Water and electrolytes

Hyperhydration and hypoalbuminemia. How to proceed?

A Sigtes-Sierra
Albumin and fluid shifts

What is albumin and what albumin is meant for?

• **STRUCTURE and KINETICS**
  - Globular protein (60,000 dalton MW)
  - Half-life of 21 days
  - Intra (40%) and extravascular (60%) pools
  - Total albumin mass = 250-300 grs.
  - Reference values for [s-alb]: 35-50 g/L

• **FUNCTION**
  - Fluid shifts across capillary membrane
  - Transport protein
Albumin as a risk factor

*Short term, general surgery*

**Albumin in composite nutrition indices**

<table>
<thead>
<tr>
<th>Author</th>
<th>Indexes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seltzer (1979)</td>
<td>$S-alb$ + lymphocytes</td>
</tr>
<tr>
<td>Buzby (1980)</td>
<td>$S-alb$ + TSK, transferrin, DHT</td>
</tr>
<tr>
<td>Detsky (1987)</td>
<td>$S-alb$ + subjective assessment</td>
</tr>
<tr>
<td>Christou (1989)</td>
<td>$S-alb$ + anergy</td>
</tr>
<tr>
<td>Windsor (1988)</td>
<td>$S-alb$ + organ failure</td>
</tr>
<tr>
<td>Buzby (1991)</td>
<td>$S-alb$ + weight loss</td>
</tr>
</tbody>
</table>
Albumin as a risk factor

VA Study. Arch Surg 1999
Albumin as a risk factor

VA Study. Arch Surg 1999
Albumin as a risk factor

The hypoalbuminaemic patient: a metabolic cripple

- Altered body composition
- Diminished muscle strength
- Higher APACHE II scores
- Deranged endocrine response
- Worse organ function
- Immunesuppression
- Comorbidity
- Old age
Albumin metabolism

Intake Muscle → Plasma amino acids → Hepatic synthesis (14g/day) → Intravascular albumin (120g; 40%) → Tissue catabolism (12g/day) → Extravascular albumin (180g; 60%) → Losses: Renal (0.4g/day), Intestinal (1.0g/day)

(Whicher, 1987)
Albumin metabolism

Pathogenesis of hypoalbuminaemia

Intake

Muscle

Plasma aminoacids

Hepatic synthesis (14g/day)

Intravascular albumin (120g; 40%)

(120g/day)

Extravascular albumin (180g; 60%)

(120g/day)

Tissue catabolism (12g/day)

Losses:

Renal (0.4g/day)

Intestinal (1.0g/day)

(Wichier. 1987)
Albumin metabolism

Pathogenesis of hypoalbuminaemia

Intake 
Muscle

Plasma aminoacids

Hepatic synthesis (14g/day)

Intravascular albumin (120g; 40%)

Extravascular albumin (180g; 60%)

Tissue catabolism (12g/day)

Losses: Renal (0.4g/day) 
Intestinal (1.0g/day)

(Whicher. 1987)
**Albumin distribution**

**Albumin in the Extracellular Water Compartment**

- Vascular space
- Available space
- Excluded space

45 (g/L)
Starling’s Law

Net filtration = $Lp*S (\Delta Oncotic P - \Delta hydraulic P)$

Net filtration = $Lp*S (\sigma (\Pi_c - \Pi_i) - (P_c - P_i))$

$\sigma$ = reflection coefficient (0-1, permeability to proteins)
probably all hypoalbuminaemic patients have ECW expansion
Albumin and ECW in cancer patients

<table>
<thead>
<tr>
<th>Albumin (g/L)</th>
<th>Haemoglobin (g/dL)</th>
<th>Ø Tumor* (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-expanded</td>
<td>Expanded</td>
<td></td>
</tr>
<tr>
<td>ECW &lt; 25 % w</td>
<td>ECW ≥ 25 % w</td>
<td></td>
</tr>
<tr>
<td>(n=20)</td>
<td>(n=30)</td>
<td>*n=23 n=12</td>
</tr>
</tbody>
</table>

