A comparison of physiological responses to percussive brain trauma in dogs and sheep

J. Eugene Millen, Frederick L. Glauser, M.D., and R. Paul Fairman, M.D.

Department of Medicine, Division of Pulmonary Diseases, Virginia Commonwealth University, Medical College of Virginia-McGuire Veterans Administration Hospitals, Richmond, Virginia

Physiological variables were monitored in dogs and sheep after exposure of the brain to a pressure wave produced by a fluid-percussion device. Mean systemic arterial pressure (SAP), mean pulmonary arterial pressure (PAP), and pulmonary wedge pressure (PWP) were recorded prior to and following trauma. Lung lymph flows (QLYM) were measured prior to and for 2 hours after trauma. Plasma catecholamine levels were quantitated prior to and at 30 seconds following trauma. In 16 dogs, SAP increased from 123 ± 14.6 to 254 ± 60.8 mm Hg (p < 0.0001), PAP increased from 17 ± 4.4 to 27 ± 10.8 mm Hg (p < 0.05), and PWP increased from 4 ± 2.4 to 15 ± 8.8 mm Hg (p < 0.0001), all at 30 seconds posttrauma. All pressures returned to near baseline values within 6 minutes. The QLYM from the right lymph duct in 12 dogs increased from 0.82 ± 0.77 to 2.7 ± 2.1 and 1.88 ± 1.82 ml/30 min, respectively, at 30 and 120 minutes. In five dogs the plasma concentrations of dopamine, epinephrine, and norepinephrine increased from 234 ± 98 to 1906 ± 1384, 609 ± 641 to 19,813 ± 10,234, and 388 ± 194 to 3223 ± 992 pg/ml, respectively (all p < 0.01). In sheep there were no changes in SAP, PAP, PWP, QLYM, or catecholamine levels in response to percussive wave trauma up to 10 atm. Ratios of lung tissue water to dry weight were not significantly different from control animals in either species. The authors conclude that in dogs there is a profound sympathetic discharge resulting in dramatic elevations in plasma catecholamines, systemic and pulmonary artery hypertension, and an increase in pulmonary lymph flow. Sheep fail to demonstrate changes in any of these variables after severe percussive wave brain trauma.

KEY WORDS • head injury • catecholamine • pulmonary blood pressure • systemic blood pressure • lymph flow • lymph plasma albumin ratio • dog • sheep

Systemic and pulmonary hypertension and, in some cases, pulmonary edema have been reported in many animal models following elevation of intracranial pressure (ICP), electrical stimulation of the sympathetic nerves, and concussive brain trauma. We have reported that marked elevations in systemic arterial blood pressure (SAP), left atrial pressure, and pulmonary artery pressure (PAP) with an increase in ratios of lung tissue water to dry weight are a consistent finding following concussive brain trauma of 3 to 4 atmospheres (atm) in the cat. Additionally, administration of phentolamine, an alpha adrenergic receptor blocker, prevented the hemodynamic changes and pulmonary edema. We concluded that induced concussive brain trauma caused severe systemic hypertension which was mediated by the release of endogenous alpha adrenergic agents.

In an effort to clarify the part that hemodynamics play in the production of pulmonary edema, we exposed additional cats to lower levels of concussive brain trauma (1 to 3 atm). Pulmonary edema developed, as shown by a marked increase in the ratio of lung tissue water to dry weight, but without appreciable elevations in pulmonary wedge pressure (PWP) or mean SAP.

While performing ongoing pilot studies of the response of various animals to percussive-wave brain trauma, utilizing a fluid-percussion device, we found that the dogs' physiological response was similar to that of the cat. Surprisingly, sheep exposed to the same type of brain trauma had no hemodynamic alterations or pulmonary edema. The present study documents and extends these observations and relates them to the literature on animal brain/head trauma which has evolved over the last several years.
Brain trauma was induced utilizing a fluid-percussion device. Its use permits the administration of graded degrees of trauma in a very reproducible fashion while simultaneously monitoring cardiorespiratory variables. The animals were placed in the supine position, and their heads were attached to a stereotaxic frame in order to facilitate attachment to the trauma device. A craniotomy was performed over the central sagittal sinus. The dura was left intact. A hollow metal tube, affixed over the craniotomy hole with dental acrylic, served as a connection between the skull and the fluid-percussion device. A Plexiglas cylindrical saline reservoir was attached to the tube by way of a transducer housing through which the force and the duration of the injury was measured on a storage oscilloscope.

