Effects of hyperbaric oxygenation and tissue oxygen studies in experimental paraplegia

DAVID L. KELLY, JR., M.D., KENNETH R. L. LASSTER, M.D., ARBHA VONGSVIVUT, M.D., AND JACK M. SMITH, M.D.

Department of Surgery, Section on Neurosurgery, Bowman Gray School of Medicine, Wake Forest University, Winston-Salem, North Carolina

This study demonstrates that the tissue pO₂ of the normal spinal cord of dogs can be modified by ventilating the animals with oxygen and carbogen. Following trauma to the cord, the tissue pO₂ responded only to hyperbaric oxygen. A series of animals rendered paraplegic and treated with hyperbaric oxygen recovered to a greater degree than those in an untreated control group.

KEY WORDS spinal cord injury · paraplegia · hyperbaric oxygen · tissue pO₂

In a previous report we demonstrated that the tissue pO₂ of the spinal cord following experimental nondisruptive trauma in dogs decreased rapidly to near zero. The hypoxic area was confined to a short segment of cord at the site of injury.

In the present study we have used identical methods to determine if the tissue pO₂ could be modified in the normal and traumatized spinal cord and to evaluate the therapeutic effectiveness of any alteration.

Tissue Oxygen Studies

Methods and Materials

In the studies of tissue oxygen tension carried out in room air and in the hyperbaric chamber, an IL 17365 pO₂ needle electrode* was modified for amperometric determination of tissue pO₂ through an IL 113 oxygen analyzer.* The electrode was first calibrated at 37°C in a solution of normal saline saturated with an oxygen-free gas. This step was repeated with a solution of normal saline saturated with room air. After stabilization up-scale and at zero slope, the electrode was checked in a saline solution of known oxygen content. At the completion of each experiment, the electrode was rechecked in vitro; if a greater than 5% error was noted, the observations were discarded. Since the electrode is so sensitive to temperature, care was taken to make all recordings at the calibrated temperature of 37°C.

Experimental Groups

Laminectomy was performed on eight dogs from T-6 through T-11. An endotracheal tube was inserted to maintain a good airway. In the experiments conducted outside the hyperbaric chamber, arterial blood pressure and pulse rate were recorded from the lower aorta through a catheter connected to a strain-gauge leading to a polygraph.
Group 1. In four animals, the dura was opened and retracted. With the in vivo needle electrode, recordings of tissue $pO_2$ were made in the normal spinal cord. When stable readings were obtained from the cord substance, the animal was ventilated with 100% oxygen for a 5-min period. Continuous recordings of tissue $pO_2$ from the spinal cord were taken. The response of the $pO_2$ in the arterial and venous blood was followed by a separate oxygen analyzer. The animal was allowed to restabilize on respired room air. When stable readings were again obtained from the cord substance, the dog was ventilated for 5 min with carbogen (95% oxygen, 5% carbon dioxide). The tissue $pO_2$ of the spinal cord and the $pO_2$ of the arterial and venous blood were again monitored. After restabilization on room air, the spinal cord was subjected to trauma of 400 GCF. The decline in tissue $pO_2$ was followed until stable. The animals were ventilated with the same gases by the previously described schedule, and the tissue $pO_2$ of the spinal cord was measured.

Group 2. In four animals, the spinal cord was subjected to trauma of 400 GCF. The dura was opened and retracted, and the tissue $pO_2$ in the traumatized cord was followed until stable. The animal was then placed in a hyperbaric chamber, measuring 18 by 36 inches. With standard rates of compression with 100% oxygen, the dog was subjected to 2 atmospheres absolute at 14.7 lb/sq in (psi) (2 ATA), and changes in tissue $pO_2$ in the traumatized cord were recorded. When these readings were stable at 2 ATA, compression was carried to 3 ATA, and changes in tissue $pO_2$ in the traumatized cord were noted. After decompression by standard rates and restabilization of the $pO_2$ needle electrode, the animals were sacrificed with an overdose of pentobarbital. To determine whether exposure of the apparatus in the open wound to hyperbaric oxygen contributed to the changes noted during compression, the dead animals were carried to 2 and 3 ATA, and the tissue $pO_2$ recordings were made as before.

