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EDITORIAL

Prehospital ventilation targets in severe traumatic brain injury

Theresa Mariero Olasveengen[1*] and Nino Stocchetti[2]

In closely monitored patients with severe traumatic brain injury (TBI) in intensive care, ventilation may be titrated to carefully balance the need for adequate cerebral perfusion while avoiding intracranial hypertension. In case of high intracranial pressure (ICP) a lower than normal arterial pCO_2, which causes cerebral vasoconstriction, might reduce ICP. This potentially beneficial effect, however, should be weighed against the risk of brain ischemia [1]. Fine tuning of pCO_2, and multimodal monitoring of brain perfusion are, therefore, recommended in guidelines [2] and expert consensus [3–5]. This is challenging in clinical practice, with recent reports from multicenter studies documenting considerable heterogeneity in arterial pCO_2 management [6].

What is difficult in specialized centers is, of course, unfeasible in the prehospital arena, where advanced neuromonitoring, or even sequential blood gas analyses are not available. Under that situation end-tidal CO_2 ($EtCO_2$) represents the best estimate and any attempt at individualizing treatment needs to be balanced against adding complexity in a time sensitive and resource limited setting.

In this issue of Intensive Care Medicine (ICM), Bossers and colleagues [7] give new insights into how severe trauma patients are actually ventilated by the Dutch Helicopter Emergency Medical Services. Their careful data collection under the constraints and pressures of emergency rescue on more than 1700 trauma patients is remarkable. Among them, more than 1300 cases have also been followed up to 30 days and one year after injury; mortality at this end-point was then included in elegant multivariable statistical models. Based on this 5-year long study the authors propose a safe zone of 35–45 mmHg $EtCO_2$ and warn that values lower than 35 mmHg were associated with a significantly increased mortality.

While this paper offers new information to the ICM readership, it has important limitations that should be kept in mind when interpreting the findings. The observational nature of the paper inherently brings with it substantial risk of bias: for instance, $EtCO_2$ values outside what is currently thought of as a "safe zone" might represent either a very sick patient or a less skilled team, independently predictive of poor outcome. As such, this paper can identify associations, as clearly stated in the title, but cannot conclude on causality. Therefore, it can't provide solid evidence on the safety limits for $EtCO_2$ for TBI patients in the prehospital setting.

On a more granular level, five aspects should be considered. First, the inclusion of patients with suspected, rather than confirmed TBI, detracts from the value of the research. Second, all case mortality is a problematic end-point for establishing a link between $EtCO_2$ and outcome. On one hand, TBI may cause significant disability and functional survival is, therefore, considered a much more appropriate outcome than mortality itself. On the other hand, an important proportion of the mortality observed in the TBI population is not directly related to the TBI itself, and will complicate the interpretation of any association. A patient may have a recoverable brain injury, but die due to sepsis or have care withdrawn due to overall frailty and co-morbidity. Third, the number of $EtCO_2$ data points collected in every single patient during the whole pre-hospital phase is limited, making a comprehensive description of CO_2 management difficult. In fact, the correlation between the pre-hospital findings and the first in-hospital blood gas analysis is very weak. Finally, patients have been ventilated not only during their prehospital care (for a limited time, we suppose in

*Correspondence: t.m.olasveengen@medisin.uio.no
[1] Department of Anesthesiology and Intensive Care, Institute of Clinical Medicine, Oslo University Hospital, University of Oslo, Oslo, Norway
Full author information is available at the end of the article

an efficient helicopter service in a relatively narrow country) but also during their acute phase in the intensive care unit (ICU), which usually takes days or weeks. The brain remains vulnerable during this critical phase, which requires a tailored ventilation. We have no information on how arterial CO_2 has been managed during those days. Assuming that the pre-hospital values, collected for a short period of time, may be directly linked to mortality regardless what has been done in the following days raises a number of questions. Importantly, it is in contrast with a recent multicenter study analyzing more than 1000 TBI patients (6) ventilated in the ICU: this study didn't find an association between the risk of mortality or unfavorable functional outcome and more frequent use of profound hyperventilation ($PaCO_2 < 30$ mmHg).

To conclude, the authors present interesting associations between prehospital $EtCO_2$ levels and all-cause mortality, but these associations are not grounded on a completely adequate data set. And while the suggested "safe zones" for $EtCO_2$ levels during prehospital management of TBI are perfectly reasonable, they are not based on high certainty data.

Author details
[1] Department of Anesthesiology and Intensive Care, Institute of Clinical Medicine, Oslo University Hospital, University of Oslo, Oslo, Norway. [2] Fondazione IRCCS Cà Granda Ospedale Maggior Policlinico, Milan and Department of Physiopathology and Transplant, Milan University, Milan, Italy.

Data availability
This paper represents the views of the authors and does not include generated or reused research data, and as such there is no data to share.

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