Experimental Treatments of Acute Spinal Cord Injury

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Although physicians have a choice of treating acute injuries of the spinal cord by realignment of the spinal column, surgical decompression, or measures that alter neuronal metabolism and prevent or reduce edema of the cord, or by combinations of these methods, the relative merits of these procedures appear to be unknown because they have not been evaluated comparatively. There is no known experimental model to assess bony alignment, but Freeman and Wright have described an experimental spinal cord concussion-contusion in which sufficient threshold trauma produces at least a moderately prolonged paraplegia and possibly a lasting neurological deficit and by which the relative efficacy of most current treatments could be compared. Using a similar experimental model, we evaluated standard dural decompression, direct local cord hypothermia, intramuscular dexamethasone, and intrathecal methylprednisolone.

Materials and Methods

We used beagle dogs raised specifically for research; all were young and weighed 8.4 to 15 kg. Most of the animals weighed approximately 12 kg and were female. They were anesthetized with intravenous sodium pentobarbital (30 mg/kg). Endotracheal tubes were placed in all the dogs, but assisted respiration was not required. Following the usual aseptic technique, a midline longitudinal incision was utilized to remove the posterior laminae of the tenth, eleventh, and twelfth dorsal vertebrae completely. The epidural fat was removed, but the dura was not opened.

The trauma was inflicted by striking the dura-covered cord with an impounder from a 25-gm weight dropped 15 cm. Thus, a 375-gm-centimeter force was delivered, which represented the minimal trauma (threshold) at which a physiological transection of the cord might be expected.

All animals remained under anesthesia and were started on the respective treatments 3 hours after the trauma. Forty-eight (48) beagles were divided at random into four groups of 12 animals.

Group 1 (4 males, 8 females). In this control group, the dura was opened over the area of trauma and over the next dorsal and ventral segments if the spinal cord. Gelfoam was placed over the dural decompression; the paravertebral musculature, fascia, and skin were closed in layers and the wound dressed.

Group 2 (3 males, 9 females). These animals received local hypothermia as described by Albin, et al., for 3 hours beginning 3 hours after injury. The dura was opened and tacked laterally to the paravertebral musculature during the treatment. Hypothermia was effected by irrigating the wound with saline circulated through tubing in an ice-water bath at 0°C at a rate of 75 to 100 ml/min. Temperature was recorded from the saline irrigation, the spinal cord, and the deep musculature 4 to 5 cm lateral to the operative site by No. 26 needle thermisters connected to the Tele-Thermometer. The temperature of the saline irrigation was always kept below 4°C. At the end of the period of cooling, the tacking sutures were cut, but the dura, which then assumed a more normal position, was not closed by suture. Gelfoam again was placed over the dural incision, and the wound closed in layers.

Group 3 (2 males, 10 females). These animals were treated with intramuscular injec-

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‡ The principles of laboratory animal care as promulgated by the National Society for Medical Research were observed.

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tions of gluco-corticoid steroids starting 3 hours after injury, after which the wounds were closed without opening the dura. The dose of dexamethasone was 0.50 mg/kg/24 hours on the day of trauma and 0.24 mg/kg/24 hours on the first postoperative day, given in divided doses, after which the medication was changed to methylprednisolone 1.3 mg/kg/24 hours, given as a single dose for 7 days.

**Group 4 (2 males, 10 females).** In this group the dura was not opened but each beagle received a single dose of methylprednisolone 8 mg/kg delivered intrathecally under direct vision directly at the site of trauma with a small curved 25-gauge needle. Thereafter the wound was closed.

Postoperatively, the animals were kept in a recovery unit for 24 hours and then transferred to cages with straw-covered bottoms for further care and evaluation. If the animals were completely paraplegic, their bladders were emptied frequently by expression during the first week after injury. The beagles were retained 5 to 6 weeks under the care and surveillance of veterinarians and the authors. The end point for results was a plateau of the neurological status for 4 to 6 weeks after injury.

**Neurological Evaluation.** To obtain objective results, only the post-trauma neurological status was judged on motor function. Sensory examination (pain perception) produced similar results not considered objective and, in addition, was poorly received by the animals. To perform effective repeated evaluations, we wished to remain on as friendly terms as possible with these animals. The end point of motor recovery was based on the degree of recovery 4 to 6 weeks after the laminectomy and trauma, after which the animals made only very slow further recovery. Grading of the neurological status was based in part on the scale of function described by Tarlov:

1. complete paraplegia, no voluntary movements; 2) perceptible movements of joints, minimal voluntary movements; 3) good movements of joints, able to right and stand, but not run; 4) ability to stand and walk with some spastic running; and 5) running with little deficit and with a near complete recovery. The animals' functional status was judged without knowledge of the treatment groups. Three identical scores in succession and all within the final week were considered as an end point; examples were recorded on movie films.

The animals were then given a fatal dose of pentobarbital, and the spinal column for two segments on each side of the injury was resected and placed in buffered formalin. After the tissues had fixed for 1 week, the spinal cord was removed, and histologic sections taken proximal and distal to the lesion as well as through it were stained with hematoxylin and eosin. Special stains for myelin were performed on occasion.

**Results**

Figure 1 shows the variation in final recovery. Nearly 90% of the animals achieved stable neurological status within the first 2 weeks after injury, but about 10% required 4 to 5 weeks for stabilization. The average grade of functional recovery is recorded in Table 1.

**Control Group.** The control group reached an average functional level of 2.1 in which the animals had minimal but definitely perceptible voluntary movements of the joint. These animals were anesthetic to pain in their hind legs and generally had a spastic bladder. Three animals spontaneously recovered to a level of 4 with ability to stand and walk with poorly coordinated spastic running, but the fact that one animal died and five others remained paraplegic indicates that the outlook of half of these animals was very poor. The animal that died, one of the few male dogs used in the experiment, developed uncontrolled spastic reflex penile erections and urological infection, and succumbed to bacteremia and septicemia caused by a Pseudomonas organism which was resistant to routine antibiotics.

**Treated Groups.** Distinctly different from the controls were the treated groups. Four animals in Group 2 (treated by local hypothermia) and four animals in Group 3 (intramuscular dexamethasone) recovered nearly completely. The average grade of functional recovery for those receiving local hypothermia was 3.5, and for those receiving intramuscular dexamethasone was 3.3. These results were significantly different from that of the controls (p < 0.01). This grade of motor function meant that the ani-