† Model 1836–150 psig Hyperbaric Chamber, Bethlehem Corporation, 225 West Second Street, Bethlehem, Pennsylvania.

Treatment with Hyperbaric Oxygen

Methods and Materials

Following the preliminary observations, the effectiveness of hyperbaric oxygen in the treatment of experimental paraplegia was studied. Forty healthy adult mongrel dogs, weighing from 12 to 17 kg, were used. They were anesthetized with pentobarbital (32 mg/kg of body weight). Anesthesia was maintained with small increments of additional pentobarbital (10 mg/kg of body weight) as needed. Endotracheal tubes were inserted to prevent obstruction of the upper airway, but assisted respiration was not required.

Spinal cord injury was produced as previously outlined with 400 GCF. The test and control animals were examined daily for 3 weeks postoperatively and twice weekly thereafter until the end of the observation period. Sensory testing was found to be unreliable. Motor function was carefully tested, and progress was recorded on film. The scale for judging recovery of motor function first proposed by Tarlov was used: 0 = no voluntary movement; 1 = perceptible movement at the joints; 2 = good movement at the joints but inability to stand; 3 = ability to stand and walk; 4 = complete recovery.

Hyperbaric oxygenation at 2 ATA was used for treatment in all test groups. After anesthesia, laminectomy from T-6 through T-11 and standard trauma to the spinal cord, the animals were placed in the hyperbaric chamber. A catheter was inserted into the femoral vein for administration of drugs through the chamber. The chamber was flushed for 10 min with 100% oxygen. Compression was carried out at a rate of 2 to 3 psi per min until 2 ATA was reached. After the treatment, decompression was carried out according to standard decompression rates.

Experimental Groups

Untreated Control Group. Ten dogs were subjected to the standard trauma. The dura was incised and left opened. After the wound was closed, the animals were given antibiotic medication postoperatively and needed supportive care but no other specific therapy. The postoperative period of observation was 3 months when possible. For humane reasons, the dogs were sacrificed ear-
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Test Group 1 (Immediate Treatment). After laminectomy, the spinal cords of 10 dogs were subjected to the standard trauma. As in the control group, the dura was incised. After good hemostasis was obtained, the wound was closed aseptically. Following a delay of 1 hour, the animals were treated with 100% oxygen at 2 ATA for 4 hours. They were followed for neurological recovery for 3 months.

Test Group 2 (Delayed Treatment). Ten dogs were subjected to laminectomy from T-6 through T-11. After a delay of 4 hours, the animals were treated with 100% oxygen at 2 ATA for 4 hours. They were observed for 3 months.

Test Group 3 (Serial Treatment). After laminectomy, the spinal cords of 10 dogs were subjected to the standard trauma. Following a 1-hour delay, the animals were treated with 100% oxygen at 2 ATA for 4 hours. This treatment was repeated in 24 and 48 hours.

Results

Tissue Oxygen Studies

Group 1. The tissue pO_2 of the normal canine spinal cord ranged from 15 to 30 mm Hg. When the animal was ventilated with 100% oxygen, there was a consistent rise in tissue pO_2 (Fig. 1). The pO_2 of the arterial blood rose from an average of 80 to 504 mm Hg, while the pO_2 of the venous blood rose from an average of 43 to 83 mm Hg. When the animals were ventilated with carbogen, arterial blood pO_2 rose to an average of 313 mm Hg, while venous blood pO_2 rose to 98 mm Hg. In spite of the lower pO_2 determinations from the blood while the animals were on carbogen, the tissue pO_2 rose significantly higher while on carbogen (Fig. 1). After standard trauma, the tissue pO_2 of the spinal cord deteriorated to near zero over the ensuing 30 min. The tissue pO_2 in the traumatized area was not affected by the animal's breathing oxygen or carbogen.

