Craniocerebral missile injuries in the monkey: an experimental physiological model

ARTHUR M. GERBER, M.D., AND ROBERT A. MOODY, M.D.
Division of Neurological Surgery, The University of Chicago Hospitals, Chicago, Illinois

Experiments were carried out on rhesus monkeys to determine what physiological parameters were most closely correlated with death due to craniocerebral missile injuries. Observations of intracranial pressure, blood pressure, carotid flow, blood gases, respiratory rate, depth and volume, and electroencephalograms were made. These parameters were compared in survivors and nonsurvivors as were the pathological injuries. The most important single parameter that correlated with death was the drop in carotid flow. As this same correlation has been observed in epidural compression experiments in the monkey, there is a strong suspicion that reduced blood flow to the brain as measured by carotid flow is a common factor in craniocerebral missile injuries and epidural compression injuries.

KEY WORDS head injury • carotid blood flow • respiration • electroencephalogram • gunshot wounds • monkey

A increasing number of head injuries, both civilian and military, are due to penetrating missiles. Most of our current knowledge about this type of head injury has been derived from clinical material obtained under military conditions. Recently, Raimondi and Samuelson published an evaluation of 150 civilian craniocerebral gunshot wounds emphasizing the less destructive effects of lower velocity missiles. Investigation of these civilian and military casualties, while affording some opportunity for the evaluation of therapy, has not added to our knowledge of the immediate post-traumatic physiological changes.

In recent years a variety of experimental models has been used to elucidate the pathophysiology of head injury. Concern about the continuing high mortality for these injuries led us to design an experimental model in an attempt to standardize the conditions of injury. This has permitted the monitoring of a variety of physiological parameters which we have correlated with survival and pathological evidence of the injury.

Materials and Methods

This report concerns 11 rhesus monkeys weighing 4 to 5 kg on whom adequate data were obtained, following establishment of the model in pilot studies. The animals were anesthetized with intraperitoneal sodium pentobarbital which was supplemented with small intravenous doses as needed. Arterial and venous catheters were placed for monitoring systemic blood pressure and administration of intravenous fluids respectively. In addition, the arterial line permitted intermittent sampling of blood, which was analyzed for PaO₂ and PaCO₂ on a Beckman 160 gas analyzer. Respiratory rate and depth were monitored by a Harvard pneumograph secured around the chest. In addition, intermittent measurements of respiratory minute
volume were made and noted, using a Bennett Respiratory Ventilation Meter. Right carotid blood flow was monitored by a Carolina square-wave electromagnetic flow meter on the common carotid, following ligation of the external carotid. Intracranial supratentorial and infratentorial pressures were recorded by epidural balloons. Biparietal EEG's referred to the vertex and obtained from epidural screws fixed to the cranium were recorded. All pressure lines and the pneumograph were attached to Statham strain gauges, and the outputs recorded continuously on a Beckman Type R Dynograph, as were the carotid flow and EEG's. The blood gases and minute volumes were manually and intermittently recorded.

The 11 animals were shot through a burr hole 7 mm in diameter and 1 3/8 cm lateral to the sagittal suture, with its posterior edge on the coronal suture. The gun was a Crossman Power Master 160 air rifle, which propelled a .17 caliber BB at a muzzle velocity of 560 feet/sec 3 cm from the skull. In all animals the head and body were fixed to avoid the effects of movement from the impact. Save for the burr hole used for shooting, the holes in the skull made for balloon placement were closed with dental acrylic cement. All animals, whether dying acutely or sacrificed at a later date, were perfused with formalin and studied pathologically.

Results

Of the 11 animals, six survived the gunshot wound until elective sacrifice 5 to 7 days later. Five died within 46 min of the injury. A sample record of the events following the injury for an animal that survived is shown in Fig. 1. All animals that survived showed evidence of a mild hemiparesis, but all were able to get about their cages easily and feed themselves. A sample record of similar events for an animal that died is shown in Fig. 2.

