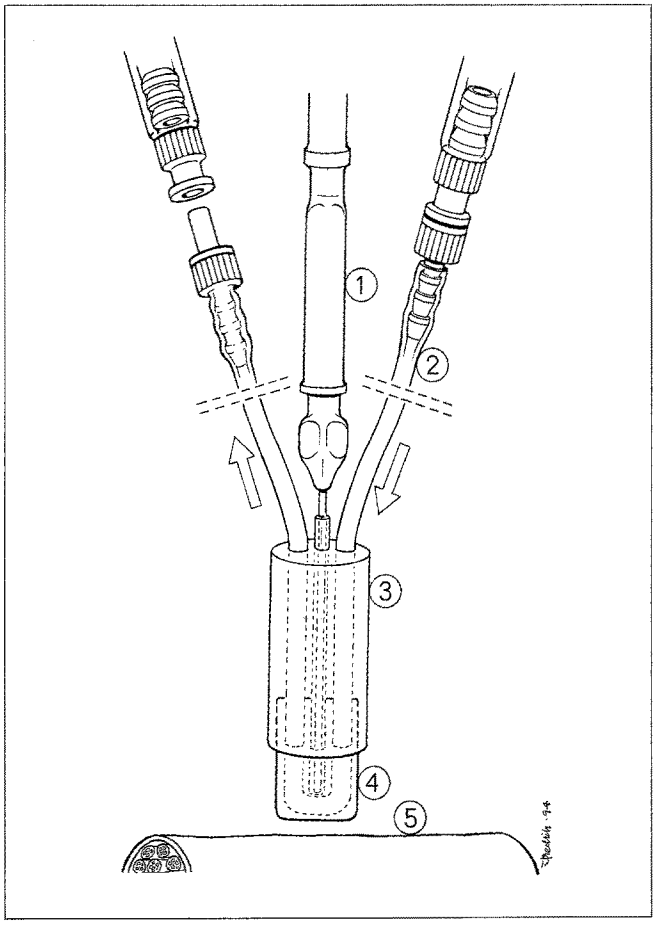

Fig. 1. Probe used for inducing heat injury to the cauda equina *(5)*. Heated water is pumped to and from the probe *(4)* through two hoses *(2)*. The probe is heat-insulated by a rubber cover *(3)*, which is also used for holding the probe. The temperature of the probe is continuously monitored via a thermistor with its recording tip placed in the center of the probe *(1)*

Co.). To ensure that only impulses from exposed nerve fibers were registered, all nerves that left the spinal canal between the cranial and the caudal stimulating electrodes were sectioned.

Muscle action potential. Stimulations were performed at both stimulation sites until the muscle action potential (MAP) amplitude had been constant for 10 min. During the experiment, stimulations were performed every 5 min. The amplitudes of the first peaks of the MAPs were measured and expressed as percentages of the baseline value. The MAP amplitude of the cranial stimulation was studied to detect any heat-induced changes in the cauda equina. The average of the recordings in the 5 pigs at the same time point in each experimental series was calculated and presented in diagram form. The MAP amplitude of the caudal stimulation was studied to ensure that there were no adverse effects in the non-heated part of the cauda equina and that the experimental conditions were stable.

Nerve conduction velocity. The same experimental set-up was also used to calculate the nerve conduction velocity (NCV) in the heated cauda equina segment. The difference in time between the first peaks of the MAP with cranial and with caudal stimulation was determined on the computer. The distance between the two stimulation site on the cauda equina was measured with calipers. The nerve conduction velocity between the two stimulation sites could thus be calculated by dividing separation distance by time difference. This was done every 5 min during the experiment. Like the MAP-amplitude recordings, the average of the recordings at the same time in all 5 pigs in each experimental series was calculated and presented in diagram form.

The statistical differences between the end-values at 40° C and the other temperature series were assessed for MAP and NCV using an unpaired Student's *t*-test.

Histological assessment

After the experiments were finished, the cauda equina was ligated in situ to a wooden stick and fixed by immersion in a mixture of 4% paraformaldehyde and 5% glutaraldehyde according to Karnovsky [2]. The specimens were dehydrated and embedded in plastic. Sections 1 µm thick were stained with methylene blue and Azur II according to the method of Richardson [6]. Coded sections were analyzed using light microscopy.

Results

There were reductions in both MAP amplitude and NCV, which were proportional to the applied temperature (Fig. 2, 3, Table 1). There was generally an initial reduction that stabilized at a slightly higher level within 15 min. The MAP amplitude seemed to be more markedly reduced than NCV. A temperature of 40° C did not induce any lasting reduction. However, a temperature of 70° C blocked the nerve function completely within 5 min.

