



Dialysis in Inborn Errors of Metabolism

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Dialysis in Inborn Errors of Metabolism

- Case presentation
- Differential Diagnosis
Hyperammonaemia
- Outcome
- Dialysis modalities available
- Local approach



Baby A B

- Presented day 3
 - Sleepy poor feeding initially treated for sepsis metabolic investigations done
 - Progressed seizure, apnoea and coma
 - Urine: red -ve ; ket -ve
 - Lactate increased, LFT =N
 - Gas: resp alkalosis, glucose normal
 - Ammonia 1300



Medical Treatment

- Na Benzoate, arginine, phenyl butarate
- Stop feeds
- Vitamins



Dialysis

- Peritoneal dialysis
- Cook catheter – placed at bedside
- Fill volume 20ml/kg; dwell time 30min
- Ammonia
 - Start of dialysis 2590
 - Stopped 49 after 4 days
- Currently:
 - 3yr well grown
 - Mild delayed language > motor
 - Maintained on medical therapy



Baby LN

- Presented to RXH at 3 months of age
- Previous admissions
 - 3/52 seizures and severe metabolic acidosis
Rx for infection- recovered
 - Seen again with seizures CT brain shrinkage
recovered
 - Since then had not been the same but still
feeding



LN Cont

- At 3/12 well grown 5kg
 - Encephalopathic, Hypotonic, Bilat UMN signs
 - Metabolic acidosis (increased AG),
 - Urea <1;
 - N glucose
 - Pancytopenia CRP 130
 - Ammonia 340-1499 , lactate normal
 - Urine Organic acid : 3-oh-propionate and methylcitrate= **propionic acadaemia**



Treatment

- Rehydration
- Stop feeds
- Glucose drip
- Antibiotics
- Medical cocktail: Biotin, Carnitine, Thiamine, Na Benzoate
- Ammonia continued to rise



Dialysis: CVVHD

- 6.5Fr catheter in L femoral by ICU consultant 4th attempt
- Neonatal lines and filter (50ml). Prime'd lines with blood
- CVVHD
 - Dialysate 500ml/hr
 - Blood speed 25ml/min(5ml/kg/min)
 - Complications: initially hypotensive required multiple boluses and inotropes
- Ammonia 1499-190 in 15 hrs
- No neurological recovery
- Therapy withdrawn



Which diseases may need dialysis

- Hyperammonaemia
- Branch chain amino acids e.g. MSUD, Isovaleric acidemia
 - Accumulation of neuro-toxic metabolites (leucine and metabolites)
- Severe Acidosis



Differential Diagnosis of Hyperammonaemia in Newborns & Young Infants

- Inborn errors of metabolism
 - Urea cycle defects
 - Amino acid transport defects
 - Organic acidaemias
 - Fatty acid oxidation disorders
 - Miscellaneous inborn errors
- Transient Hyperammonaemia of the newborn
- Severe infection
- Liver failure
- Urinary tract infection associated with congenital ureteral obstruction

Mathis RS AJKD 2001

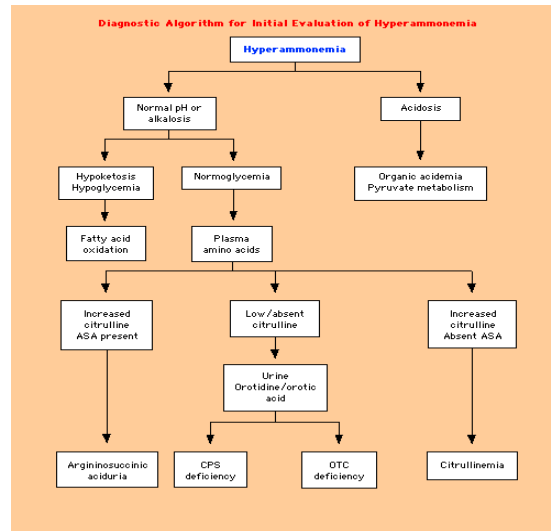


Differential Diagnosis of Hyperammonaemia in Older Children & Adults

- Reye's syndrome (post viral aspirin-induced)
- Liver failure
 - Acute or chronic hepatitis
 - Wilson's disease
 - Alpha-1-Antitrypsin deficiency
 - Alcoholic cirrhosis
 - Drug-induced (anti-seizure medications)
- High-dose chemotherapy
- Later onset urea cycle defects
- Infection

