Intensive Care Med. 7, 187 – 191 (1981)

Intensive Care Medicine

Positive End-Expiratory Pressure (PEEP) and Cerebrospinal Fluid Pressure During Normal and Elevated Intracranial Pressure in Dogs

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Abstract. The effect of up to 15 cm H_2O positive end-expiratory pressure (PEEP) on cerebrospinal fluid pressure (Pcsf) was investigated in five anaesthetised, mechanically ventilated dogs during normal and then elevated (40 – 50 cm H_2O) intracranial pressure (ICP). Stepwise elevations of PEEP in 5 cm H_2O increments resulted in small rises in Pcsf at normal ICP and in significantly larger rises when ICP was elevated. The regression equations for the relationships between Pcsf and end-expiratory pressure (EEP) were as follows: Pcsf = 12.95 + 0.82 EEP for normal ICP, and Pcsf = 46.41 + 2.06 EEP for elevated ICP. Mean $PaCO_2$ rose from 39.7 ± 2.5 to 47.6 ± 5.0 torr during normal ICP, and from 34.2 ± 2.9 to 50.9 ± 5.3 torr at elevated ICP as PEEP was elevated to 15 cm H_2O. We conclude that PEEP raised Pcsf, and that this increase is more severe under conditions of elevated ICP. The rise in Pcsf due to PEEP may be explained by either the rise in intrathoracic pressure or the rise in $PaCO_2$, or both.

Key words: Positive end-expiratory pressure – Cerebrospinal fluid pressure – Intracranial pressure

Introduction

The incorporation of positive end-expiratory pressure (PEEP) into the ventilatory circuit is now an accepted mode of therapy for resistant hypoxaemia associated with acute respiratory failure [4, 6, 12]. However, when PEEP is used with controlled mechanical ventilation (CMV), there can be reduction in venous return and cardiac output secondary to increased mean intrapleural and thoracic venous pressure [13, 17]. The degree of this effect is dependent on the compliance of both the lungs and the thoracic cage [5]. Increased central venous pressure (CVP) can be expected to raise cerebral venous pressure and cerebral blood volume, thus increasing intracranial volume and pressure (ICP) and decreasing cerebral perfusion pressure. Positive end-expiratory pressure, when used with CMV, may also increase ICP indirectly by increasing wasted ventilation and $PaCO_2$ [19].

Frequently, patients suffering from multiple trauma have both acute respiratory failure and intracranial injury. If PEEP and CMV increase ICP, their use in the treatment of hypoxaemia under these circumstances may be relatively limited. The present study was undertaken to clarify further the effects of CMV combined with PEEP on ICP and to demonstrate the possible influence that an initially elevated ICP may have on these effects.

Methods

Anaesthesia and Technique

Five mongrel dogs weighing 18.2 to 26.0 kg were anaesthetised with sodium pentobarbital, 25 mg/kg, IV, and were paralyzed with 0.1 mg/kg pancuronium bromide. Their tracheae were intubated and their lungs ventilated with a volume preset ventilator (Emerson Volume Controlled Ventilator, J. H. Emerson Co., Cambridge, MA) set at 12 breaths per minute. A tidal volume of 12 to 15 ml/kg body weight was measured at the airway with a Wright respirometer. An F_IO_2 was maintained between 0.45 and 0.55 throughout the experiment. Additional increments of sodium pentobarbital and pancuronium bromide were used as necessary to maintain light anaesthesia and muscle paralysis. The dogs were placed in the prone position with the head elevated 5 to 7 cm above the trunk.

0342-4642/81/0007/0187/$01.00

A catheter was threaded via the femoral artery into the descending aorta for blood sampling and for systemic blood pressure (SBP) monitoring. For monitoring CVP, another catheter was introduced through the external jugular vein into the superior vena cava or right atrium. The lowest deflection recorded on the polygraph records was taken as the CVP, since the higher, or "systolic" values depend on the exact catheter position. Lactated Ringer's solution (5 ml/kg/h) was infused into a forelimb vein. Core body temperature (T) was recorded continuously from a thermistor probe placed in the oesophagus at heart level. Airway pressure (Paw) and vascular pressures were measured with pressure transducers (Model P23D6, Statham Instruments Inc., Oxnard, CA). A 22-gauge spinal needle was introduced into the cisterna magna and zeroed to the level of the base of the skull for monitoring cerebrospinal fluid pressure (Pcsf). All pressures were recorded continuously on a Grass Model 5 polygraph.