All animals manifested some alteration of respiration at the moment of impact. Two of the nonsurvivors did not recover spontane-

Fig. 1. Record for animal surviving gunshot wound 5 days. Respiration (RESP), systemic blood pressure (BP), carotid blood flow (CBF), supratentorial intracranial pressure (AF ICP), infratentorial intracranial pressure (PF ICP), and biparietal electroencephalograms (EEG LT and EEG RT) during and after the gunshot wound (GSW) are continuously recorded.
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Fig. 2. Record of animal dying within 27 min of gunshot wound. Parameters are as in Fig. 1.

ous respirations, while in two others there was a period of apnea lasting for at least 12 sec. Only one of the six animals that survived was apneic for more than 12 sec.

The two animals whose carotid flow at the end of 3 min was zero were the only nonsurvivors still breathing at this time. They had respiratory minute volumes of at least 200 cc /min and the highest PaO₂ values for the nonsurvivors. These observations did not correlate with any other physiological parameters monitored.

Eight animals showed an alteration in EEG, consisting of slowing and flattening of the baseline pattern. This was most pronounced in four of the five nonsurvivors. In four instances the EEG changes followed both apnea and decreased carotid flow to 50% of baseline or less. Neither apnea alone nor reduction in flow alone appeared to have a predominant effect on the EEG.

The record of blood gases, intracranial pressure, blood pressure, carotid flow, and respiratory minute volumes are summarized in Table 1. In general, blood gases, respiratory minute volumes, and apnea as measured by the pneumograph are all essentially congruent. In Fig. 3 the averaged data are plotted against blood pressure and intracranial pressure in the anterior and posterior fossa. Flow is plotted as the average per cent of the baseline. These graphs show trend only, and highlight the contrast between survivors and those that died acutely. Figure 4 shows the flow separately for each group, with standard deviations plotted. It is plain that statistical significance becomes evident only after 2 min. The flow at 3 min furnished the most significant prognostic data; no surviving animal with a flow at 3 min of less than 60% of baseline survived, and no animal who died had a flow above 25% of baseline.

Three of the animals that survived manifested an initial drop in flow after the injury, while the remaining three had an increase in carotid flow at this time. Among the animals that died, two showed initial post-injury flows as high as four times the baseline, while three showed a drop in flow. There was no correlation between these earlier flow changes and the corresponding systolic or diastolic blood pressures.
TABLE 1
Changes in physiological parameters due to craniocerebral gunshot wounds

<table>
<thead>
<tr>
<th>Animal No.</th>
<th>Respiratory Volume (cc/min)</th>
<th>PaO₂ (mm Hg)</th>
<th>PaCO₂ (mm Hg)</th>
<th>Carotid flow (% of baseline)</th>
<th>Anterior Fossa Pressure (mm Hg)</th>
<th>Posterior Fossa Pressure (mm Hg)</th>
<th>Blood Pressure (mm Hg)</th>
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<tr>
<td></td>
<td>base-line 3 min base-line 3 min base-line 3 min 30 sec 3 min 30 sec 3 min 30 sec 3 min 30 sec 3 min</td>
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* Shot through intact skull.

Both supratentorial and infratentorial pressures at 30 sec were much higher, on the average, in the animals that died than in survivors. To a lesser extent this was also true of the blood pressure. At 3 min, supratentorial pressure was essentially the same in both groups, but infratentorial and blood pressures continued to show a differential.

Pathological study of the brains showed an entrance wound in the right frontal cortex with the exit located in the midportion of the temporal lobe on the same side just above the tentorial notch. All of the brains showed a small amount of blood in the subarachnoid space, but there was no indication of massive hemorrhage. There was no sign of the missile directly injuring the cerebellum. The uncus on the side of the injury was slightly more prominent than on the contralateral side, but there was no other evidence of herniation.

On cut section the missile tract was observed to pass through the putamen down to the medial temporal lobe. The brains of those animals that survived revealed some proteinaceous casting of the ipsilateral ventricle and some areas of infarction adjacent to the missile pathway. Contusions were frequently observed in the lateral pons on both sides as well as in the region of the mammillary bodies.

Discussion

The single parameter that correlated most closely with survival or death was the carotid blood flow monitored 3 min after the gunshot wound. There appeared to be quite a sharp difference in the flow between the two groups. At 3 min after injury, the lowest flow for the survivors was at least 60% of the baseline value while the highest for nonsurvivors was 23% of the baseline. It is recognized that this measurement may not reflect the actual cerebral blood flow under these conditions. The higher intracranial pressure shortly after injury in those animals that did not survive is of interest, but it is not possible to be certain what role, if any, this had to play in the flow reduction. One might speculate that it was responsible for reduced perfusion of vital cerebral tissue.

