**Glucose and Lactate Concentrations in Cerebrospinal Fluid after Traumatic Brain Injury**

*Angels LOZANO1,2, MD, Federico FRANCHI1,3, MD, Ramon Joel SEASTRES 4, MD*

*Mauro ODDO5, MD, Olivier LHEUREUX1, MD, Rafael BADENES2, MD, PhD, Sabino SCOLLETTA3, MD, Jean-Louis VINCENT1, MD, PhD, Jacques CRETEUR1, MD, PhD, Fabio Silvio TACCONE1, MD, PhD*

*1Department of Intensive Care*

*Erasme University Hospital, Université Libre de Bruxelles*

*Route de Lennik, 808*

*1070, Brussels, Belgium*

*2Department of Anesthesia and Intensive Care*

*Hospital Clinic Universitari*

*Valencia, Spain*

*3Department of Anesthesia and Intensive Care*

*Università di Siena – Azienda Ospedaliera Universitaria Senese*

 *Siena, Italy*

*4Department of Intensive Care Medicine*

*The Royal Melbourne Hospital*

*300 Grattan Street, Parkville*

*Victoria, Australia 3050*

*5Department of Intensive Care Medicine*

*Centre Hospitalier Universitaire Vaudois (CHUV),*

*Lausanne University Hospital*

*Lausanne, Switzerland*

Corresponding author:

Pr. **Fabio Silvio TACCONE**, MD, PhD

Department of Intensive Care

Erasme Hospital

Université Libre de Bruxelles (ULB)

Route de Lennik, 808

1070 – Brussels (BELGIUM)

email: ftaccone@ulb.ac.be

tel: +322 555 5587

fax: +322 555 4698

**Supplemental Table 1.** Differences in blood and cerebrospinal fluid (CSF) data collected on the first day after placement of extra-ventricular drainage, according to the concomitant use of insulin therapy.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Insulin therapy****(n=46)** | **No insulin therapy****(n=10)** | **P Value** |
| **CSF-Glucose, mmol/L** | 4.9 [3.8-5.5] | 4.7 [3.7-5] | 0.078 |
| **CSF-Lactate, mmol/L** | 2.5 [1.9-4.2] | 2.9 [2.3-4.2] | 0.772 |
| **CSF-Glucose/Lactate ratio** | 1.51 [1.04-2.12] | 1.85 [1.09-2.35] | 0.433 |
| **Blood-Glucose, mmol/L** | 7.3 [6.5-9.1] | 7.3 [5.8-8.2] | 0.955 |
| **Blood-Lactate, mmol/L** | 1.2 [0.9-2.0] | 1.0 [0.8-1.9] | 0.792 |
| **Glucose CSF/Blood ratio** | 0.65 [0.47-0.72] | 0.60 [0.58-0.74] | 0.257 |
| **Lactate CSF/Blood ratio** | 2.06 [1.54-3.43] | 2.10 [1.45-3.30] | 0.250 |

**Supplemental Table 2.** Glucose and lactate concentrations in the cerebrospinal fluid (CSF) in all patients and in different subgroups over the 4 days after insertion of an extraventricular drain

