Therapeutic Value of Oxygen at Normal and Hyperbaric Pressure in Experimental Head Injury*

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Previous work reported from this laboratory with a model that simulates an expanding extradural hematoma has shown a profound alteration in blood gases and respiration during head injury in dogs. It seemed reasonable to investigate the therapeutic benefits associated with improving the blood oxygen in the post-compression period.

Material and Method

Group 1 (Controls). The previously designed model of head injury was established in 20 dogs used as controls. After Nembutal anesthesia, bilateral fluid-filled extradural balloons were placed, a large one for compression by adding increments of fluid, and a smaller one connected to a Statham strain gauge for pressure measurements. Biparietal dural EEG leads were also placed and referred to the vertex. The balloons and EEG leads were fitted in place, and bone openings closed with acrylic cement. Arterial blood pressure was monitored by a femoral catheter attached to a Statham strain gauge, and respirations by a pneumotachygraph attached to a strain gauge. Fluid was added to the compressing balloon in small increments over a 1½ to 2½-hour period until we obtained both a flat EEG bilaterally for 3 minutes and a spontaneously rising intracranial pressure that corresponded to the blood pressure, reflecting vasoparesis. The balloon was then deflated. When these criteria were met, a 95% mortality was obtained, usually within 24 hours post-decompression, and at the longest, within 30 hours. Figure 1 shows the record of an animal at vasoparesis with rising intracranial pressure and flat EEG's.

Three additional groups of 10 dogs each were compared with the control group.

Group 2. These 10 dogs had respirations supported by a Bird respirator adjusted to deliver 100% oxygen at a rate and depth comparable to that recorded in the anesthetized dog prior to compression; the respirator was maintained for 4 hours following balloon decompression. Arterial PaCO₂ was monitored to be sure that a level above 25 mm Hg was maintained; we have found that this is the lower limit of normal range in the spontaneously respiring dog.

Group 3. These 10 dogs were allowed to respire 100% O₂ spontaneously for 4 hours at ambient pressure following balloon decompression.

Group 4. These 10 dogs spontaneously respired 100% O₂ at 2 atmospheres absolute pressure for 4 hours following balloon decompression in a small animal hyperbaric chamber.

Results

The results as compared to the controls in Group 1 are summarized in Table 1. The animals whose respirations were artificially supported (Group 2) showed a reduction in mortality of 70%. The quality of survival was very poor in five animals, however, and only two (20%) were able to feed themselves or ambulate.

The dogs in the groups spontaneously respiring 100% oxygen (Group 3) were progressively improved in quality of survival. With 100% O₂ at ambient pressure there was a 30% survival, and all dogs could walk, eat, and drink. Although the mortality rate was high, the length of time until death was increased to 3 to 5 days.

The group receiving 100% O₂ at 2 atmospheres (Group 4) showed still more reduction in the mortality to 50%, and the quality of survival was good in all. Even several of

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the dogs that later died looked much better initially than the control dogs on first being removed from the chamber. Death occurred at 3 to 5 days, as it did in the animals receiving 100% O₂ at ambient pressure.

**Discussion**

In a separate study⁹ we have reported the effect of the balloon compression injury on cerebral blood flow and arterial sagittal sinus oxygen difference. In that study it was shown that, following balloon decompression, the arteriovenous oxygen difference progressively widens and the cerebral blood flow falls. Oxygen consumption, as the product of these functions, remains constant for a time until the increased oxygen extraction, as measured by the widening arteriovenous oxygen difference, can no longer compensate for the reduced flow. When this stage is reached, the oxygen consumption falls and shortly after the animal dies.

The primary problem in this form of injury, as we see it, is a metabolic one, with lack of sufficient available tissue oxygen. It is clear that the situation could be improved either by increasing the flow to the tissue, or by leaving the flow unchanged but increasing the amount of oxygen available per unit of blood flow. The effect of improving the flow reported in our previous paper⁵ resulted in a reduction in mortality of 50%, the survivors being of good quality. The present study makes no attempt to change blood flow or composition directly but, rather, to increase the amount of available oxygen carried in the blood.

It has been shown¹¹ that increasing the inspired O₂ to 100% at ambient pressure, as in our Group 3, adds 2.28 cc of O₂ to the
total \( O_2 \) content of blood, providing there is no change in lung function or hematocrit. Breathing 100% \( O_2 \) at 2 atmospheres absolute results in an increased oxygen content of 4.56 cc. Not only is this oxygen very easily available, as it represents oxygen that is dissolved and not bound, but it increases the vessel-to-tissue oxygen gradient and extends the distance into the tissue from the vessel at which a critical \( O_2 \) tension can be maintained.\(^1\)

Jacobson, et al.,\(^1\) have reported a reduction in cerebral blood flow at 2 atmospheres absolute of 100% \( O_2 \) in the normal dog that was more than compensated by increased blood oxygenation as measured by sagittal sinus \( PO_2 \). Furthermore, the same authors have shown that when cerebral autoregulation is impaired, as in hemorrhagic hypotension, hyperbaric oxygen no longer reduces the cerebral blood flow over that noted in air alone. It is the general opinion\(^4,6,7,8\) that a similar loss of autoregulation is to be found in the dogs compressed with the extradural balloon. While the observations regarding autoregulation apply primarily to the period of vasoparesis, it is very possible that some degree of autoregulatory dysfunction persists following decompression of the balloon. We would presume, therefore, that the reduction in cerebral blood flow at high oxygen tensions in these animals would be less than that in the normal animal.