In one additional sheep and two additional dogs the following studies were performed. In the sheep, sodium thioptental was used only during the actual surgical manipulation and thereafter nitrous oxide (N₂O) was administered at a ratio of 6:1 with oxygen for 1½ hours prior to trauma. This animal was added to the series to assure that sodium thiopental had not masked or blunted any animal's physiological response to trauma. In order to verify that canine QLYM from the right lymph duct reflected lung fluid dynamics, lymph ducts of the left lung were cannulated in two dogs using a modification of the technique of Parker, et al., which is reported to be free of cardiac and chest wall lymph contributions.

In five sheep and five dogs, 10 ml of arterial blood was obtained for determination of dopamine, epinephrine, and norepinephrine concentrations employing a radioenzymatic technique.

**Materials and Methods**

*Animal Preparations*

Twelve sheep and 16 dogs were studied before, during, and 2 hours after percussive-wave brain trauma. Both species were anesthetized intravenously with 30 mg/kg of sodium thiopental and secured to the operating table in the supine position. In the sheep a standard cuffed endotracheal tube was passed through a tracheostomy, and in the dogs an oral endotracheal tube was inserted. Tidal volume in both species was set at 12 cc/kg and was delivered with a Harvard animal ventilator; a pulmonary end-expiratory pressure of 5 to 7 cm H₂O with an inspired O₂ concentration of 0.8 to 1.0. Through a vascular cutdown procedure, a balloon-tipped flow-directed catheter was passed via a femoral vein to the pulmonary artery for recording mean PAP and mean PWP. Through an adjacent femoral artery a polyethylene catheter (PE-160) was directed into the lower thoracic aorta for recording mean SAP. Pressure monitoring was achieved with a transducer and physiological recorder.*

Acute lung lymph fistulas were created in six of the sheep using a technique similar to that reported previously. In 13 of the dogs the right lymph duct was cannulated as described previously. Lymph flow (QLYM) was collected in calibrated test tubes at 30-minute intervals. Arterial blood samples were obtained at the end of each QLYM collection. Lymph to plasma (L/P) albumin ratios were determined by means of a fluorometric technique.

*Statham Db transducer manufactured by Gould, Inc., Medical Products Division, 1900 Williams Drive, Oxnard, California: physiological recorder, Model DR-8, manufactured by Electronics for Medicine, Inc., White Plains, New York.

**Time of Measurements**

After the animals were attached to the fluid-percussion device, baseline SAP, PAP, and PWP were obtained. Following concussive brain trauma, SAP and PAP were recorded continuously for 10 minutes and thereafter at 30-minute intervals. The PWP was recorded at 30 seconds, 1, 5, 10, and 30 minutes, and thereafter at 30-minute intervals. The QLYM and L/P albumin ratios were determined in six sheep and 14 dogs for a minimum of 2 hours or until stable prior to brain trauma, and thereafter at 30-minute intervals. Arterial catecholamine levels were determined at baseline and at 30 seconds posttrauma. Ratios of lung tissue water to dry weight were obtained at the end of each experiment, as described by Pearce, et al.,

**Statistical Analysis**

Statistical analysis was performed by Student's t-test and regression analysis was performed where indicated. Means and standard deviations were used exclusively. Differences between groups were considered significant when p < 0.5.

*Cat-a-Kit radioenzymatic technique developed by Upjohn Diagnostic, Kalamazoo, Michigan.
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**Results**

**Sheep Studies**

In sheep, SAP did not change significantly in response to an average trauma level of 4.06 atm. Control SAP was 79 ± 13.9 mm Hg, compared to 71 ± 23.9 mm Hg at 30 seconds posttrauma and remained at this level for the duration of the study. At 30 seconds (Fig. 1) and throughout the remainder of the study, PWP and PAP were unchanged from control values. The QLYM did not change appreciably, control values were 1.97 ± 1.03 ml/30 min, and following trauma, QLYM values were 2.37 ± 0.83 ml/30 min. The L/P albumin ratio remained relatively constant throughout this period (Fig. 2). The sheep anesthetized with nitrous oxide also had no appreciable change in pressures 30 seconds following trauma: SAP, PAP, and PWP were 66, 14, and 4 mm Hg, compared to control values of 62, 13, and 4 mm Hg, respectively. The QLYM was not measured in this animal.

