High positive fluid balance could be harmful for the brain in shock patients

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Brain dysfunction in the ICU

Up to 70% of ICU patients and multifactorial

Hypotension

Hypoxia

Excessive brain inflammation

Harmful excessive stress hormones release (cortisol)

Aging with previous brain degenerative disorders

Sedatives and anesthesia administration

Sonneville R et al. Ann Intensive Care 2013
Background

• Although vital for resuscitation does fluid administration have any harmful effect on the brain?

• High positive fluid balance is harmful and aggravates ICU mortality.
  
  Maccagan BA et al. World J Crit Care 2015; 4: 116-129

• Aggravation acute lung injury and deteriorates kidney function.
  
  Wiedermann HP et al. NEJM 2006; 354: 2564-2575
  Texeira C et al. Crit Care 2013; 17: R14

• Negative fluid balance is associated with worse outcome after traumatic brain injury.
  

• Positive fluid balance can aggravates cognitive dysfunction and delirium in surgical patients.
  

• Positive fluid balance likely do not influence ICP and CPP in sepsis
  
Aim of the study

Investigate if high positive fluid balance was associated with brain dysfunction (coma, stroke, and delirium) in shock patients.
Inclusion following standard criteria and within 24 hours after ICU admission

190 patients in shock

104 Medical
86 Surgical

86 Septic shock
80 Cardiogenic shock
24 Hemorrhagic shock
Exclusion criteria

- Age < 18
- Pregnancy
- Advanced malignancy
- Non-survivors in the first five days in the ICU
- Cardiorespiratory arrest
- Post-neurosurgical patients
- Primary brain disorders: meningitis, trauma, bleeding, stroke
- Dementia, disabled neuromuscular or severe psychiatric disorders
- Liver cirrhosis
- Terminal kidney failure
- Non operable cardiac valvulopathy or coronary disease
- Polytrauma
- Congenital bleeding disorders
Fluid administration

• Cristalloids and colloids
• Correction of hypotension and restore urine output
• Daily fluid intake: sum of all IV and oral fluids
• Daily fluid output: urine output, ultrafiltration fluid, drain fluid, gastrointestinal losses
• Daily fluid balance: difference between fluid intake and output
• Investigate the impact of positive fluid balance in the first 5 days after ICU admission on the development of brain dysfunction
Brain dysfunction assessment

- Glasgow Coma Scale < 13 at admission
- Richmond Agitation Sedation Scale (RASS) score
- Confusion Assessment Method in the ICU (CAM-ICU)

_Ely W et al. JAMA 2004; 14: 1753-1762_

24 hours after sedation withdrawal
- Delirium if RASS > -3 and CAM-ICU positive for at least 2 consecutive days
- Coma if RASS ≤ -4 or throughout ICU stay
- Stroke was confirmed by brain CT scanner

- Measurement of S100B protein (biomarker of brain injury) during the first three days after ICU admission (N < 0.105 µg/L).

SERUM OR CSF BIOMARKER OF BRAIN INJURY

S100B
CSF/serum = 18

Brain and CSF

S100B NSE GFAP

Serum

BBB
S100B protein

BRAIN

Stress inflammation
With transient BBB
leakage

Injury
cell death

Serum

Transient
S100B
elevation

Prolonged
S100B
elevation

Blood-brain-
barrier

Nash DL et al. Neurocrit Care 8: 301-307
Results

190 patients in shock

No brain dysfunction
n= 57 (30%)

Brain dysfunction
n= 133 (70%)

Coma: 28 (20%)
Stroke: 8 (2%)
Delirium: 117 (78%)

Brain CT 66 (50%):
Normal 22 (38%)
Ischemia 18 (31%)
Atrophy 17 (29%)
Bleeding 1 (2%)

Hypoactive delirium: 50 (26%)
Hyperactive delirium: 53 (28%)
Mixte delirium: 13 (7%)
## Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No brain dysfunction n= 57 (30%)</th>
<th>Brain dysfunction n= 133 (70%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years</strong></td>
<td>62 ± 12</td>
<td>70 ± 15</td>
<td>0.013</td>
</tr>
<tr>
<td><strong>Gender M/F, n (%)</strong></td>
<td>39/18 (68/32)</td>
<td>89/44 (67/34)</td>
<td>0.841</td>
</tr>
<tr>
<td><strong>Septic/non-septic, n (%)</strong></td>
<td>25/32 (44/56)</td>
<td>61/72 (46/71)</td>
<td>0.799</td>
</tr>
<tr>
<td><strong>Medical/surgical, n (%)</strong></td>
<td>27/30 (47/53)</td>
<td>59/74 (44/56)</td>
<td>0.703</td>
</tr>
<tr>
<td><strong>AHT, n (%)</strong></td>
<td>29 (51)</td>
<td>79 (59)</td>
<td>0.277</td>
</tr>
<tr>
<td><strong>COPD, n (%)</strong></td>
<td>14 (25)</td>
<td>43 (32)</td>
<td>0.284</td>
</tr>
<tr>
<td><strong>Sepsis history, n (%)</strong></td>
<td>14 (25)</td>
<td>28 (21)</td>
<td>0.593</td>
</tr>
<tr>
<td><strong>Neurological history, n (%)</strong></td>
<td>9 (16)</td>
<td>37 (28)</td>
<td>0.076</td>
</tr>
<tr>
<td><strong>APACHE III</strong></td>
<td>72 ± 34</td>
<td>79 ± 31</td>
<td>0.189</td>
</tr>
<tr>
<td><strong>SOFA admission</strong></td>
<td>7 ± 3</td>
<td>7 ± 3</td>
<td>0.368</td>
</tr>
<tr>
<td><strong>GCS admission</strong></td>
<td>13 ± 3</td>
<td>12 ± 4</td>
<td>0.045</td>
</tr>
</tbody>
</table>
## ICU EVOLUTION