Mathis RS AJKD 2001

Diagnosis Hyperammonaemia



Emergency Medical Management of Hyperammonaemia

- ✦ Minimize endogenous ammonia production and promote anabolism
 - Stop protein intake
 - High caloric intake(120Kcal/kg/day +/-with insulin)
- ✦ Supply coenzyme: Thiamine, Biotin, VitB12 (affected in some OA)
- ✦ Carnitine
- Prime the urea cycle
 - ✦ Arginine Intravenous/oral or
 - Citrulline
 - Carbamylglutamate
- ✦ Treat suspected intracranial pressure
- ✦ Ammonia removal
 - Alternative pathway
 - Na Benzoate IV/oral; Na phenylbutyrate IV/oral



Outcome

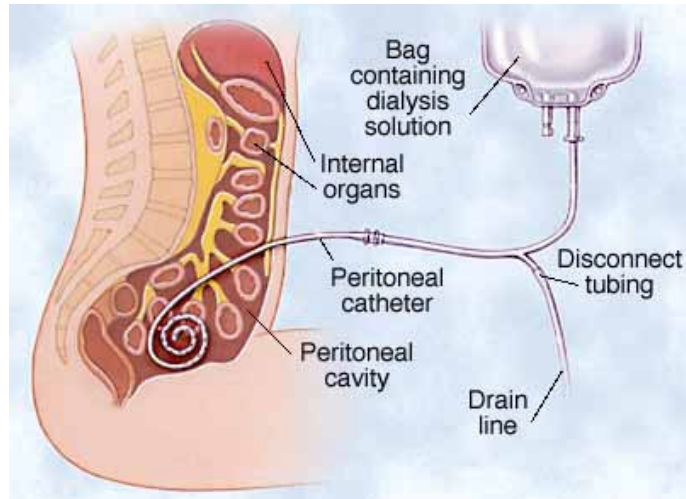
- **Coma**
 - Coma duration
 - Coma >30hrs prior to dialysis
No correlation with peak levels - *Picca Pediatr Nephrol 2001*
 - Prolonged coma severe neuro outcome
-*Msall M NEJM 1984 Surtees RA, Pediatr Neurol 1992; Hilliges. Eur J Pediatr 1993*
- **Peak**
 - <180mmol/L no neuro handicap
 - > 350mmol/L severe neuro handicap
-*Urchino T J inherited metab Dis 1998 (japan)*
 - Levels >1000 Micromol/l less likely to survive
-*Enns NEJM 2007*
- **Rapid removal** -*Schaefer Nephrol Dial Transplant 1999*
- **Prospectively** treated patients-outcome better
-*Maestri NE J Paedr 1991*



Dialysis Modalities available in Cape Town

- Peritoneal Dialysis
- Haemodialysis
- CVVHD

Peritoneal Dialysis

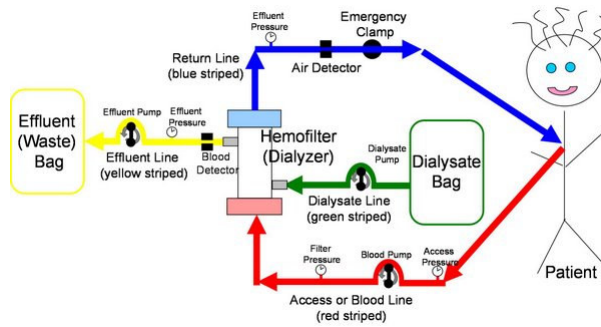


Peritoneal Dialysis

- Bedside placement of PD catheter Cooke
- Up and running within the hour
- Nurses in ICU proficient in use
- Home choice Continuous Cyclor
- Safe
- Low cost in our setting



CVVHD /Haemodialysis





Efficiency of dialysis

- Ammonia
 - HD was 10 times more efficient than PD
Donn SM J Pediatr 1979;Wiegand C J Pediatr 1980
 - CVVHD 2-5 times greater clearance vs PD
Wong KY Pediatr Nephrol 1998

NB Flow dependant *Schaefer Nephrol Dial Transplant 1999*
- Branch chain amino acid
 - Rabbits 100-150% increase in clearance CVVHD v s PD [Gouyon JB](#) *J Inherit Metab Dis. 1996*
 - Neonate leucin reduction time 2.1 hr (CVVHD) vs 16-36hr(PD) *Schaefer Nephrol Dial Transplant 1999*