Since there were no alterations in hemodynamics or QLYM in the above animals, we exposed four additional sheep to percussive-wave brain trauma at extremely high levels (6.5, 7.5, 8.5, and 10 atm) in order to determine if, in the previous animals, the level of percussive trauma had not been high enough. In these four additional animals, mean baseline pressures were as follows: SAP 82 ± 15 mm Hg, PWP 7 ± 2 mm Hg, and PAP 15 ± 4 mm Hg; these values did not change significantly following any level of trauma. The QLYM did not change from a control value of 2.1 ± 1.2 ml/30 min.

There was no significant change from baseline in plasma dopamine, epinephrine, or norepinephrine concentrations following trauma (Fig. 3). The ratio of lung tissue water to dry weight was 3.10 ± 0.45, which is not significantly different from control values in this laboratory (3.6 ± 0.6).

**Dog Studies**

Following induced percussive-wave trauma averaging 3.16 atm in dogs, SAP increased from a control value of 123 ± 14.6 to 254 ± 60.8 mm Hg at 30 seconds posttrauma (p < 0.0001), and returned to near control levels by 6 minutes. The PAP also increased at 30 seconds posttrauma to 27 ± 10.8 mm Hg from a control level of 17 ± 4.4 mm Hg (p < 0.05). The PWP increased from 4 ± 2.4 to 15 ± 8.8 mm Hg at 30 seconds (p < 0.0001) (Fig. 1). Both PAP and PWP returned to near control levels at 6 minutes after trauma.

In the 12 dogs with right lymph duct cannulation, the QLYM increased from an average control level of 0.82 ± 0.77 to 2.7 ± 2.1 and 1.88 ± 1.82 ml/30 min, respectively, at 30 and 120 minutes after trauma averaging 2.93 atm (all p < 0.02). The L/P albumin ratios remained relatively constant throughout this period (Fig. 2). Electroencephalograms (EEG's) performed in two additional dogs demonstrated profound depression of electrical activity with gradual but incomplete recovery after 25 minutes.
Left lung QLYM was increased in two additional dogs. In one, there was an increase from a baseline of 2.6 to 23.7 and 21.1 µl/hr at 60 and 90 minutes post-trauma, respectively. Due to technical difficulties, during the 90 to 120-minute interval, QLYM ceased. In the second dog, QLYM increased in response to 4 atm of trauma from a baseline of 400 µl/hr to 800, 1400, and 1200 µl/hr at 60, 90, and 120 minutes, respectively. It is interesting that during the first 30 minutes following trauma, QLYM was the same as six successive baseline values (400 µl/hr). During that interval (at 30 seconds following trauma), SAP, PAP, and PWP were at their highest. Ratios of lung tissue water to dry weight were 2.92 ± 0.52, which is not significantly different from our control values of 3.17 ± 0.35.

In five dogs, the plasma catecholamine concentrations increased dramatically in response to an average of 2.94 atm of brain trauma. At 30 seconds posttrauma, dopamine values increased from 234 ± 98 to 1906 ± 1384 pg/ml, epinephrine content from 609 ± 641 to 19,813 ± 10,234 pg/ml, and norepinephrine values from 388 ± 194 to 3223 ± 992 pg/ml (all p < 0.01) (Fig. 3).

Discussion

This study documents that sheep and dogs do not have the same hemodynamic, lung lymph flow, or catecholamine response to percussive-wave brain trauma. The dogs’ hemodynamic response was similar to that previously described for cats,11 in that SAP, PAP, and PWP increased dramatically within 10 seconds of receiving an average 3.16-atm percussive brain trauma (Fig. 1). At the peak of the pressure response (at 30 seconds posttrauma), arterial dopamine, epinephrine, and norepinephrine levels determined in five dogs increased between nine- and 30-fold (Fig. 3), similar to findings in cats when head trauma was delivered by a captive bolt blow.1

In contrast, sheep exposed to 4.06-atm head trauma demonstrated no significant change in either dopamine, epinephrine, or norepinephrine concentrations, or in SAP, PAP, or PWP after percussive-wave brain trauma (Figs. 1 and 3). It is not surprising that systemic and pulmonary vascular pressures remained constant with stable blood catecholamine levels. What is surprising is that sheep did not have hemodynamic or catecholamine responses similar to dogs and cats exposed to similar or lower levels of percussive-wave brain trauma.