A skin and temporal muscle flap was elevated over the cranium on one side and a burr-hole was drilled into the cranial bone. After haemostasis was achieved, a latex rubber balloon (Foregger mountable soft-cuff, Allentown, PA) was introduced carefully between the cranial bone and the dura. The bone defect was then covered with a layer of methyl methacrylate and was allowed to set and seal, leaving the catheter of the intracranial balloon outside the cranium for inflation later in the experiment.

Experimental Procedure

In each animal PEEP was incorporated into the ventilatory circuit (Emerson PEEP valve, J. H. Emerson Co., Cambridge, MA) and raised to 15 cm H_2O in increments of 5 cm H_2O, as confirmed by the recording of Paw. After each raising of PEEP, 15 min were allowed to achieve a steady-state ICP plateau at which time SBP, CVP, Pcsf, Paw and T were recorded and arterial blood samples obtained. Blood gas tensions and pH measurements were immediately performed (Blood gas analyzer Modell 113, Instrumentation Laboratory Inc., Lexington, MA) and were corrected for the animal's temperature.

End-expiratory pressure was then returned to zero. After allowing about 15 min to return to steady state conditions, ICP was elevated gradually by inflating the intracranial balloon with air. Initially small (0.5 – 1 ml) increments of air injected into the balloon resulted in a sharp rise in ICP that very rapidly returned towards baseline. With each additional introduction of air, however, the rate of fall of ICP decreased, and the previous baseline was never reached. This procedure of gradually elevating ICP was continued until ICP reached 40 to 50 cm H_2O and remained at a steady state level for at least 5 to 10 min. Once steady state elevated ICP was achieved, the entire procedure of obtaining PEEP/ICP response curves was carried out exactly as described for normal ICP.

Student's t test was applied for statistical significance between groups.

Results

The effect of incremental raising of PEEP in five dogs with normal and elevated ICP on SBP, CVP, Paw, Pcsf and $PaCO_2$ are shown in Table 1 and Figs. 1 and 2. Neither systolic nor diastolic SBP changed significantly with changes in EEP. Central venous pressure rose by the incremental elevation of PEEP in each dog during both normal and elevated ICP, although the rise in CVP was always smaller in magnitude than that induced in EEP. The relationships between EEP and CVP are described by the following equations:

$CVP = -3.44 + 0.27$ EEP for normal ICP, and $CVP = 2.90 + 0.53$ EEP for elevated ICP. The difference in the slopes of these lines was statistically significant ($p < 0.02$).

The elevation of EEP caused a rise in Pcsf at normal and elevated ICP (Fig. 2). The rise in Pcsf when PEEP was applied at elevated ICP's was larger with each step augmentation of PEEP than in the normal ICP stage of the experiment ($p < 0.001$). Each elevation of PEEP of 5 cm H_2O brought about a mean increase in Pcsf of about 10 cm H_2O, which was at least twice as large as that occurring when the dogs had normal ICP's. The equation for these relationships are as follows: $Pcsf = 12.95 + 0.82$ EEP for normal ICP, and $Pcsf = 46.41 + 2.06$ EEP for elevated ICP. The difference in the slopes of these lines is also significant ($p < 0.001$).

The $PaCO_2$ response to elevation of PEEP was often unpredictable. Some dogs exhibited no significant rise in $PaCO_2$ during elevation of EEP, while others showed $PaCO_2$ increases to as high as 60 torr during CMV when PEEP equaled 15 cm H_2O. Mean $PaCO_2$'s were 39.7 and 34.2 torr at normal and elevated ICP's, respectively, before PEEP was applied. The mean rises in $PaCO_2$ were larger during elevation of EEP at elevated ICP as compared with those occurring when ICP was low. Because of the divergent $PaCO_2$ response to EEP in individual dogs, the increase in mean $PaCO_2$'s was not statistically significant except in animals with elevated ICP when PEEP was raised from 0 to 15 cm H_2O ($p < 0.05$) (Table 1).

