Workshop
The Liver and the Kidney - 2

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Liver support

- Synthesis
- Detoxification
- Regulation

Liver cells

Adsorber

Dialysis

- ammonia
- bilirubin
- endotoxins
- aromatic amino acids
- toxins
- acid-base-status
- electrolytes
- amino acids
- CNS energy supply
- CNS transmitter precursors
- albumin
- amino acids
- glucose, lipids
- coagulation factors
- unknown substances
Renal support

Dialysis therapies

- Peritoneal dialysis
- Intermittent HD/HF/HDF
- Hybrid techniques
- CAVHF
- CVVHF
- CVVHF high volume
  - plasma exchange
Peritoneal dialysis

Acute or AonCLD

• **advantage**
  - no anticoagulation
  - glucose based

• **disadvantages**
  - clearance
  - fluid balance
  - hyponatraemic
Urea clearance ml/min

- EDD
- CVVHDF
- CAVHDF
- PD
- HVHF
- CAVHF

* indicates significant difference.
Peritoneal dialysis

CLD

• awaiting transplantation
  • risk of peritonitis?
  • splenic vein thrombosis

• not for transplantation
  • no increased infection risk
  • no increased protein losses
Cerebral edema
Start of hemodialysis

During hemodialysis

End of hemodialysis

↓↓↓↓ urea
↓↓ urea
↓ urea
↓ urea
↓↓↓↓ osmolality
↓↓ osmolality
↓ osmolality
↑ idiogenic osmoles
↑ osmolality

H₂O

H₂O
Brain water post hemodialysis

Measured brain water
L/kg dry wt

uremic controls slow fast urea high Na
hemodialysis

dogs
2 hrs
hemodialysis
plasma urea
72→24 mmol/l
* p < 0.05

gray matter
white matter

Arieff et al KI 1973
Ammonia clearance

Arterial NH₃, ug/l

Time h

CVHHF

SJUH
45 yr pt
Acetaminophen
CVVHF
1.5 /h
65 yr pt
4 hr HD
CLD
CVVH for acute liver failure

Matsubara et al CritCareMed 1990

Tohoku Univ
Sendai, Japan
ALF
CVVH
Polysulfone
0.6m²
500-600 ml/min
Nafamostat
30-40 mg/h
Apnoeas during haemodialysis

DeBacker et al AmRevRespirDis 1987
Start of dialysis:
- HCO$_3^-$ in capillary
- During dialysis:
  - ↑HCO$_3^-$
  - ↑pH
- End of dialysis:
  - H$_2$O + CO$_2$ to cerebrospinal fluid

Cerebrospinal fluid:
- HCO$_3^-$
- pH↓

Brain:
- pH↓
- ↑H$^+$
- ↑Idiogenic osmoles
Changes in ICP with HD
Change in ICP with falling MAP

ICP mmHg

ABP mmHg

SJO₂ % ICP mmHg

Time min
CVVH vs intermittent HD

John et al NephrolDialTransplant 2001

- CVVHF 2l/h lac
- 4 h HD bic
- UF 0.25-0.5 l/h

Change in Systolic BP mmHg

Univ Frankfurt
Univ Erlangen
Nürnberg
30 pts septic shock AKI
PS /heparin
Q_b 250 ml/min
mean (SD)
* p < 0.05
Cerebral perfusion during PD

- MAP mmHg
- epinephrine
- norepinephrine
- GTN
- colloid
- fixed dilated pupils
- cardiac arrest & death
- CCPD 2 l cycles

Time (hrs): 0 4 8 12 16
DYNAMICS OF BLOOD VOLUME RESPONSE

\[ \Delta BV \ (\%) \]

\[ t \ (\text{min}) \]

-20 -15 -10 -5 0 5

UFR = 2 l/h
UFR = 0.85 l/h
UFR = 0.3 l/h

Lopot et al. Hemodial Int 2000
Slope RBV with UF

The graph shows the relationship between RBV [%] and time [mins] with UFR [ml/hr]. The lines represent different sodium levels: Na 136, Na 142, and Na 147.
CRRT for acute liver failure

