Therapeutic Blood Glucose Control Effects Cerebral Glycolysis Following Traumatic Brain Injury

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Purpose

Energy crisis after traumatic brain injury (TBI) is associated with poor neurologic outcomes [1,2]. Managing glucose is a major concern in the critical care setting. Maintaining blood glucose levels within the range of 80-110 mg/dL (tight glycemic control) has been investigated for therapeutic benefits in intensive care unit patients but conflicting clinical outcome studies on tight glycemic control in TBI patients have generated controversy. The objective of this study is to determine the relationship between systemic glucose and metabolic pathway activity after TBI. We hypothesize that cerebral glucose is metabolized differently depending on plasma glucose levels and that lactate is increasingly metabolized when systemic glucose is low.

Methods

Our group has conducted a prospective within-patient and randomized crossover study on patients consented to two study days (day 1: post-injury hour 111±29, day 2: 148±24) at tight or loose (120-150 mg/dL) glycemic control. 7 severely injured TBI (age=45.4±16.3, 1 female) participated in C1 ^{13}C-labeled glucose infusion studies ([1-^{13}C]glucose) which was infused continuously for 3 hrs. Arterial and jugular venous plasma were collected simultaneously before infusion and 3 hrs post-infusion while cerebral microdialysate was collected hourly. Glucose and lactate concentrations (mM) and isotopic enrichments (%) in plasma were determined by quantitative ^{1}H and ^{13}C NMR spectroscopy; microdialysate by CMA600. Statistics were computed robustly and, considering that the following complex analysis is performed on a relatively small sample size, results are supported by mixed model analysis.

Results and discussion

Arterial plasma glucose concentrations were significantly lower under tight glycemic control. Lactate concentrations were significantly decreased in cerebral microdialysate and in jugular venous plasma and were trending toward significance in arterial plasma under tight glycemic control. Glucose metabolized through glycolysis produces C3 ^{13}C-labeled lactate ([3-^{13}C]lactate) when infusing [1-^{13}C]glucose and tight glycemic control leads to increased enrichment of [3-^{13}C]lactate compared to loose glycemic control 3 hrs post-infusion.

	Tight glycemic control	Loose glycemic control	p-value
Glucose (mM) – Arterial plasma	11.4±4.2	14.8±4.8	0.049
Lactate (mM) – Cerebral microdialysate	3.26±1.30	4.71±0.89	0.023
Lactate (mM) – Jugular venous plasma	1.59±0.56	2.58±0.81	0.015
Lactate (mM) – Arterial plasma	1.53±0.53	2.08±0.59	0.085
Lactate ^{13}C3 enrichment (%) – Jugular venous plasma	3.20±0.74	1.67±0.41	0.053

Conclusion

Increased enrichment of [3-^{13}C]lactate under tight glycemic control suggests increased cerebral glycolytic activity in this TBI population. Decreased jugular and cerebral concentrations of lactate under tight glycemic control suggest lactate generated through glycolysis is not simply a waste product but may be an important fuel source after TBI. Previously we have shown that tight glycemic control correlated with increased glucose uptake and increased cerebral metabolic crisis [3] which may be explained by increased glycolytic glucose metabolization in order to generate energy from lactate.

References

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