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **Day 1** | **Day 2** | **Day 3** | **Day 4** |
| **CSF-Glucose, mmol/L** | **All patients (n=56)** | 4.8 [3.7-5.5] | 4.9 [4.2-5.3] | 4.6 [4.0-5.1] | 4.4 [3.8-5.0] |
|  | **Survivors (n=36)** | 4.9 [3.7-5.2] | 4.9 [4.4-5.3] | 4.6 [4.1-4.9] | 4.3 [4.0-5.0] |
|  | **Non-survivors (n=20)** | 4.8 [3.9-5.8] | 4.3 [3.9-5.4] | 4.8 [3.2-5.7] | 5.0 [3.3-5.1] |
|  | **Favorable outcome (n=23)** | 4.9 [3.7-5.2] | 4.9 [4.3-5.3] | 4.6 [4.1-4.9] | 4.4 [3.8-5.0] |
|  | **Unfavorable outcome (n=33)** | 4.8 [3.7-5.5] | 4.8 [4.2-5.3] | 4.6 [3.9-5.2] | 4.4 [3.7-5.0] |
| **CSF-Lactate, mEq/L** | **All patients (n=56)** | 2.8 [2.2-4.2] | 2.8 [2.2-3.5] | 2.7 [1.9-3.8] | 2.3 [1.7-3.4] |
|  | **Survivors (n=36)** | 2.3 [2.0-3.7] | 2.3 [2.1-3.1] | 2.3 [1.9-3.0] | 2.1 [1.6-2.8] |
|  | **Non-survivors (n=20)** | 4.1 [2.9-6.0] | 3.7 [2.8-5.1] | 3.7 [2.5-5.6] | 3.6 [2.7-5.6] |
|  | **Favorable outcome (n=23)** | 2.2 [1.8-2.6] | 2.3 [2.0-3.0] | 2.3 [1.9-2.9] | 2.1 [1.6-2.7] |
|  | **Unfavorable outcome (n=33)** | 3.8 [2.8-5.9] | 3.2 [2.3-4.0] | 3.2 [2.1-4.4] | 2.9 [2.0-4.7] |
| **CSF-Glucose/Lactate ratio** | **All patients (n=56)** | 1.56 [1.10-2.13] | 1.73 [1.29-2.24] | 1.63 [1.21-2.27] | 1.80 [1.08-2.35] |
|  | **Survivors (n=36)** | 1.94 [1.35-2.34] | 1.93 [1.65-2.39] | 1.88 [1.48-2.36] | 2.11 [1.66-2.46] |
|  | **Non-survivors (n=20)** | 1.03 [0.82-1.67] | 1.16 [0.85-1.80] | 1.22 [0.80-1.83] | 1.12 [0.77-1.64] |
|  | **Favorable outcome (n=23)** | 2.12 [1.53-2.58] | 2.12 [1.73-2.58] | 1.87 [1.49-2.54] | 2.11 [1.65-2.91] |
|  | **Unfavorable outcome (n=33)** | 1.12 [0.85-1.77] | 1.54 [0.96-1.98] | 1.44 [1.00-2.08] | 1.55 [0.93-2.19] |