Haemodialysis

- Main problems:
 - Access difficult 6,5Fr double lumen
 - Cardiovascular instability
 - Poor flow through catheter
 - Anticoagulation
- May take several hours to set up lines, setting up, getting technologists etc
- Small neonatal lines Fx baby= lines 50 mls



CVVHD

- Setup time similar to HD
- BM25 machine
- Volume of lines similar to baby HD lines
- Because no UF hemodynamic instability can be expected to be similar to HD but poorer clearance



How dialysis prescription differs from ARF

- No ultra filtration
- Phosphate
- Potassium
- Prime lines with blood



When to start and when to stop

Picca S. Semin Nephrol. 2008-Italy

- **Start**
 - Only if not responding to medical therapy during a four hour trial period
 - Persistently above 500
- **Stop**
 - Persistently <100micromol/L
- **Withdraw**
 - Depends on response to feeding

Mathis RS AJKD 2001- San Francisco

- **Start dialysis**
 - Ammonia levels 2-3 x normal
 - rising rapidly (>100micromol/L/2-3hrs
 - encephalopathy
- **stop** when reach normal levels and continue with medical therapy

Personal communication Andrew Morris Manchester

- CVVHD/HD insert lines at 350
- PD earlier -250
- Comatose



Which modality is best ?

- Take in to account:
 - difficulties associated haemodialysis
 - Theatre time
 - Expertise: lines, monitoring, ped haemo techs
 - Time to initiate
 - Complications
 - Cost
 - No studies have shown a relationship between dialysis modality and survival

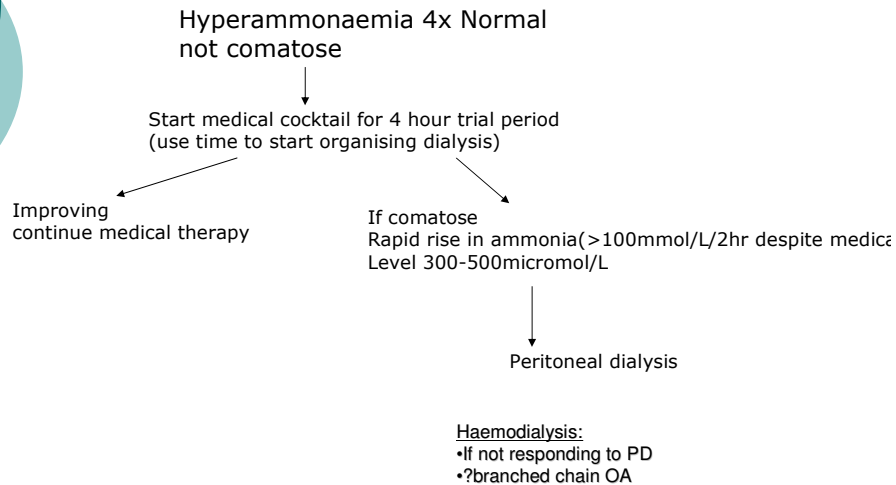
“local expertise and available facilities remain, at the moment, the main determinant for the choice of dialysis modality. ”

Picca Semin Nephrol. 2008

Western Cape Renal service

- PD
 - Method of choice
 - Most experience easiest and safest in small babies
 - Implementation time fastest
 - Have had numerous success
- CVVHD/HD is available
 - Only in Red Cross ICU
 - Lines insertion major problem
 - Haemodynamic instability
 - Babies >3kg


Protocol for western Cape Renal Services treatment of Hyperammonaemia



○ The end



Thank you

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-
- Phenyl Butyrate section 21 –named patient basis 10 000 rand /bottle 170g can get
 - Arginine IVI can get some in pharmacy but is expiring soon
 - Carnitine no prob contains Mg



Western Cape Renal service

- Guidelines Practical for a SA setting
- Hyperammonaemia 3-4x Normal not encephalopathic
 - Start medical cocktail 4 hour trial period (use time to start organising dialysis)
 - If improving continue medical therapy
 - If rapid rise >100mmol/L/3hr
 - encephalopathy
 - level > 300-peritoneal dialysis
 - level >500 -haemodialysis

Then start dialysis

CVVHF