Table 1. Effect of increasing end-expiratory pressure on systemic blood pressure, central venous pressure, airway pressure, cerebrospinal fluid pressure and arterial CO_2 tension in dogs with both normal and elevated intracranial pressure

	SBP systolic (torr)	SBP diastolic (torr)	CVP (cm H_2O)	Paw inspiration (cm H_2O)	Paw expiration (cm H_2O)	Pcsf (cm H_2O)	$PaCO_2$ (torr)
Normal ICP							
ZEEP	173 ± 5.0[+]	123.4 ± 4.6	−1.2 ± 0.7	11.2 ± 0.7	0.7 ± 0.2	10.9 ± 0.9	39.7 ± 2.5
PEEP (5 cm H_2O)	179 ± 5.4	128 ± 4.2	0.4 ± 1.0	16.8 ± 0.6	5	13.8 ± 1.5	37.5 ± 2.6
	N.S.[#]	N.S.	N.S.	****		N.S.	N.S.
PEEP (10 cm H_2O)	182 ± 4.9	130 ± 3.7	2.3 ± 1.0	23.3 ± 1.2	10	16.9 ± 1.5	42.9 ± 4.1
	N.S.	N.S.	*	****		*	N.S.
PEEP (15 cm H_2O)	175 ± 6.1	126 ± 7.1	4.0 ± 1.4	30.3 ± 1.7	15	22.0 ± 2.5	47.6 ± 5.0
	N.S.	N.S.	*	****		***	N.S.
Elevated ICP							
ZEEP	177 ± 2.0	122 ± 3.7	−0.4 ± 0.9	11.2 ± 2.0	0.1 ± 0.2	43.8 ± 1.3	34.2 ± 2.2
PEEP (5 cm H_2O)	181 ± 6.2	124 ± 3.7	1.5 ± 1.4	15.3 ± 0.9	5	53.8 ± 2.4	37.9 ± 2.9
	N.S.	N.S.	N.S.	****		**	N.S.
PEEP (10 cm H_2O)	183 ± 6.4	124 ± 3.2	3.3 ± 1.6	23.4 ± 0.9	10	64.0 ± 4.8	42.7 ± 4.0
	N.S.	N.S.	N.S.	****		****	N.S.
PEEP (15 cm H_2O)	179 ± 8.9	116 ± 6.2	7.8 ± 2.1	31.2 ± 1.2	15	74.8 ± 4.8	50.9 ± 5.3
	N.S.	N.S.	**	****		****	*

[+] = ± SEM

[#] = levels of statistical significance refer to the comparison in each case to the corresponding mean values at ZEEP

N.S. = not significant; * = $p < 0.05$ ** = $p < 0.01$ *** = $p < 0.005$ **** = $p < 0.001$

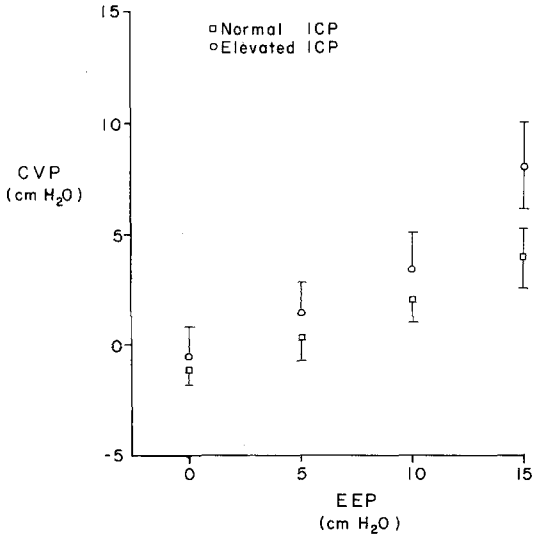

Fig. 1. The effect on CVP (mean ± SEM) of raising EEP from 0 to 15 cm H_2O at normal and elevated ICP

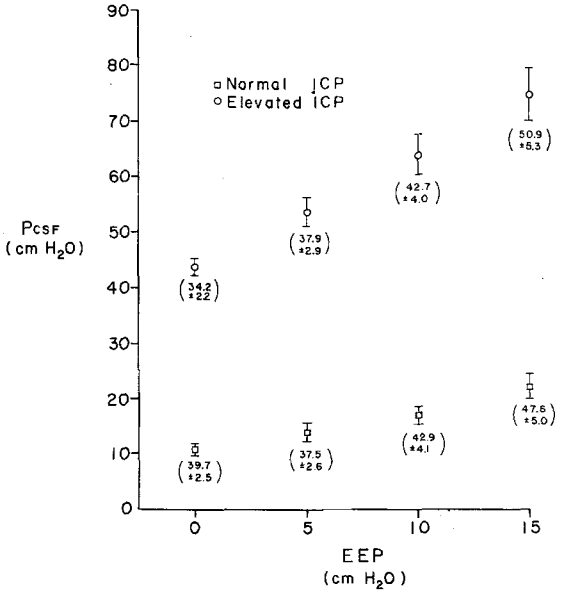

Fig. 2. The effect on Pcsf of raising EEP from 0 to 15 cm H_2O at normal and elevated ICP. The corresponding mean values (± SEM) for $PaCO_2$ (torr) are in parentheses