**Supplemental Table 3.** Characteristics of the study population, according to low CSF glucose/lactate ratio (< 0.78) or high CSF lactate (> 3.0 mmol/L).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **CSF Glu/Lact ≤ 1.47 (n=24)** | **CSF Glu/Lact > 1.47 (n=32)** | **CSF Lactate < 3.0 mmol/L (n=30)** | **CSF Lactate** ≥**3.0 mmol/L (n=26)** |
| **Age, years** | 36 [24-64] | 44 [31-68] | 34 [25-50] | 41 [27-65] |
| **Male, n (%)** | 16 (67) | 24 (75) | 24 (80) | 16 (61) |
|  |  |  |  |  |
| **COMORBID DISEASES** |
| **Heart disease, n (%)** | 0 (0) | 4 (12) | 3 (10) | 1 (4) |
| **Hypertension, n (%)** | 4 (17) | 8 (25) | 5 (17) | 7 (27) |
| **Diabetes, n (%)** | 2 (8) | 3 (9) | 2 (7) | 3 (11) |
| **COPD/asthma, n (%)** | 0 (0) | 1 (3) | 0 (0) | 1 (4) |
| **Chronic renal disease, n (%)**  | 1 (4) | 1 (3) | 0 (0) | 2 (8) |
| **Liver cirrhosis, n (%)** | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| **Previous neurological disease, n (%)** | 1 (4) | 2 (6) | 2 (7) | 1 (4) |
|  |  |  |  |  |
| **TBI CHARACTERISTICS** |
| **Fall, n (%)** | 9 (37) | 20 (62) | 17 (57) | 12 (46) |
| **Traffic accident, n (%)** | 14 (58) | 11 (34) | 12 (40) | 13 (50) |
| **Others, n (%)** | 1 (4) | 1 (3) | 1 (3) | 1 (4) |
| **Hypotension before admission, n (%)** | 6 (25) | 3 (9) | 3 (10) | 6 (23) |
| **Hypoxemia before admission, n (%)** | 4 (17) | 4 (12) | 4 (13) | 4 (15) |
| **GCS on admission** | 4 [3-9]  | 7 [4-11] | 7 [4-10] | 4 [3-10] |
| **Pupils*** **Not reacting**
* **Only one reacting**
* **Both reacting**
 | 4 (17)19 (79)1 (4) | 6 (19)26 (81)0 (0) | 4 (13)26 (87)0 (0) | 6 (23)19 (73)1 (4) |
| **Marshall CT-scan score*** **I**
* **II**
* **III**
* **IV**
* **V**
* **VI**
 | 0 (0)2 (9)5 (21)5 (21)5 (21)7 (29) | 0 (0)2 (6)5 (16)7 (22)8 (25)10 (31) | 0 (0)2 (7)4 (13)6 (20)6 (20)9 (30) | 0 (0)2 (8)6 (23)6 (23)7 (27)8 (31) |
| **Intracranial hemorrhage on CT-scan, n (%)** | 20 (83) | 26 (81) | 25 (83) | 21 (81) |
| **Glucose on admission, mmol/L** | 8.7 [7.4-10.6] | 7.9 [6.7-10.1] | 7.9 [6.7-10.2] | 8.7 [7.2-10.1] |
| **Hemoglobin on admission, g/dL** | 10.6 [9.0-13.0] | 12.4 [9.7-14.4] | 12.4 [9.8-14.2] | 11.0 [8.7-13.1] |
| **ISS score** | 50 [36-57] | 41 [34-57] | 42 [36-57] | 46 [32-57] |
|  |  |  |  |  |
| **DURING ICU STAY** |
| **Enteral nutrition, n (%)** | 9 (37) | 8 (25) | 8 (27) | 9 (35) |
| **Parenteral nutrition, n (%)** | 15 (62) | 24 (75) | 22 (73) | 17 (65) |
| **Insulin therapy, n (%)**  | 21 (87) | 25 (78) | 24 (80) | 22 (85) |
| **Infections, n (%)** | 14 (36) | 25 (78) | 26 (87) | 13 (50) \* |
| **Ventriculitis, n (%)** | 3 (12) | 5 (16) | 6 (20) | 2 (8) |
| **Shock, n (%)** | 3 (12) | 2 (6) | 3 (10) | 2 (8) |
| **Hydrocephalus, n (%)** | 1 (4) | 2 (6) | 1 (3) | 2 (8) |
| **Intracranial hypertension, n (%)** | 17 (71) | 22 (69) | 21 (70) | 18 (69)  |
| **Seizures, n (%)** | 7 (29) | 11 (34) | 10 (33) | 8 (31) |
| **Hyponatremia, n (%)** | 9 (38) | 14 (44) | 13 (43) | 10 (38) |
| **Fever, n (%)** | 15 (62) | 28 (88) \* | 28 (93) | 15 (58) |
|  |  |  |  |  |
| **DATA ON DAY 1 AFTER EVD PLACEMENT** |
| **Body Temperature, C°** | 37.3 [35.1-37.9] | 37.2 [36.4-37-9]  | 37.5 [36.7-38.0] | 37.0 [34.6-37.7] |
| **Mean arterial pressure, mmHg** | 94 [79-103] | 98 [89-109] | 96 [87-106] | 95 [82-105] \* |
| **Intracranial pressure, mmHg** | 14 [9-20] | 13 [9-20] | 13 [9-19]  | 14 [8-21] |
| **Cerebral perfusion pressure, mmHg** | 75 [64-93] | 81 [72-97] | 79 [70-97] | 78 [67-96] |
| **CSF-Red blood cells, n/μl** | 100 [57-159] | 109 [57-208] | 100 [62-213] | 110 [47-150] |
| **CSF-White blood cells, n/μl** | 25 [12-45] | 36 [18-55] | 33 [15-54] | 26 [16-46] |
| **CSF-Proteins, mg/dl** | 86 [42-219] | 42 [12-67] \* | 42 [12-66] | 83 [37-233] \* |
| **CSF-Glucose, mmol/L** | 4.7 [3.4-5.3] | 4.9 [4.0-5.5] | 4.7 [3.6-5.3] | 4.9 [4.1-5.7] |
| **CSF-Lactate, mmol/L** | 4.6 [3.8-6.1] | 2.3 [2.0-2.6] \* | - | - |
| **CSF-Glucose/Lactate ratio** | - | - | 2.1 [1.8-2.5] | 1.1 [0.8-1.4] |
| **Blood-Glucose, mmol/L** | 7.7 [6.5-9.2] | 7.3 [6.4-8.9] | 7.4 [6.3-8.8] | 7.5 [6.5-9.1] |
| **Blood-Lactate, mmol/L** | 1.6 [0.9-3.3] | 1.0 [0.8-1.4] \* | 1.0 [0.8-1.4] | 1.6 [1.1-3.3] \* |
| **Glucose CSF/Blood ratio** | 0.6 [0.5-0.7] | 0.6 [0.5-0.8] | 0.6 [0.5-0.7] | 0.6 [0.5-0.7] |
| **Lactate CSF/Blood ratio** | 2.5 [1.7-3.9]  | 1.9 [1.5-2.9] \* | 1.9 [1.4-3.0] | 2.6 [1.6-3.9] \* |

COPD = chronic obstructive pulmonary disease; EVD = external ventricular drain; GCS = Glasgow coma scale; CT = computed tomography; ISS = injury severity score; ICU = Intensive Care Unit.

\* p < 0.05 for CSF Glu/Lact ≤ 1.47 vs. CSF Glu/Lact > 1.47 or CSF Lactate < 3.0 mmol/L vs. CSF Lactate ≥3.0 mmol/L (univariate analysis)