Effects of acetazolamide on brain tissue oxygenation in ICU patients with Acute Brain Injury

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Introduction

Acetazolamide is a carbonic anhydrase inhibitor which determines the acidification of intracellular and extracellular environment of the central nervous system.

In consideration of the key role of pH in modulating **cerebral vascular tone**, acetazolamide contributes to the regulation of cerebral blood flow (CBF), intracranial pressure (ICP), and thus brain tissue oxygenation ($PbtO_2$), which are all factors potentially affected in conditions of decreased intracranial compliance.

Hence, the **aim** of the study was to evaluate the impact of acetazolamide on ICP, CBF and $PbtO_2$ in patients with acute brain injury (ABI).

Methods

Inclusion criteria: a) >18 years, b) admitted to ICU for ABI, c) mechanical ventilation in controlled modality, d) continuous monitoring of ICP and $PbtO_2$, e) baseline ICP < 20mmHg.

The **protocol** is represented in Fig.1.

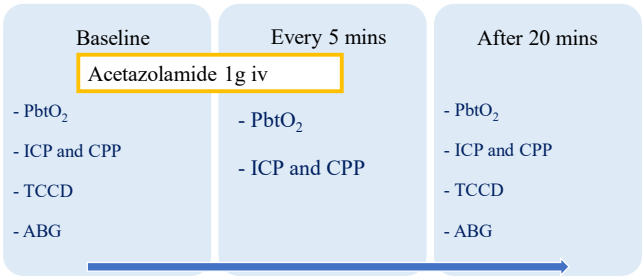


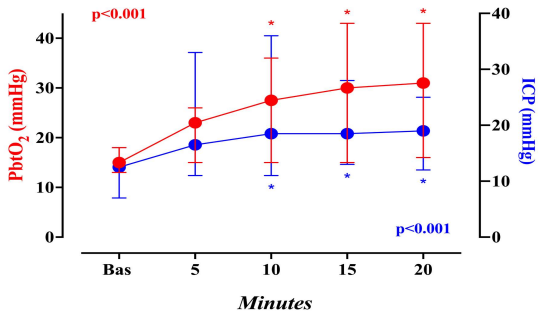
Fig.1. ABG: Arterial Blood Gas analysis; CPP: Cerebral Perfusion Pressure; ICP: Intracranial Pressure; PbtO2: brain tissue oxygenation; TCCD: Transcranial color-coded duplex .

Results and discussion

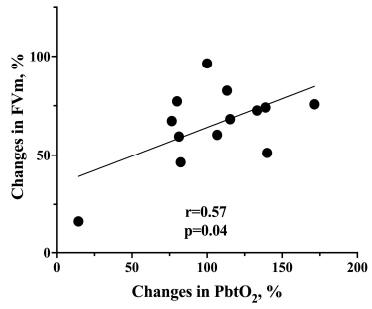
Among the 143 patients screened, **14** fulfilled the eligibility criteria (64% male, median age 44 [35-51] years). The admission diagnosis were: traumatic brain injury (**TBI**) (n=7, 50%), subarachnoid hemorrhage (**SAH**) (n=6, 43%) and intracranial hemorrhage (**ICH**) (n=1, 7%).

Non parametric Friedman's test showed that acetazolamide determined a **significant increase of both $PbtO_2$ and ICP** (p <0.001), which started from ten minutes after the injection and remained stable over the observation time (Fig.2, Tab.1). This is consistent with the hypothesis that acetazolamide increases $PbtO_2$ mainly through a mechanism of vasodilation, and thus CBF. Consequently to increased CBF, ICP could rise as well, yet in our population only 4 patients needed an adjustment of respiratory rate (+3 [2-3] breaths per minute) to maintain ICP < 25mmHg.

Both transcranial color-coded duplex (TCCD), with the detection of **incremented flow velocities** (FV) and **reduced Pulsatility Index (PI)** (Tab.1), and the **significant correlation between variation of mean FV (FVm) and of $PbtO_2$** (r=0.57, p=0.04) (Fig.3) confirmed that **acetazolamide causes a significant increase of CBF, and hence $PbtO_2$**.



▲ Fig.2
ICP: Intracranial Pressure;
PbtO2: brain tissue oxygenation.



◄ Fig.3
FVm: mean Flow Velocity;
PbtO2: brain tissue oxygenation

	Baseline	5 min	10 min	15 min	20 min	*p* value
$PbtO_2$ (mmHg)	15 [15-17]	23 [22-24]	28 [26-29]	30 [29-32]	31 [29-35]	<0.001
ICP (mmHg)	13 [10-14]	17 [15-18]	19 [17-21]	19 [17-24]	19 [16-21]	<0.001
CPP, (mmHg)	85 [81-91]	85 [78-88]	84 [76-87]	83 [79-89]	83 [81-87]	0.08
FVs (cm/s)	109 [98-125]	-	-	-	171 [157-183]	<0.001
FVd (cm/s)	51.00 [49-58]	-	-	-	100 [92-107]	<0.001
FVm (cm/s)	72 [67-78]	-	-	-	127 [116-130]	<0.001
PI	0.74 [0.69-0.89]	-	-	-	0.58 [0.51-0.69]	<0.001
pH	7.44 [7.43-7.45]	-	-	-	7.38 [7.37-7.41]	0.003
$PaCO_2$ (mmHg)	50 [49-55]	-	-	-	51 [48-57]	0.32
PaO_2 (mmHg)	110 [103-135]	-	-	-	119 [112-151]	0.02
Lactate, (mmol/L)	0.8 [0.7-0.9]	-	-	-	0.6 [0.5-0.7]	0.45
$PbtO_2/PaO_2$	0.14 [0.12-0.15]				0.26 [0.23-0.29]	<0.001

Tab.1
CPP: Cerebral Perfusion Pressure; FV: Flow Velocity (d: diastolic; m: mean; s: systolic); ICP: Ictracranial Pressure; PI: Pulsatility Index.

Conclusions

Among patients with ABI, the administration of intravenous acetazolamide determined a significant improvement of brain oxygenation along with increased ICP and FV at TCCD, indicative of cerebral vasodilation. These findings suggest that acetazolamide may serve as a valuable therapeutic option for enhancing brain oxygenation in this specific clinical context.

References

[1] Severinghaus JW, Cotev S. Carbonic acidosis and cerebral vasodilation after Diamox. Scand J Clin Lab Invest Suppl. 1968;102:I:E.
[2] Vorstrup S, Henriksen L, Paulson OB. Effect of acetazolamide on cerebral blood flow and cerebral metabolic rate for oxygen. J Clin Invest. 1984 Nov;74(5):1634-9
[3] Wolf ME. Functional TCD: regulation of cerebral hemodynamics--cerebral autoregulation, vasomotor reactivity, and neurovascular coupling. Front Neurol Neurosci. 2015;36:40-56.
[4] Zirak P, Delgado-Mederos R, Martí-Fàbregas J, Durduran T. Effects of acetazolamide on the micro- and macro-vascular cerebral hemodynamics: a diffuse optical and transcranial doppler ultrasound study. Biomed Opt Express. 2010 Nov 19;1(5):1443-1459.
[5] Kaminogo M, Ichikura A, Shibata S, Toba T, Yonekura M. Effect of acetazolamide on regional cerebral oxygen saturation and regional cerebral blood flow. Stroke. 1995 Dec;26(12):2358-60.