The ICP/CBF Effects of Volume Loading during PEEP Administration

To the Editor:—The study of Doblar et al.1 may have important implications with regard to the care of neurosurgical patients. Certain aspects of their study, however, invite comment.

If the increases in CSFP which the authors observed when they restored cardiac output to pre-PEEP levels with saline infusion were the result of increased brain interstitial fluid as the authors suggest, how did the extravasation occur? Their data show that cerebral perfusion pressure was not altered as compared with the zero PEEP state, so it did not occur along a hydrostatic gradient. With the infusion of normal saline significant extravasation should not occur along an osmotic gradient. That leaves only an oncotic gradient resulting from dilution of serum proteins. Were oncotic pressures measured? Should the important conclusion drawn from the saline-treated animals (Group 2 of the study) be that colloid might be a better choice than isotonic crystalloid for volume augmentation in the patient with reduced intracranial compliance? The study would have been improved by the inclusion of a colloid-treated group.

Interpretation of the CBF data from the mannitol-treated animals (Group 3 of the study) is also difficult. There are explanations for the greater CBFs (as compared with Groups 1 and 2) which the authors observed other than the suggested differences in interstitial fluid volume. These include a mannitol-related reduction in blood viscosity2 and a direct mannitol-induced vasodilation. These possibilities make a mechanistic interpretation of their observations difficult, if not impossible.

While the data suggest an advantage of uncertain cause for mannitol under stabilized conditions, the authors make no mention that the advantage may not be apparent when the drug is first administered or following a major diuresis. The administration of mannitol has been reported to produce transient increases in ICP3 and hence initially may cause reductions in cerebral perfusion pressure. The CBF technique employed permits the recording of transients. What were the initial effects of mannitol infusion?

The important conclusions of this study must lie in the intergroup comparisons, yet only intragroup statistical comparisons are provided. At what PEEP levels and at what levels of statistical significance did intergroup differences in CBF and CSFP occur?

We second the authors' suggestion that any conclusions drawn from their study using animals with normal lungs may not necessarily be applicable in situations of reduced pulmonary compliance. The transmission of airway pressures to the intrathoracic and cerebral vessels may be markedly attenuated by a poorly compliant lung.

We observe two apparent inconsistencies among the reported results. The hemodynamic data reveal that the saline (Group 2) and mannitol (Group 3) infusions used to return cardiac output to pre-PEEP levels did so without producing elevations in CVP or PAP over those observed in their control (Group 1) animals. Given that increasing right heart output by volume loading requires generating an increase in right ventricular end-diastolic volume, and hence right ventricular end-diastolic pressure, mean right atrial pressure and mean CVP, we are concerned that there has been an error in the determination of either CVP or cardiac output.

If the CVP data are accepted, one must reconcile the small or absent gradient between the CSFPs (used as a measure of ICP) and the CVPs reported for both the control (Group 1) and mannitol (Group 3) animals. (We assume in the absence of information to the contrary that the animals were studied in a horizontal position.) CSF absorption requires a gradient of approximately 5 cmH2O across the arachnoid villi. This gradient might be abolished by an acute elevation of venous pressure (as with the sudden application of PEEP), but ICP would continue to rise thereafter as a result of continued CSF secretion and no “steady state” would be observed until the gradient was reestablished.

Our final concern is the influence of the level of stress to which these animals were subjected. It appears that these investigations were performed on paralyzed, unanesthetized, unsedated goats. If this is the case, we must wonder whether any conclusions that can be drawn should be extrapolated to anything but extremely high-stress states. We therefore must wonder whether this study should have been undertaken at all. Studies of this nature will become appropriate grist for the mill of the ever more vocal animal welfare advocates.

The study of Doblar et al. asks a question relevant to the care of the neurosurgical patient. Pending clarification of the questions raised above, we must consider the question unanswered.

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In reply.—The objective of our study was to examine the effect of PEEP on cerebral blood flow (CBF) and cerebrospinal fluid pressure (CSFP) with and without the maintenance of mean arterial pressure (BP) at pre-PEEP levels. With the application of PEEP, decreases in BP were prevented by gradual infusion of intravenous fluid titrated against BP changes at each of the three levels of PEEP applied. This required approximate infusion volumes of 11 per cent of the estimated blood volume in the saline group and 4 to 7 per cent in the mannitol group.\(^1\) We did not, as stated in the letter above, “return cardiac output (CO) to pre-PEEP levels” with volume infusion: BP, and not CO, was the controlled variable and only small decreases in BP were permitted before volume infusion was increased. Concerning the mechanism of the increase in CSFP in the saline group, we agree that the most likely explanation is an onotic pressure gradient given the available data, but we cannot exclude shifts in intracranial contents resulting in regional differences in perfusion pressure which are known to occur.\(^2\) We regret that onotic pressure data are not available and we also agree that additional studies should be done using colloid for BP control as it may offer advantages over hyperosmotic and crystalloid solutions.

With reference to the mannitol data, the paper by Burke et al. (reference 2 of the above letter), which was not available to us as it was published a month after ours, examines several mechanisms for blood flow increases with mannitol but does not permit any conclusions as to which of the effects of mannitol (decreased viscosity and red cell volume, increased red cell deformability, direct vasodilating effects, and brain dehydration) predominates in the CBF response to mannitol.

In the early period of the infusion of mannitol we did not observe significant increases in CSFP probably because of the slow rate of injection and the low total volume infused. We did not cite the paper by Cottrell et al. (reference 3 of the above letter) because their use of a bolus injection of mannitol and the lack of supporting hemodynamic data did not permit comparison of our results. It should not be surprising that the difference in technique of administration of mannitol might result in a difference in the CSFP responses as similar results have been reported for nitroprusside by one of the authors of the above letter.\(^3\)

We take issue with the “apparent inconsistencies” in the central venous pressure (CVP), pulmonary arterial pressure (PAP), and cardiac output data suggested above. It appears that the authors above, without supporting data, expected to see additive effects of PEEP and volume infusion on central venous pressure. We did not observe this, rather we found that proportional increases in CVP and PAP with PEEP occurred in all three groups. Our data are consistent with those of Sykes et al.\(^4\) who demonstrated that the small increases in CVP with the addition of PEEP (10 cmH\(_2\)O) in euvoolemic dogs contrasted with decreases in CVP in hypervolemic dogs placed on PEEP.

The literature is replete with conflicting reports of the effects of PEEP on hemodynamics and ventricular function.\(^5\)\(^-\)\(^8\) Both increases\(^5\) and decreases\(^4\) in transmural right ventricular pressure have been documented with PEEP therapy suggesting that the prevailing conditions of the study exert significant influence on the resulting data. In this regard, we are not aware of data from a study which closely matched our protocol which would allow comparison of the data.

We see no reason to reconcile the small or absent gradients between CSFP and CVP reported for the control group (Group 1) and the mannitol group (Group 2) animals as they pertain to the existence of steady state conditions during our data collection. As stated in our manuscript, the animals were studied in a position where the head was at the same level as the heart (horizontal). In this position we found that the progressive application of PEEP did reduce the gradient between CSFP and CVP from 4.1 to 0 cmH\(_2\)O in Group 1 and from 5.6 to \(-0.7\) cmH\(_2\)O in Group 3. As we stated in the text, during the 30-min equilibration period no significant changes in the measured variables were observed. It is likely that small changes in CSFP were occurring due