While the data in Table 1 indicate that a high differential between diastolic blood pressure and intracranial pressure results in the highest flow rates among the nonsurvivors 30 sec after the injury, this is not true for the survivors. It is possible that this variation of flow with the pressure difference may indicate the presence of vasoparesis in the nonsurvivors. At the 3-min period such a correlation is no longer apparent in either group. While this might be expected in the survivors who never manifested this phenomenon, in the nonsurvivors it may represent irreversible changes in the cerebral circulation such as those described by Ames, et al.¹

Using a similar monitoring setup, we have noted this same correlation of carotid flow with survival after a different injury, namely,
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Fig. 3. Comparison between survivors and nonsurvivors for averaged values of carotid blood flow (CBF), supratentorial intracranial pressure (AF ICP), infratentorial intracranial pressure (PF ICP) and systemic blood pressure (BP) during and after the gunshot wound (GSW).

that of epidural compression. The gunshot wound apparently telescopes into a very brief period the events noted over 2 hrs with compression. It appears that the reduced flow to the brain, as measured in the carotid artery, is a common factor in these two quite different injuries. That this is not merely a reflection of decreased heart action is shown by the maintenance of an average systemic, systolic blood pressure of over 100 mm Hg even in the animals that died.

While respirations were altered in all animals at the time of the gunshot wound, apnea and low blood gases did not appear to be as closely correlated with death as flow, many of the animals having quite adequate minute volumes of PaCO₂ and PaO₂ measurements at the 3-min interval despite a marked reduction in carotid flow. This again, does not necessarily reflect cerebral oxygenation. The relative preservation of respiratory function until late is also similar to that seen with epidural compression, and suggests that respiratory function itself may
be altered as a reflection of reduced cerebral perfusion.

Ommaya, in experiments on monkeys, observed similar respiratory changes in concussive injuries. In those animals suffering fatal or severe concussion, there was an apneic pause from which either the animal did not recover, or the return of an irregular respiratory pattern preceded a second apnea and death. Up to 3 hrs of artificial respiration was attempted on these animals without reversing the situation.

Unlike the compression injury, where the flattening of the EEG appeared closely correlated with apnea, we were unable to see a clear correlation of altered EEG function in this injury with either flow or respiratory function alone. Others have shown in rabbits and dogs that EEG alteration is more rapid following an ischemic injury to the brain than an asphyxic one. Certainly, the findings of the most severe EEG changes early in the animals that died is compatible with cortical ischemia, and may further support the idea that the reduced carotid flow in our animals reflects such an ischemia. In Ommaya's experimentally induced concussive injuries, a similar flattening of the EEG followed complications such as hemorrhage or fracture, however, in their animals without these complications the injury was immediately followed by high-amplitude slow activity.

Pathological studies failed to yield a positive correlation with the changes in various parameters, probably because the injury was extensive and nonspecific. It was, in fact, surprising how well some of the survivors were despite extensive injury to the cortex, midbrain, and, in one case, the cerebellum. There was, however, a tendency for those with pontine or hypothalamic injuries to
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have higher intracranial pressure, and this is being further investigated in a separate series.

Summary

Eleven rhesus monkeys were shot in the brain with a 0.17 caliber air rifle. Five of the animals died within 46 min while the remaining six survived and were sacrificed 5 to 7 days later. The physiological parameter most closely correlated with these two groups was the carotid blood flow 3 min after the injury. While EEG changes and apnea occurred, they were not closely correlated with the survival of the animals. Increased intracranial pressure was most closely correlated with damage to the pons and hypothalamus. Death was more closely correlated to lesions in the pons and basal ganglia.

Ideally one would like to be able to produce two controlled missile injuries, one producing death and the other compatible with survival. The initial pilot study proved quite discouraging in this aspect since seemingly identical injuries one monkey would die while another would survive. Observation of the carotid flow, however, did provide a parameter by which death could be consistently predicted.

References


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Address reprint requests to: Robert A. Moody, M.D., Division of Neurological Surgery, The University of Chicago Hospitals, 950 East 59th Street, Chicago, Illinois 60637.