RENAL DISORDERS IN INTESTINAL FAILURE PATIENTS

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Renal disorders in intestinal failure patients

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Renal disorders in IF

- Intercurrent / unrelated renal disease
- Short-term acute kidney injury from hypovolaemia
- Longer-term (cumulative) chronic kidney disease from prolonged low level hypovolaemia
- Consequences of other complications of IF
Different types of IF

- Short bowel syndrome
- Intestinal failure without short bowel
Different types of IF

- Short bowel syndrome
- Intestinal failure without short bowel

- When no short bowel then management is largely as for renal disease in any other context
ESPEN GUIDELINES

ESPEN Guidelines on Enteral Nutrition: Adult Renal Failure

N. Cano\textsuperscript{a,\,*}, E. Fiaccadori\textsuperscript{b}, P. Tesinsky\textsuperscript{c}, G. Toigo\textsuperscript{d}, W. Druml\textsuperscript{e}, DGEM: ☆☆ M. Kuhlmann, H. Mann, W.H. Hörl

Parenteral Nutrition in Adult Renal Failure

NJM Cano, M Aparicio, G.Brunori, JJ Carrerro, B Cianciaruso, E Fiaccadori, B Lindholm, V Teplan, D Fouque, G Guarnieri

Clinical Nutrition 2009; 28:401-414
Different types of CKD

• Renal failure still trying to avoid dialysis
• End-stage disease on dialysis
• Protein restriction vs protein supplements
• These approaches also apply in intestinal failure but may be difficult to implement
The two most common types of short bowel

- **Jejuno-colic anastomosis**
  - Ileum and some of jejunum resected leaving jejuno-colic anastomosis

- **Jejunostomy**
  - Colon, ileum and some of jejunum resected, leaving a jejunostomy
Different types of short bowel

Key elements

• Is the colon present?

• Is the patient a net secretor?
Normal physiology

- Osmotic and sodium gradients
- Proximal intestinal response is secretory
- Sodium and water move into lumen
- Threshold for absorption is a luminal sodium concentration of about 100mmol/L
Net absorber/net secretor?

• Healthy person is net absorber
  Drinks more → absorbs more

• Dehydration → Thirst → Drinking
  → Increased fluid retention
  → Resolution
Net absorber/net secretor?

- If <1.5m small intestine
  → Normal proximal secretion is not compensated by distal absorption
Net absorber/net secretor?

- If <1.5m small intestine
  - Normal proximal secretion is not compensated by distal absorption
- Drinks more → absorbs LESS
- Dehydration → Thirst → Drinking
  - Increased fluid loss
  - Deterioration
Net secretors and fluid restriction

- Fluid restriction is central challenge
- Thirst requires LESS drinking
  - iv “saline”
  - oral rehydration solutions
  - limit (sodium-free) fluids
- Risk to kidneys is clearly apparent
The colon in short bowel

- Retained colon (>half) equivalent to ~50cm small intestine
- Value mainly in fluid balance
- Some nutritional gain from fermentation
- Potential problem from oxalate
Urine sodium

- Marked sodium retention in dehydration
- Very early feature
- Simple untimed sample sufficient
- $< 20$ mmol/L almost diagnostic

- Only in hepatorenal syndrome is this potentially misleading
Urine sodium

- Ceases to be helpful in established renal failure (no concentrating capacity)
- Falsely high with diuretics
- Caution about diuretics in intestinal failure
Clinical case

- 62 year-old woman with Crohn’s disease
- Multiple intestinal resections
- 55cm to jejunostomy since 1996
- HPN since 1996
- No major problems (urine volume ~800ml)
- Now has only 4th central catheter
- Family history of cardiovascular disease
- Smoker
Clinical case

• 2014: myocardial infarction
• 2015: congestive cardiac failure
• 2016: 5 admissions with fluid balance problems
• Oedema and hypovolaemia – iatrogenic?
• Rising “recovery” creatinine
Clinical case

2017

- Best creatinine 2 x ULN
- Intractable dependent oedema
- Unable to lie flat
- During admission combination of furosemide, amiloride and reduced Na\(^+\) in PN effective
- Rapid partial relapse at home
Clinical case

2017

- Best creatinine 2 x ULN
- Intractable dependent oedema
- Unable to lie flat
- During admission combination of furosemide amiloride and reduced Na+ in PN effective
- Rapid partial relapse at home
- Rising “recovery” creatinine
  - 4 x ULN by end of the year
Clinical case

2018

- Much discussion about haemodialysis
- Nephrologists less keen
- Progressive azotaemia and acidosis
- Shunt created
- HD commenced in June
- Immediate benefit
  - Biochemical, clinical and psychosocial
Epidemiology of renal failure in IF