Light microscopy revealed significant nerve fiber damage in three of five specimens exposed to 60° C and in all four specimens exposed to 70° C (Table 2). The majority of the damaged nerve fibers showed axonal swelling and an attenuation of the myelin sheath, and light microscopy indicated severe vacuolization in some myelin sheaths (Fig. 4). The nerve fiber damage was most severe in small fascicles. No structural changes were found in axons or myelin sheaths from specimens exposed to lower temperatures (Table 2). A slight or moderate endoneurial hyperemia was seen in nerve roots exposed to 50° C, 60° C, and 70° C. There were no significant differences

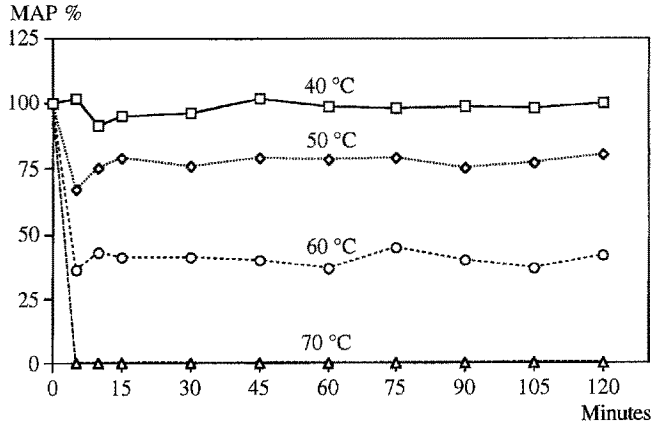

Fig. 2. Changes in muscle action potential amplitude induced by exposure to various temperatures for 5 min. There is a reduction proportional to the temperature. After 15 min, there is a new baseline as the result of the temperature exposure indicating a loss of axons contributing to the action potential

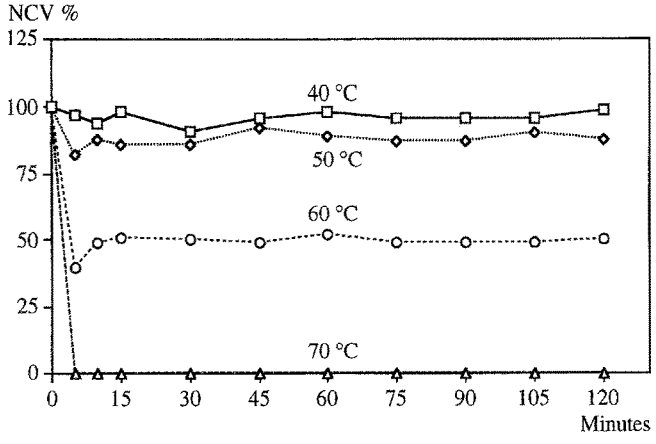

Fig. 3. As with the muscle action potential in Fig. 2, the nerve conduction velocity declines in proportion to the temperature applied. After the temperature exposure, a new baseline is also established after 15 min

Table 1. Reductions in muscle action potential (MAP) and nerve conduction velocity (NCV) following exposure to different temperatures for 5 min

Temperature	MAP	NCV
40° C	100 ± 5	99 ± 4
50° C	80 ± 20 (NS)	88 ± 18 (NS)
60° C	42 ± 39*	50 ± 50 (NS)
70° C	0 ± 0***	0 ± 0***

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$

Table 2. Nature and severity of nerve damage following exposure to different temperatures for 5 min

Temperature	Nerve fibre damage[a]	Schwann cell swelling[a]	Endoneurial hyperemia[b]	Epidurial hyperemia[b]	Epidurial inflammation[b]
40° C	0	++	0	+++	+
	0	++	0	+++	+
	0	+	0	+++	+
	0	0	0	++	+
	0	0	0	+++	+
50° C	0	0	++	+++	+
	0	+	0	++	+
	0	++	+	++	++
	0	0	+	++	+
	0	0	+	+++	++
60° C	0	+	0	+++	+
	++	0	+	+++	+
	0	+	+	+++	+
	++	+	+	+++	++
	++	+	++	+++	++
70° C	++	++	+	+++	+
	++	++	++	+++	+
	+	+	+	+++	+
	+	0	0	++	++
	*	*	*	*	*