<table>
<thead>
<tr>
<th></th>
<th>No brain dysfunction n= 57 (30%)</th>
<th>Brain dysfunction n= 133 (70%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AKI, n (%)</td>
<td>18 (32)</td>
<td>43 (33)</td>
<td>0.893</td>
</tr>
<tr>
<td>ARDS, n (%)</td>
<td>10 (18)</td>
<td>21 (16)</td>
<td>0.764</td>
</tr>
<tr>
<td>Surinfections, n (%)</td>
<td>21 (37)</td>
<td>73 (55)</td>
<td><strong>0.022</strong></td>
</tr>
<tr>
<td>MV length, days</td>
<td>9 ± 6</td>
<td>13 ± 11</td>
<td><strong>0.007</strong></td>
</tr>
<tr>
<td>Sedation length, days</td>
<td>7 ± 1</td>
<td>8 ± 1</td>
<td>0.08</td>
</tr>
<tr>
<td>Midazolam (mg/h)</td>
<td>3 ± 3</td>
<td>3 ± 3</td>
<td>0.292</td>
</tr>
<tr>
<td>Fentanyl (mg/h)</td>
<td>1.45 ± 1.77</td>
<td>1.53 ± 1.34</td>
<td>0.722</td>
</tr>
<tr>
<td>Propofol (ml/h)</td>
<td>4 ± 3</td>
<td>3 ± 3</td>
<td>0.728</td>
</tr>
<tr>
<td>Ramifentanil (µg/kg/h)</td>
<td>0.06 ± 0.03</td>
<td>0.07 ± 0.03</td>
<td>0.668</td>
</tr>
<tr>
<td>ICU stay, days</td>
<td>14 ± 13</td>
<td>19 ± 14</td>
<td><strong>0.021</strong></td>
</tr>
<tr>
<td>ICU mortality, n (%)</td>
<td>15 (26)</td>
<td>55 (41)</td>
<td><strong>0.040</strong></td>
</tr>
<tr>
<td>In-hospital mortality, n (%)</td>
<td>1 (3)</td>
<td>11 (16)</td>
<td><strong>0.038</strong></td>
</tr>
</tbody>
</table>
RESULTS

S100B protein values (µg/L) over the first three days

$p = 0.012$
Fluid balance (ml) over the first five days

p = 0.023
SOFA score without the Glasgow Coma Scale over the first five days

\[ p < 0.01 \]
Episodes of mean blood pressure < 60mm Hg

p < 0.01
Cardiovascular SOFA score over the first five days

\[ p < 0.01 \]
Respiratory SOFA score over the first five days
Minimal PaO2 values (mm Hg) over the first five days
CRP values (mg/L) over the first five days

\[ p = 0.726 \]
# Logistic regression results

<table>
<thead>
<tr>
<th>Covariates</th>
<th>OR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOFA score admission</td>
<td>1.17</td>
<td>1.06, 1.32</td>
<td>0.004</td>
</tr>
<tr>
<td>Hypotension</td>
<td>1.41</td>
<td>1.22, 1.67</td>
<td>0.01</td>
</tr>
<tr>
<td>Positive fluid balance</td>
<td>1.08</td>
<td>1.01, 1.21</td>
<td>0.025</td>
</tr>
</tbody>
</table>
Fluid administration and brain dysfunction

- Excessive Fluid administration
- Brain injury
  - Endothelium dysfunction
  - Hypotension
    - Blood-brain- barrier leakage
    - Interstitial edema
      - Cells dysfunction due to reduction oxygen transport
      - Ischemia
        - reduction organ perfusion presssure
Conclusions

High positive fluid balance administration to correct hypotension is associated with the development of brain dysfunction in patients in shock
I d’ont care
WHERE ARE THE BABES?