Outcome of kidney function in adults on long-term home parenteral nutrition based on eGFR

Prospective observational study (n=72) over 30 months with additional baseline retrospective
Normal: ≥90; chronic kidney disease (CKD): <60ml/min

eGFR <90 in 41.7% of patients at baseline
53.4% to 56.6% during prospective period
CKD rose from 20.1% to 35.9%

Agostini et al, Nutrition 2019
Incidence of chronic renal disease on HPN

Agostini et al, Nutrition 2019
Epidemiology of renal failure in IF

Probability of maintaining eGFR ≥60 in HPN
- 98% at 1 year
- 82% at 5 years
- 79% at 10 years

Development of CKD significantly associated with increasing age
- urological diseases

CKD numerically associated with episodes of catheter sepsis
- short bowel syndrome
- low volume HPN
True in children too

70 Finnish children on PN for IF
   short bowel (n = 59); primary motility disorder (n = 11)

At median age of 5.7 and PN duration of 3.2 years
   20 patients (29%) had decreased eGFR

These patients had
   significantly longer duration of PN (3.2 vs 0.9y; p = 0.03)
   shorter intact age-adjusted small bowel (22 vs 32%; p = 0.04)

No other predisposing factors for decreased eGFR were identified.

Ylinen 2018
Renal failure after intestinal transplant

US incidence of CKD at 1, 5, and 10 years after transplant was 3.2%, 25.1%, and 54.1%

Significantly associated with female gender (HR 1.34) age (HR 1.38/10 year increment) catheter-related sepsis (HR 1.58) steroid maintenance (HR 1.50) graft failure (HR 1.76) need for IV fluids (HR 2.12) or PN (HR 1.94) diabetes (HR 1.54).

CKD linked to a significantly higher risk of death (HR 6.20)
Renal failure after intestinal transplant

Pittsburgh: median follow-up of 5.7 years

24.7% patients required dialysis,
13.2% required long-term dialysis

1, 3 and 5-year risks of ESRD were 2%, 7%, and 14%

More likely if
Higher baseline creatinine (HR 3.4)
Graft included liver (HR 2.01)

Median survival on dialysis was 6 months
3-year survival was 21%

Puttarajappa 2018
Intradialytic parenteral nutrition

To be covered later
In specific context of IF and HPN:

- Disappointing
- Difficult to arrange logistically
- Difficult to ensure adequate nutrition when given concurrently with dialysis
- Often tried and abandoned
Nephrolithiasis in IF

Urinary tract stones are common in IF
up to 25% prevalence
Most are related to chronic dehydration

Special case of oxalate in those with colon
<table>
<thead>
<tr>
<th>Factor</th>
<th>Cause</th>
<th>Type of stone</th>
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<tbody>
<tr>
<td>↓ urine volume</td>
<td>↑ intestinal fluid losses</td>
<td>Uric acid</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Calcium oxalate</td>
</tr>
<tr>
<td>↓ urine pH</td>
<td>Metabolic acidosis</td>
<td>Uric acid</td>
</tr>
<tr>
<td>↓ urine citrate</td>
<td>GI loss of bicarbonate</td>
<td>Calcium oxalate</td>
</tr>
<tr>
<td>↓ urine Mg(^{2+})</td>
<td>Magnesium malabsorption</td>
<td>Calcium oxalate</td>
</tr>
<tr>
<td>↑ urine calcium oxalate</td>
<td>↑ colonic absorption “Enteric oxaluria”</td>
<td>Calcium oxalate</td>
</tr>
<tr>
<td>Pyridoxine deficiency</td>
<td></td>
<td>Calcium oxalate</td>
</tr>
<tr>
<td>Thiamine deficiency</td>
<td></td>
<td></td>
</tr>
<tr>
<td>↑ ascorbate intake</td>
<td></td>
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Oxalate stones in IF

Promoting factors
Low luminal calcium
Non-absorbed fats in colon
FFAs form soaps with calcium
Luminal oxalate no longer calcium bound
Available for absorption in colon

Influence of Oxalobacter formigenes
Unabsorbed bile acids increase colonic permeability
Oxalate stones in IF – new approach

Modulation of gut microbiota

Confirmed effect of antibiotics on intestinal barrier integrity - improved by antibiotics
To date no confirmed effect on progression of CKD or on stone formation

Potential for manipulation by selected probiotics?

Konrad 1919
Oxalate stones in IF – management

Optimise management of IF / SBS
  maximise intestinal absorption
  reduce intestinal losses
  provide sufficient iv volume

Dietary management
  increase dietary calcium
  reduce dietary oxalate
  substitute MCT for some dietary fat

Metabolic elements
  Avoid systemic acidosis (sodium bicarb and citrate)
  Add bile salt sequestrants (which also bind oxalate)