Intensive Care Med (2014) 40:919
DOI 10.1007/s00134-014-3297-5

Carl-Henrik Nordström
Troels Halfeld Nielsen

Exogenous lactate supplementation to the injured brain: misleading conclusions with clinical implications

Accepted: 7 April 2014
Published online: 1 May 2014

A reply to these comments can be found at doi:10.1007/s00134-014-3312-x.

Dear Editor,

In their study Bouzat et al. [1] conclude that following traumatic brain injury lactate may be used by the brain as a preferential energy substrate and that intravenous infusion of hypertonic sodium lactate had positive effects on cerebral energy metabolism and intracranial pressure (ICP). The biochemical conclusions are based on data obtained from microdialysis (MD) indicating that the therapy increased the intracerebral levels of glucose and pyruvate while glutamate and ICP decreased. The conclusions are partly misleading which may lead to inappropriate clinical decisions.

The lactate/pyruvate (LP) ratio obtained during MD reflects cytoplasmatic redox state which can be described according to the equation

$$[\text{Lactate}]/[\text{Pyruvate}] \times K_{\text{LDH}} = [\text{NADH}][\text{H}^+]/[\text{NAD}^+] \quad (1)$$

In this reaction NADH obtained in an earlier step of glycolysis (GAP → 1,3DPG) is oxidized to NAD^+ necessary for continued cytoplasmatic glycolysis. It is well documented that a net transport of lactate from plasma across the blood–brain barrier (BBB) to the cerebral compartments occurs when the plasma concentration exceeds the intracerebral level [2]. The ensuing increase in intracerebral lactate concentration will shift Eq. 1 towards a more reduced state which will limit glycolytic degradation of glucose [3]. The increase in cerebral glucose level described in the study is explained by this redox shift. However, the energy yield when glucose is completely metabolized to carbon dioxide and water is greater than that obtained from degradation of lactate. We question that lactate may be described as the "preferential" energy substrate and that the observed increase in cerebral glucose is interpreted as a positive effect on cerebral energy metabolism. If we regard increasing intracerebral glucose level as desirable, why not increase glucose delivery to the brain by increasing blood glucose level?

The observed increase in intracerebral pyruvate was also considered to be beneficial. The increase was most prominent in patients with elevated LP ratio (Fig. 5 [1]) "suggesting that metabolic conversion of lactate into pyruvate during sodium lactate therapy was more pronounced in patients who had a higher degree of cerebral energy demand". As in the present study the patients did not display low tissue PO_2 the elevated LP ratio was probably caused by mitochondrial dysfunction. During mitochondrial dysfunction an increase in pyruvate is regularly obtained [4] and can hardly be described as beneficial when augmented by the therapy given.

The decrease in glutamate did not reach statistical significance and the concentration given in the text and in the table is probably erroneous (approximately 1,000 times higher than expected). If we accept that the level should have been given in μmol/L instead of mmol/L then the reported change is in agreement with the spontaneous decrease often observed when no specific therapy is given.

We do not agree with the conclusion that increased levels of glucose and pyruvate during exogenous lactate supplementation may be interpreted as "improved brain energetics during the early phase of TBI". The significant decrease in ICP is explained by the fact that the BBB reflexion coefficient for sodium is 1.0 [5].

Conflicts of interest None to declare.

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C.-H. Nordström (✉) · T. H. Nielsen
Department of Neurosurgery, Institute of Clinical Science, Odense University Hospital, Odense, Denmark
e-mail: carl-henrik.nordstrom@med.lu.se
Tel.: +46-46-146974;
+46-46-705655785