Mean PaO_2 values during all our measurements ranged between 243 ± 8.2 (SEM) and 264 ± 3.5 torr at normal ICP, and between 247 ± 10.6 and 258 ± 3.9 torr at elevated ICP. None of the changes in PaO_2 during administration of PEEP or during elevation of ICP were statistically significant.

Discussion

Previous experimental data reported by Aidinis, Lafferty and Shapiro [1] indicated variable responses of ICP to the raising of EEP in cats. Their findings depended to some extent on the initial ICP prior to

the institution of PEEP. Additionally, in their experimental model SBP often fell with the elevation of EEP, associated with a fall in ICP while EEP was raised. Huseby et al. [10] demonstrated in dogs that the degree of rise in ICP due to the introduction of PEEP is dependent on pulmonary compliance.

The results of our experiment indicate that the use of PEEP of up to 15 cm H_2O combined with CMV results in an increase in ICP in dogs. There was a consistent rise in CVP, but it was never as large as the initiating elevation of PEEP. Similarly, the rise in ICP was smaller than the amount of PEEP applied, as long as ICP was within normal ranges. At elevated initial ICP's, however, any additional rise in ICP because of PEEP was about twice as large as the amount of PEEP applied.

The consistency of the PEEP effect on ICP might be attributed primarily to the stability of SBP associated with elevation of EEP in our experimental model, although cerebro-vascular autoregulation may have been impaired after the acute introduction of the intracranial mass by balloon inflation [2, 15]. Stability of SBP probably prevented alterations in cerebral blood flow and volume, even if autoregulation was lost, and thus allowed the demonstration of the expected rise in ICP whenever EEP was raised. This consistent trend was not found in the experiments of Aidinis and his colleagues [1], where hypotension often accompanied the introduction of PEEP. Hypotension superimposed on loss of autoregulation in their experiments would account for their observing an occasional fall in ICP during elevation of EEP. Probably because SBP remained stable during our experiments, we never observed the rises in ICP associated with the removal of PEEP, which occurred in their studies.

A larger increase in CVP occurred when PEEP was raised from 10 to 15 cm H_2O at elevated ICP's than when ICP was normal. This may be attributed to pulmonary venous constriction secondary to acute elevation of ICP [16] although no other evidence of the development of neurogenic pulmonary oedema [14, 20] such as decreasing arterial oxygenation or elevated peak inspiratory pressure (consistent with decreased pulmonary compliance) could be demonstrated.

The effect of PEEP on raising ICP was found to be greater when ICP was elevated as compared to when it was normal. These findings are in agreement with the type II response of Aidinis et al. [1] and with similar findings in man reported by Apuzzo and his associates [3]. Presumably, when the initial ICP was 40 to 50 cm H_2O, intracerebral compliance was reduced significantly, so that each incremental elevation in intracerebral volume resulted in larger

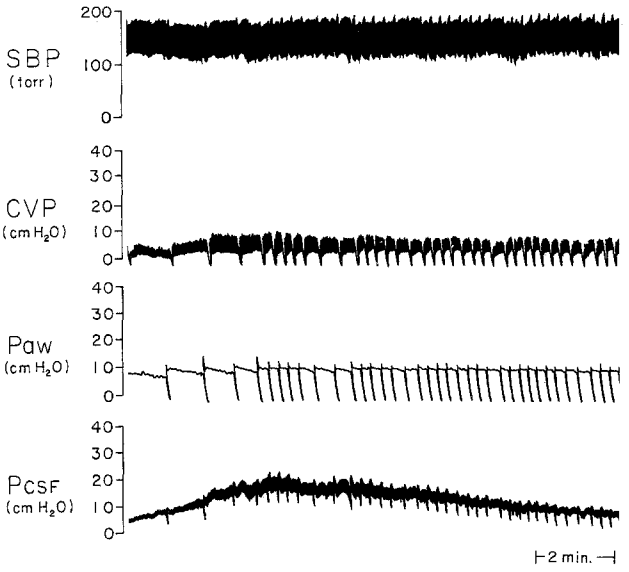

Fig. 3. Polygraph record from a pilot study in a spontaneously breathing dog. See text for discussion

increases in ICP [18]. An additional explanation that may explain, in part at least, the larger rise in ICP with the institution of PEEP when ICP is elevated, is the more pronounced effect of PEEP on CVP under these circumstances (Table 1 and Fig. 1).