*, No histologic evaluation was possible due to severe fixation artefacts

[a] 0, None; +, few scattered; ++, < 25% of myelinated axons

[b] 0, None; +, slight; ++, moderate; +++, severe

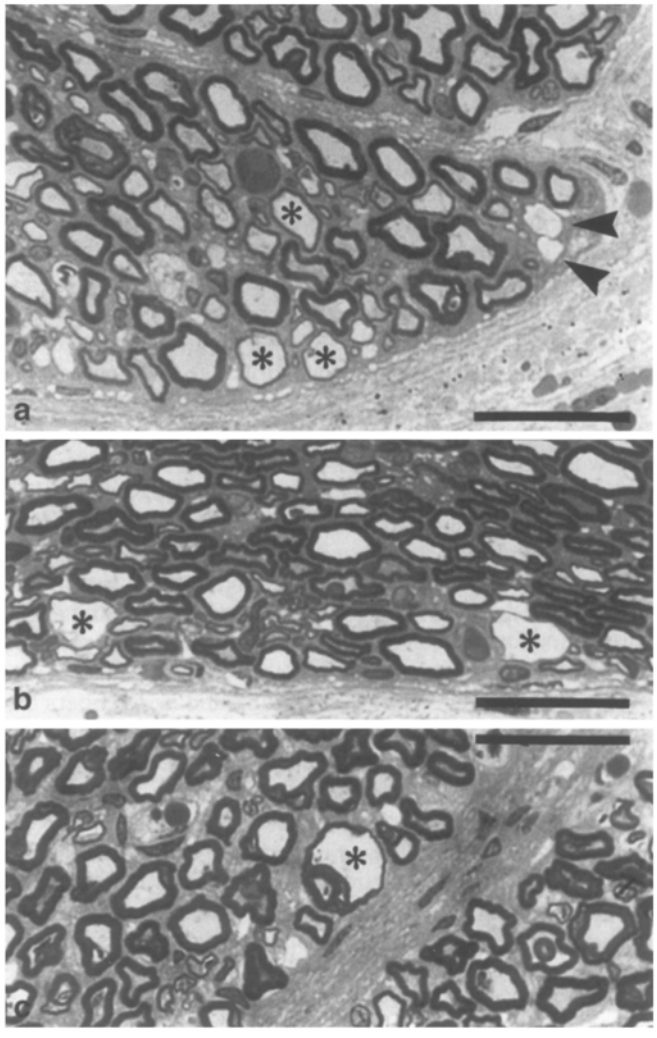

Fig. 4a–c. Semithin sections. *Bars*, 25 µm. **a** Spinal root exposed to 60° C for 5 min. Note nerve fibers with attenuated myelin sheaths (*) and swollen axons without visible myelin *(arrowheads)*. **b** Spinal nerve root exposed to 60° C for 5 min. Swollen nerve fibers with severely attenuated myelin sheaths (*) are seen near the root sheath. **c** Vacuoles (*) indicating intramyelin edema in spinal nerve root exposed to 70° C for 5 min

between the groups in epidural hyperemia, epidural inflammation or Schwann cell swelling between the groups (Table 2).

Discussion

The surgical treatment of malignant tumors in the spine consists in excision of neoplastic tissue with an inevitable loss of substance, which is usually replaced with bone cement [1, 7, 8]. Furthermore, bone cement is sometimes used to provide better fixation between inadequately fixed pedicular screws and the vertebral bone. However, since the temperature of the bone cement reaches more than 70° C during polymerization, there is a potential risk of heat-induced nerve injury [11]. The literature contains no specific recommendations on the critical temperature/time threshold for inducing heat injury in intraspinal nervous

tissue. A previous experimental study showed changes in the spinal evoked potential after the application of acrylic cement over the spinal dura [12]. However, in that study the temperature elevation was not recorded. Histological lesions were demonstrated in the spinal cord after the dura had been heated to 45°C or more for 30 min [10], In vitro studies on the heat emission characteristics of bone cement during polymerization have shown that a significant increase in temperature will only last for up to 5 min [4]. Therefore, the experiments in the present study were performed with a constant duration of 5 min.

The present experimental study demonstrated reductions in MAP and NCV proportional to the increase in temperature and indicated the critical thresholds for heat-induced nerve root injury for the first time. Baseline values were obtained for both MAP and NCV after 5 min exposure to 40°C, which ensures that the pressure applied via the probe was not responsible for the changes seen at higher temperature levels.

The histological examination demonstrated significant nerve fiber damage after the exposure to 60°C and 70°C for 5 min. Thus, even a moderate increase in temperature could induce structural injury to the nervous tissue. However, since the majority of the myelinated nerve fibers did not display changes detectable with light microscopy, additional explanations for the reduction in MAP and NCV should be sought at the subcellular level.

According to the present results, direct contact between nerve roots and bone cement would be deleterious to the structure and function of the nervous tissue. However, biological tissues are generally poor conductors of heat, and it can therefore be assumed that the temperature will drop substantially with increasing distance from the point of application. Based on the results of the present investigation, it may be relevant to study the critical minimum thickness of bone required for complete heat insulation of different volumes of polymerizing bone cement.

To conclude, the present study provides basic knowledge of heat-resistance properties of spinal nerve root, which might be directly applicable as guidelines for the safety margins during spinal surgery. However, it must also be taken into account that the threshold level for thermal damage might be lowered by the surgical trauma and by preoperative vascular injury of devacularization.

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