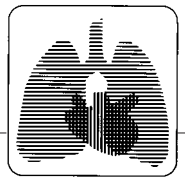

reviews

Hyperventilation in Head Injury*

A Review

Nino Stocchetti, MD; Andrew I.R. Maas, MD, PhD; Arturo Chieregato, MD; and Anton A. van der Plas, MD

The aim of this review was to consider the effects of induced hypocapnia both on systemic physiology and on the physiology of the intracranial system. Hyperventilation lowers intracranial pressure (ICP) by the induction of cerebral vasoconstriction with a subsequent decrease in cerebral blood volume. The downside of hyperventilation, however, is that cerebral vasoconstriction may decrease cerebral blood flow to ischemic levels. Considering the risk-benefit relation, it would appear to be clear that hyperventilation should only be considered in patients with raised ICP, in a tailored way and under specific monitoring. Controversy exists, for instance, on specific indications, timing, depth of hypocapnia, and duration. This review has specific reference to traumatic brain injury, and is based on an extensive evaluation of the literature and on expert opinion. ***(CHEST 2005; 127:1812–1827)***

Key words: cerebral ischemia; hyperventilation; intracranial pressure; traumatic brain injury

Abbreviations: $AVDO_2$ = cerebral arteriovenous difference of oxygen content; CBF = cerebral blood flow; $CMRO_2$ = cerebral metabolic rate of oxygen; CPP = cerebral perfusion pressure; CSF = cerebrospinal fluid; DPG = diphosphoglycerate; ICP = intracranial pressure; ITP = intrathoracic pressure; LV = left ventricle, ventricular; NO = nitric oxide; $Pbro_2$ = brain tissue oxygen tension; PET = positron emission tomography; RV = right ventricle, ventricular; SjO_2 = jugular bulb oxygen saturation; TBI = traumatic brain injury

Modulation of $Paco_2$ has been used for >40 years,[1] first in neuroanesthesia and subsequently also in neuro-intensive care. Preliminary work has shown that the volume of the swollen brain could be decreased by lowering $Paco_2$. With the realization that raised intracranial pressure (ICP) is a significant, treatable problem in patients with traumatic brain injury (TBI), hyperventilation became a cornerstone in the management of TBI and has remained so for decades. Hyperventilation lowers ICP by the induction of cerebral vasoconstriction with a subsequent decrease in cerebral blood volume.[2] The downside of hyperventilation, however, is that cerebral vasoconstriction may decrease cerebral blood flow (CBF) to ischemic levels. Already in 1942, a slowing of the EEG was observed during active hyperventilation and was interpreted as a sign of cerebral ischemia, thus illustrating the potentially harmful effects of hypocapnia.[3] Over the past decade, relatively more attention has been paid to the adverse effects of hyperventilation and concern seems to exceed enthusiasm. This change in attitude would appear more emotional than data-driven and reflects the lack of conclusive data.

The aim of this review was to consider the effects of induced hypocapnia both on systemic physiology and on the physiology of the intracranial system, with specific reference to TBI. We chose to focus this review on TBI, as much of the research on hyperventilation has been conducted in this field and less information exists on other acute cerebral disorders, such as aneurysmal subarachnoid hemorrhage or

*From the Neuroscience ICU (Drs. Stocchetti and Chieregato), Ospedale Maggiore Policlinico, Milan University, IRCCS, Milan; Department of Intensive Care Medicine (Dr. Chieregato), Ospedale Bufalini, Cesna, Italy; the Departments of Neurosurgery (Dr. Maas) and Intensive Care Medicine (Dr. van der Plas), Erasmus Medical Center, Rotterdam, the Netherlands.

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Correspondence to: Nino Stocchetti, MD, Terapia Intensiva Neuroscienze, Padiglione Beretta Neuro, Ospedale Maggiore Policlinico, Via F. Sforza 35, 20122 Milan, Italy; e-mail stocchet@policlinico.mi.it

stroke. This review is based on an extensive evaluation of the literature, and to this purpose we selected relevant experimental and clinical articles on hyperventilation from among > 5,000 citations found on MEDLINE since 1966. We have indicated explicitly in the text when expert opinion is being expressed rather than available evidence being quoted.