Positive end-expiratory pressure may elevate ICP by raising intrathoracic pressure [8], thus impeding venous return to the heart and elevating cerebral venous pressure and blood volume. Indirectly, PEEP combined with CMV may also elevate cerebral blood volume due to an associated rise in $PaCO_2$ as it occurred in our experiments.

Pilot experiments which were carried out prior to establishing the protocol of this report indicated that PEEP increases ICP through its mechanical effects on cerebral venous drainage, as well as by occasionally raising $PaCO_2$, and that both these mechanisms may work simultaneously. Figure 3 illustrates the polygraph record from a spontaneously breathing dog in whom PEEP was raised from 5 to 10 cm H_2O. The dog became apnoeic for over one minute, at which time ICP rose significantly. The resumption of spontaneous respiration, and presumably the return of $PaCO_2$ towards control, were associated with a fall in ICP towards the initial level, which it never reached, while EEP was kept elevated and unchanged. The combined direct and indirect effects of PEEP on ICP are probably demonstrated in this experimental record. Figure 4 is taken from the record of another pilot study during a time in which ICP was high because the intracranial balloon was inflated. Mechanical breathing kept alveolar ventilation constant. Occasional, free, unobstructed, spontaneous

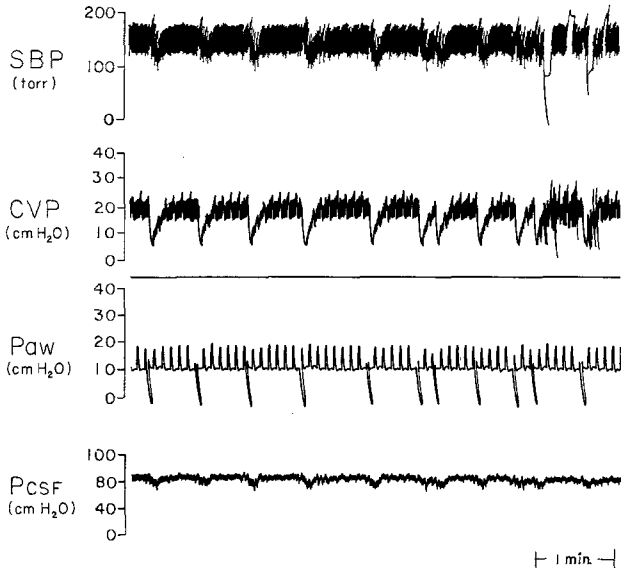

Fig. 4. Polygraph record from a pilot study in a mechanically ventilated dog in whom ICP was elevated by inflating an intracerebral balloon. A few spontaneous breaths are seen as decreases in Paw. See text for discussion

breaths were accompanied by small but definite declines in ICP, indicating direct effects of airway pressure on ICP. The data obtained from our experiments does not allow evaluation of the relative contributions of the increased airway pressure and the rise in $PaCO_2$ to the elevation of Pcsf.

Our experimental results substantiate the studies reported in man by Apuzzo and his collaborators [3] and the case described by James et al. [11], and should alert the clinician to the complications that may occasionally be associated with the use of PEEP and CMV in patients with increased intracranial pressure. They are inconsistent with those of Frost [9] who could not demonstrate significant increases in ICP with CMV and PEEP in traumatized patients, some of whom had decreased intracerebral compliance. When PEEP is indicated in the treatment of patients with elevated intracranial pressure, its use ought to be guided by the monitoring of intracranial pressure whenever possible. Additionally, even small rises in $PaCO_2$ may be extremely hazardous under these circumstances.

It should be emphasized that our study combined the use of PEEP with CMV. The use of PEEP with spontaneous respiration is known to raise mean intrapleural pressure less than CMV and PEEP [8]. It may be assumed, therefore, that the effect of PEEP on ICP may be less when used with spontaneous respiration or intermittent mandatory ventilation (IMV) [7] under circumstances of elevated ICP as long as $PaCO_2$ remains unchanged.

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