Group 2. The spinal cord pO_2 was again noted to decline to near zero during the 30 min following trauma. When the animals were carried to 2 ATA, the tissue pO_2 in the traumatized area rose sharply and remained at a high level during that period of compression (Fig. 2). An even higher level was attained at 3 ATA. After the animals were sacrificed, no response was obtained by exposure of the animals and instrumentation to 2 and 3 ATA.

Treatment with Hyperbaric Oxygen

In all groups, the spinal cord appeared to be contused with subpial hemorrhage within
15 min after trauma. A stable neurological status developed in most animals within 3 weeks following trauma. On rare occasions, neurological progress occurred over a 6-week period, but in no instance was there appreciable change after 6 weeks.

Untreated Control Group. Only one dog made a good recovery following the standard trauma (Fig. 3). Nine animals were unable to walk, and four of these were completely paraplegic.

Test Group 1 (Immediate Treatment). Hyperbaric oxygen at 2 ATA was started 1 hour after trauma to the spinal cord. Seven of these dogs made a good recovery, and four of these were considered to be normal (Fig. 3).

Test Group 2 (Delayed Treatment). Nine of the animals treated after a 4-hour delay made a good recovery. One animal was greatly impaired and had abnormal function of the urinary bladder (Fig. 3).

Test Group 3 (Serial Treatment). These animals tolerated serial anesthesia for hyperbaric oxygen treatment well. Their rate of recovery was identical to that of Group 2 (Fig. 3).

Discussion

Studies of oxygen tension in living tissues were first described by Davies and Brink. Since then, the electrochemical and physical properties of the oxygen electrodes have been studied extensively. Pilot studies in our laboratory indicated that the membrane-covered needle electrode was the most stable for measurement of tissue oxygen tension in the canine spinal cord.

Oxygen tension has been studied in many organs including the brain. The problems of controlling temperature, calibration, and electrochemical instability introduce many potential errors. The introduction of the needle electrode into the cord substance also modifies the architecture of the capillary bed. For these reasons, it is apparent that no claim to absolute measurements of oxygen tension in tissue can be made in our experiments. Because of the consistency of our results, however, we believe that our data reflect relative quantitative changes in the tissue PO2 measured.

We noted that the traumatized spinal cord became quite hypoxic over a 30-min period after injury. Inhalation of 100% oxygen or
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carbogen did not affect this level of tissue hypoxia. With hyperbaric oxygen at 2 ATA, it was possible to raise the pO₂ of the traumatized spinal cord to well above the tissue pO₂ in the nontraumatized cord.

Our previous studies,⁷ those of Albin, et al.,² and of Ducker and Hamit,⁵ have indicated that local hypothermia to the spinal cord following trauma increases the rate of recovery, possibly by decreasing metabolic demands. Our preliminary studies indicated that at least one deficiency, low tissue pO₂, could be replaced with oxygen under high pressure.

The test groups treated by hyperbaric oxygen differ from the controls in their eventual functional status. Twenty-five of the 30 treated dogs had a significant recovery of function. The remaining five had weakness of gait, sensory changes, and disturbances of the bladder. The schedule of treatment with hyperbaric oxygen did not greatly influence the speed or the degree of neurological recovery.

Recovery of neurological function following experimental paraplegia treated with hyperbaric oxygen was equal to recovery following treatment with glucocorticoid steroids, intrathecal depomethylprednisolone, and hypothermia. Further studies with subhuman primates will have to be carried out, and a clinical trial of treatment with hyperbaric oxygen should be considered.

Summary

We have demonstrated that the tissue pO₂ in the normal spinal cord of dogs can be increased by ventilating the animals with 100% oxygen or carbogen. The tissue pO₂ of the traumatized spinal cord, however, responded only to hyperbaric oxygenation. The results of treatment of experimental paraplegia with hyperbaric oxygen are equal to those of local hypothermia in this experimental model.

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References


Address reprint requests to: David L. Kelly, Jr., M.D., Department of Surgery, Section on Neurosurgery, Bowman Gray School of Medicine, Wake Forest University, Winston-Salem, North Carolina 27103.