It could be argued that, due to the sheep’s cranial anatomy, higher levels of trauma are needed to produce a response similar to those found in dogs. To test this hypothesis we exposed four additional sheep to extremely high levels of percussive trauma, ranging from 6.5 to 10 atm (approximately 7600 mm Hg pressure). Once again there were no hemodynamic or lymph flow changes compared to baseline values. In addition, EEG monitoring in several sheep failed to show any changes in electrical response (in contrast to findings in dogs, see above) at any severity of brain trauma. Gross pathological examination of the brain in these animals revealed subarachnoid and petechial hemorrhage of the pons and medullary reticular formation and an occasional midline hemorrhage of the midbrain as well, but there were no apparent surface brain-stem contusions. This finding is not unexpected since brain-stem involvement was grossly apparent in only 40% of a large series of cats exposed to percussive trauma (GT Povlishock and LD Jenkins, personal communication, 1982). However, in their series all animals displayed dramatic hemodynamic derangement secondary to percussive brain trauma produced by a fluid-percussion device. Their study would seem to indicate that gross brain-stem damage is not necessary for concussive brain trauma.

Mechanically elevating ICP elicits a dramatic increase in SAP and pulmonary edema in dogs,4-11 cats,7 monkeys,4 and rats.7 In sheep, the response to mechanically increasing ICP has not been consistent. Bowers, et al.,2 found no significant increase in mean SAP when the ICP was elevated to 96 mm Hg in sheep. Van der Zee, et al.,19 demonstrated a dramatic increase in SAP (from 73 to 177 mm Hg) after increasing the ICP to 142 mm Hg. A second group of sheep exposed to ICP levels of 70 mm Hg did not demonstrate a significant increase in SAP.

From these findings and studies with other animals, it appears that a threshold ICP level must be reached before a massive sympathetic discharge occurs. There is evidence, however, that extreme increases in ICP are not needed to elicit this response. In cats exposed to severe concussive trauma, SAP increased from 128 to 229 mm Hg while ICP increased only to 38 mm Hg from a control level of 6 mm Hg.11 This ICP level is similar to values (30 to 40 mm Hg) reported in patients with head trauma.12 In the present study, ICP was not quantitated in either sheep or dogs.

Lung lymph flow increases have been reported following mechanical elevation of ICP in sheep.2,3,7,17 Jones, et al.,4 attributed this to increased perfusion of pulmonary vascular surface area and van der Zee, et al.,19 confirmed these findings. In contrast, our study does not demonstrate any significant change in QLYM in sheep following percussive-wave brain trauma. The increase in QLYM found in our dogs indicates either an increase in pulmonary microvascular permeability or an increased pulmonary vascular surface area. Although right lymph duct flow can be contaminated by cardiac or chest wall lymph, the two additional dogs with cannulae in a left lung lymph duct demonstrated an increase in QLYM of the same order of magnitude as the others. These two additional studies do not clearly differentiate between increased microvascular permeability or recruitment of vascular surface area, but they do suggest that the increased lymph flow in this report reflects lung lymph dynamics. In addition, they do not support the conclusion that the lymph flow increase was due to elevated pulmonary vascular pressures.
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In fact, in more than half of the dogs, PAP and PWP were lower and the QLYM was higher at 1 and 2 hours posttrauma than at 30 minutes.

The lack of significant increases in lung tissue water to dry-weight ratios in our dogs was unexpected. Cats exposed to concussive brain trauma of the same or lower level demonstrated a significant increase in lung tissue water to dry-weight ratios. The difference found in this species may be attributed to a more efficient lung lymph clearance system in dogs.

The results of this report document the physiological response of dogs exposed to percussive-wave brain trauma, and reveal that sheep do not respond in a similar fashion, even when exposed to percussive trauma of more than 10 atm (10 atm is more than four times the level sufficient to elicit a response in either cats or dogs). Since the sheep is a butting animal, its lack of response may be an adaptive mechanism. From this study, it is apparent that the sheep is not a good model for studies of the physiological effects of percussive-wave brain trauma on the genesis of neurogenic pulmonary edema.

References


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