The upper limit of 2 atmospheres absolute of 100% \( O_2 \) was chosen in this series to avoid as far as possible any chance of central nervous system oxygen toxicity. It is generally believed that 3 atmospheres of oxygen are necessary before this occurs.\(^3\) Likewise, the period of exposure was limited to 4 hours to avoid pulmonary toxicity. Although special studies of the lungs were not undertaken, none of the animals appeared grossly to have any respiratory difficulties under these conditions. We chose to carry out treatment one time only, and that early, on the basis of our physiological studies, which indicated that the irreversible changes in cerebral metabolism occurred within the first 8 hours.

In a previous study\(^10\) we noted that in animals with severe head injury there may be a switch to oxygen drive. Apnea may then result if the animal is allowed to breath 100% oxygen spontaneously, either at ambient pressure as in Group 3 or at 2 atmospheres absolute as in Group 4. This apnea could account for the high mortality (70% and 50% respectively) of these two groups. The excellent quality of the survivors in the hyperbaric group (Group 4) probably represents those animals that retained their \( CO_2 \) drive and were able to avail themselves of the increased oxygen supplied.

The lower mortality in Group 2, artificially respirated with 100% \( O_2 \), simply indi-

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### TABLE 1

**Summary of oxygen treatment in 50 dogs**

<table>
<thead>
<tr>
<th>Group No. (controls)</th>
<th>No. of Dogs</th>
<th>Treatment</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20</td>
<td>brought to vasoparesis and flat EEG for 3 min, then balloon deflated and removed</td>
<td>Deaths (within 10 days)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>19 (95%)</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>same as Group 1, then placed on respirator with 100% ( O_2 ) for 4 hrs</td>
<td>3 (30%)</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>same as Group 1, then placed in hyperbaric chamber at atmospheric pressure with 100% ( O_2 ) for 4 hrs</td>
<td>7 (70%)</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>same as Group 1, then placed in hyperbaric chamber at 2 atmospheres pressure with 100% ( O_2 ) for 4 hrs</td>
<td>5 (50%)</td>
</tr>
</tbody>
</table>

* Dogs lived 3 to 5 days compared to 24 to 36 hrs in Group 1.
icates that these animals were not allowed to become apneic. The very high morbidity of the survivors is less easy to understand. One explanation may be that, although the PaCO₂ was maintained at the pre-injury level, a higher figure may be necessary in the post-injured animal to maintain adequate flow.

Others have shown a reduction in mortality with hyperbaric oxygen, using different models. Coe and Hayes,² with rats, and Dunn and Connolly,³ with dogs, have used a cold injury. While both show a reduction in mortality with hyperbaric oxygen, Dunn and Connolly showed no improvement in 100% O₂ at 2 atmospheres over 100% O₂ at ambient pressure.

Sukoff, et al.,¹² have used a very slowly expanding mass produced by psyllium seeds, and a rapid injury utilizing an epidural balloon inflated over a 10-min period. They have used 3 atmospheres absolute of 100% O₂ repeated two to three times daily to reduce the later mortality and edema produced with these forms of injury. They have noticed a reduction in mortality similar in degree to that reported in our study.

We believe that the common factor in all these injuries is reduced available tissue oxygen. The present work shows only one possible approach to altering this. We have already alluded to a series of experiments in which cerebral flow has been improved with a reduction in mortality and morbidity. That the improvement in flow and improvement in oxygenation are separate and additive effects has been shown in the same report. The addition of hyperbaric oxygenation of 2 atmospheres absolute of 100% O₂ for 4 hours to hemodilution resulted in a further reduction in mortality to 20%, greater than that obtained with either method alone. It is recognized that the present schedule of administration, pressure, or gas composition is not necessarily optimal, and further work is going on to investigate these aspects.

Summary

A model of head injury in dogs that simulates an epidural hematoma has established a mortality of 95%. The use of assisted ventilation with 100% O₂, and spontaneous respiration with 100% O₂, at both 1 and 2 atmospheres absolute, showed that the greatest reduction in mortality was obtained with assisted respirations, although morbidity remained high. The best reduction in morbidity was obtained in animals spontaneously respiring 100% O₂ at 2 atmospheres absolute for 4 hours. We have concluded that the hyperbaric oxygen produces better tissue oxygenation during the low cerebral flow syndrome seen following this head injury.

References