24 yr old pt acetaminophen CVVHF 1.5 /h
RBV change %

ACTUAL BV (%)

DESIR ED BV (%)

UF rate

UF rate l/h

0  50  100  150  200  250

0  -6  -12  -18  -24

0  1  2  3

treatment time (mins)
Biofeedback controlled HD-Hemocontrol

Upper tolerance
Actual value
Objective
Lower tolerance
Ideal trajectory

BV (%) 0 30 60 90 120 150 180 210

time (min)

0 30 60 90 120 150 180 210

BV (%) 0 5 10 15 20 25

0 60 120 180 240

WLR

0 60 120 180 240

DC

0 60 120 180 240
Sudden catastrophic hypotension
**Cardiac perfusion**

- Chesterton LJ et al. Hemodial Int 2009
- Hothi MD thesis UCL 2009
Elapsed time

Jones et al Nephrol Dial Transplant 1992

Elapsed time

Oxygen saturation %

% interval
Plasma kallikrein activity kinetics with AN69 membrane: Influence of diluted plasma pH

Plasma Kallikrein (UKK/l)

Time (min)

- pH = 7.2
- pH = 7.4
- pH = 7.6
- pH = 7.8

Bunchman
Hypersensitivity reaction

Blood - membrane interaction

Patient acidosis

Diluted Blood - Membrane interaction

Rinsing solution (pH, buffer, dilution)

Dialysate

Composition (acetic acid ...)

Heparins

Bacterial contamination exotoxins

Water treatment system
Heparin reactions

- Very charged membrane
- \( \text{C3a} \leftarrow \text{C3} \)
- \( \text{C5a} \leftarrow \text{C5} \)
- bradykinin
- HMW+ kininogen
- plasma kallikrein
- plasma prekallikrein

Contact coagulation pathway

XII

XIIa

XI

XIa
Osmotic demyelination syndrome

Hart NEnglJMed 1995
Central pontine myelinosis

Image from WebPath, courtesy of Edward C. Klatt MD, Florida State University College of Medicine.
Recovery of Brain Osmolytes

A patient with serum sodium 101 mEq/L
10 days after correction of hyponatremia
2 months after correction of hyponatremia

Haussinger, Gastroenterology 1994;107:1475-1480
Correction of hyponatraemia


Serum sodium mmol/l

140
130
120
110

0 5 10 15 20

time days

CAVHF

Birmingham adult F
CLF
Extracorporeal liver support

CRRT

- homeostasis
  - electrolytes
  - acid–base
  - fluid balance
  - cardiovascular stability
Liver failure

- hydrophilic toxins
  - Ammonia

- lipophylic or hydrophobic toxins
  - Protein bound
Risk

Bleeding vs Clotting

Do liver failure patients need to be anticoagulated?
Liver synthesis

- natural anticoagulants
  - antithrombin
  - proteins S & C
Clotting in CRRT circuits
Coagulation during RRT

- Artificial surface
- XIIa
- Endotoxin
  - Toll 4R
- PMN
- IXa - VIIIa
- platelet
- Xa - Va
- Thrombin
- Fibrin
- Fibrinogen
CRRT circuit life

**groups**

- liver
  - ALF
  - AonCLD
  - post LTx
- controls
  - systemic sepsis
  - haematological malignancy
CRRT circuit life

- Haem
- ALF
- CLD
- LTx
- SS

* Indicates a significant difference.
Number of CRRT circuits in 48 hrs
Anticoagulation?

![Bar chart showing the comparison between 'none' and 'anticoagulation'. The 'anticoagulation' group has a significantly higher value (*) than the 'none' group.]
Anticoagulants for ALF and AonCLD

Options depend upon institution

- **Japan**
  - nafamostat maleate

- **Europe**
  - prostanoids
  - citrate
  - heparin

- **USA**
  - heparin
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