- Albumin: Non-expanded ECW < 25 % w (n=20) vs. Expanded ECW ≥ 25 % w (n=30) p = 0.02
- Haemoglobin: Non-expanded ECW < 25 % w (n=20) vs. Expanded ECW ≥ 25 % w (n=30) p = 0.02
- Ø Tumor*: Non-expanded ECW < 25 % w (n=20) vs. Expanded ECW ≥ 25 % w (n=30) p = 0.002

* n=23 n=12
Distributional hypoalbuminaemia

Pathophysiology

29 (g/L)

High/Normal/Low plasma volume

Expanded interstitial volume
Increased available space

Reduced excluded space

ECW
A. Interstitial illness

- ECW increase
- ...oedema develops
- ...albumin shifts

B. Capillary leak syndrome

- Endotoxin / Cytokines
- ...albumin shifts
- ...oedema develops
Distributional hypoalbuminaemia

Convective transport of albumin
(Fluid (over)loads)

Fluid load → Fluid load → Fluid load

...oedema develops

...albumin shifts

Mullins RJ 1989
Distributional hypoalbuminaemia

Convective transport of albumin
(2L/1h fluid load in normal volunteers)

Lobo et al., Clin Sci 2001
Distributional hypoalbuminaemia

Convective transport of albumin
(2L/1h fluid load in normal volounteers)

Lobo et al., Clin Sci 2001
Hypoalbuminaemia

**Therapeutic approaches**

- Treat fundamental illness
- Negative ECW balance
  - Diuretics
  - Water and Na restriction
- Combination therapy
- Nutrition support if malnutrition
- Human serum albumin?
Hypoalbuminaemia

Therapeutic approaches in different scenarios

- Elective cancer surgery
- Obstructive jaundice
- Acute injury:
  - Polytrauma
  - Burns
  - Infectious disease
- Postoperative complications
- Malabsorption/SBS
Hypoalbuminaemia in gastric cancer

A patient with gastric cancer

- 76 yr. old male with epigastric pain
- Gastric adenocarcinoma (body)
- Weight loss of 16%
- S-alb 28 g/L
- Hb 9 g/dl
- Candidate for total gastrectomy
Hypoalbuminaemia in gastric cancer

A patient with gastric cancer

- ECW measurement (bioimpedance)
- Oral/Enteral refeeding
- Iron/Blood transfusion
- Omeprazol
- Physiotherapy
- Furosemide (10-40 mg/day)
Hypoalbuminaemia in obstructive jaundice

A patient with obstructive jaundice

- 68 yr. male with malignant obstructive jaundice
- Cholangiocarcinoma (distal 1/3 CBD)
- Weight loss 18%
- S-alb 31 g/L
- No clinical signs of cholangitis
- Potential candidate to pancreaticoduodenectomy
# Hypoalbuminaemia & jaundice

<table>
<thead>
<tr>
<th></th>
<th>Benign</th>
<th>Malignant</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ideal body weight</strong></td>
<td>97±11</td>
<td>88±15</td>
<td>.03</td>
</tr>
<tr>
<td><strong>Bilirubin mg/dl</strong></td>
<td>9±6</td>
<td>15±9</td>
<td>.04</td>
</tr>
<tr>
<td><strong>Alk Phos U/L</strong></td>
<td>366±330</td>
<td>1068±910</td>
<td>.003</td>
</tr>
<tr>
<td><strong>Endotoxin (EU/ml)</strong></td>
<td>17±10</td>
<td>10±9</td>
<td>NS</td>
</tr>
<tr>
<td><strong>TNF-α (pg/ml)</strong></td>
<td>32±26</td>
<td>87±67</td>
<td>.01</td>
</tr>
<tr>
<td><strong>CCK (pmol/L)</strong></td>
<td>2.5±2</td>
<td>3.9±1.4</td>
<td>.05</td>
</tr>
<tr>
<td><strong>S-albumin (g/L)</strong></td>
<td>35±3</td>
<td>30±4</td>
<td>0.005</td>
</tr>
</tbody>
</table>