Definition of Hyperventilation

A remarkable confusion exists on terminology. What is usually referred to as hyperventilation is, in fact, hypocapnia. Since a reduction of $Paco_2$ below the normal level (40 mm Hg) is obtained by increasing the alveolar ventilation, hyperventilation became synonymous with hypocapnia. In this review, we will use the less precise (but much more common) term *hyperventilation*. Hyperventilation may be defined as "the induction and/or maintenance of levels of CO_2 tension in the arterial blood below the normal range." In this sense, normal levels of $Paco_2$ should be corrected for barometric pressure at different altitudes.

Pathophysiology

CBF Regulation and CO_2 Reactivity

The CNS, accounting for 2% of body weight (average weight of the brain, 1,300 to 1,500 g), has a high energy requirement. The cerebral oxygen consumption is 3.5 mL per 100 g/min, which corresponds to 20% of total body oxygen consumption. Under normal conditions, CBF is maintained at a constant flow rate of 50 to 60 mL per 100 g/min, with 50 mL of oxygen being extracted every minute from 700 to 800 mL of blood (Table 1). The extraction rate for oxygen is high, and the mean arteriovenous difference of O_2 for the CNS is 6.3 mL per 100 mL of blood. CBF depends on the differential pressure between the arterial and the venous side of the cerebral circulation, and is inversely proportional to cerebral vascular resistance. Pressure on the venous side of the capillary bed cannot be measured, and ICP, which is extremely close to venous pressure, is used for estimating the cerebral perfusion pressure (CPP). CPP is calculated as the difference between mean arterial pressure and ICP.

Table 1—*Normal Values and Ischemia Thresholds for the Main Cerebral Variables

Variables	Normal Value	Threshold for Ischemia
Brain weight, g	1,300–1,500	
CBF	50–60 mL/100 g/min brain tissue	< 18 mL/100 g
OEF	30%	
$AVDO_2$	6.3 mL O_2/100 mL blood	> 9 mL O_2/100 ml blood
SjO_2, %	55–75	< 50
$Pbro_2$, mm Hg	> 20	15
ICP, mm Hg	≤ 10	
CPP, mm Hg	60	< 55–60

*OEF = oxygen extraction fraction.

Normal ICP values in adults are < 10 mm Hg, and a threshold of 20 mm Hg is usually accepted for starting active treatment. A CPP of 60 mm Hg is commonly accepted as the minimum value necessary for adequate cerebral perfusion.[4] Two important concepts are:

1. the Monro-Kellie doctrine; and
2. the volume-pressure curve.

The Monro-Kellie doctrine states that the total volume of the intracranial contents (*ie*, brain tissue, blood, and cerebrospinal fluid [CSF]) remains constant as these are contained within a rigid compartment (the skull), as follows:

$$V_C = V_{brain} + V_{blood} + V_{CSF}.$$

An increase in the volume of one of these compartments can initially be compensated for by the displacement of parts of the other components. Cerebral veins can be compressed, resulting in decreased cerebral blood volume, and the volume of the CSF compartment can decrease due to a combination of increased resorption and the displacement of CSF toward the spinal compartment. As volume increases, compensatory mechanisms are exhausted, and a further increase in volume results in a sharp rise of ICP, leading to the volume-pressure curve depicted in Figure 1.

The high metabolic demands of the brain in combination with the limited storage of substrates necessitate maintaining CBF levels within normal ranges. In physiologic circumstances, this is effected through a number of mechanisms, which are commonly referred to as *autoregulation*. CBF increases with vasodilatation and decreases with the constriction of cerebral arteriolae, termed *cerebral resistance vessels*. These vessels respond to changes in systemic BP (pressure autoregulation), blood viscosity (viscosity autoregulation), and metabolic demand, maintaining CBF levels within limits that are appropriate to meet metabolic demands. Pressure autoregulation is shown in Figure 2.

CBF is functionally coupled to the regional cerebral metabolism as expressed in the Fick equation $CMRO_2 = CBF \times AVDO_2$, in which $CMRO_2$ is the cerebral metabolic rate of oxygen and $AVDO_2$ is the