*Padillo J et al., World J Surg 2001*
Hypoalbuminaemia in obstructive jaundice

Improved food intake after internal biliary drainage

Padillo FJ et al, 2001
Hypoalbuminaemia after resuscitation

Problems after an anterior resection for rectal cancer

- 69 yr. female with postoperative peritonitis
- BP 90/50 mmHg, metabolic acidosis, oliguria
- Resuscitation: fluids, antibiotics, surgery
- Day 3: S-alb 21 g/dl, dependent oedema
- Postoperative course: BP unstable, oliguria
- Ventilator and dopamine required
Hypoalbuminaemia after resuscitation

Do not use albumin for resuscitation
Negative or inconclusive data

Human albumin solution for resuscitation and volume expansion in critically ill patients.

Hypoalbuminemia in acute illness: is there a rationale for intervention? A meta-analysis of cohort studies and controlled trials.

A comparison of albumin and saline for fluid resuscitation
Hypoalbuminaemia after resuscitation

Problems after an anterior resection for rectal cancer

Guirao et al., J Surg Res 1995

Na balance 0-3d TPN (mEq/3d)

Albumin decrease pre-TPN (g/l)

$r^2 = 0.87$

$p = 0.0007$
Hypoalbuminaemia after resuscitation

Problems after an anterior resection for rectal cancer

Guirao et al., J Surg Res 1995

ECW / kg end TPN (ml/kg)

Albumin decrease pre-TPN (g/l)

$r^2 = 0.9$

$p = 0.0001$
Hypoalbuminaemia after resuscitation

Problems after an anterior resection for rectal cancer

Management of hypoalbuminaemia

- Improve haemodynamics
- Enhance diuresis
- Promote a negative ECW balance
- Start TPN in a stable patient
- Low sodium/water TPN
Hypoalbuminaemia in malabsorption

Short bowel syndrome

- 54 yr. male with massive SB resection
- Venous thrombosis. 45 cm. SB with colon
- Postoperative diarrhea. TPN for 2 mos.
- 2 mos. after weaning: ankle oedema, 15% weight loss, paresthesiae, s-alb: 22 g/L. Ca: 6.5 mg/dl. Mg: 0.5 mg/dl
- Admitted for lobar pneumonia
Hypoalbuminaemia & TPN

Hypoalbuminaemia during i.v. refeeding

Responders
Non-responders

Starker et al., Ann Surg 1983
Hypoalbuminaemia & TPN

Hypoalbuminaemia during i.v. refeeding

\[ \Delta \text{ in albumin (g/l)} \]

\[ \Delta \text{ in weight (kg)} \]

R = -0.61

P = 0.003

Lobo et al., Clin Nutr 1999
## Hypoalbuminaemia & TPN

### Hypoalbuminaemia during i.v. refeeding

Preoperative malnutrition. TPN for 10 days

<table>
<thead>
<tr>
<th></th>
<th>Standard Diet</th>
<th>Low Na-water diet</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>S-albumin (g/L)</td>
<td>31.7±4.1</td>
<td>35.3±3.8</td>
<td>0.008</td>
</tr>
<tr>
<td>Δ S-albumin (g/L)</td>
<td>-0.7±2.8</td>
<td>2.3±3.5</td>
<td>0.006</td>
</tr>
<tr>
<td>Δ Weight (Kg)</td>
<td>0.8±0.9</td>
<td>-1.5±1.1</td>
<td>0.0001</td>
</tr>
<tr>
<td>Daily diuresis (mL)</td>
<td>1,230±310</td>
<td>959±245</td>
<td>0.003</td>
</tr>
<tr>
<td>Water balance (10 d)</td>
<td>478±1134</td>
<td>-1091±1256</td>
<td>0.001</td>
</tr>
<tr>
<td>Na balance (mEq/day)</td>
<td>40±3</td>
<td>-27±18</td>
<td>0.0001</td>
</tr>
<tr>
<td>Urea (mg/dL)</td>
<td>41±12</td>
<td>61±34</td>
<td>0.02</td>
</tr>
</tbody>
</table>