Aims of Treatment

Prevention of thirst & dehydration

Stomal output <2L/day or manageable diarrhoea

Prevention of electrolyte deficiencies
Drugs used in IF

- Electrolyte mix
- Dioralyte® (double strength)

Oral hypertonic solutions

- Omeprazole
- Octreotide
- Racecadotril

Antisecretory

Supplements

- Magnesium

Antimotility

- Loperamide
- Codeine phosphate
Patient types
Respond differently to medications

<table>
<thead>
<tr>
<th></th>
<th>Absorbers</th>
<th>Secretors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Residual small</td>
<td>&gt;100 cm</td>
<td>&lt;100 cm</td>
</tr>
<tr>
<td>Bowel length</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Net Na &amp; H₂O balance</td>
<td>Intestinal output &lt; oral intake</td>
<td>Intestinal output &gt; oral intake</td>
</tr>
<tr>
<td>Jejunostomy output</td>
<td>~2 L/day</td>
<td>~4-8 L/day</td>
</tr>
</tbody>
</table>
Antisecretory Drugs

- **Ranitidine**
  - Competes with histamine for receptor site
  - Less effective in food-stimulated secretion

- **Omeprazole**
  - Irreversible inhibition of proton pump preventing secretion of H⁺ ions

- **Octreotide**
  - Somatostatin analogue
Mechanism of action

Parietal Cell

Proton pump inhibitors
Omeprazole

H2 receptor antagonists
Ranitidine
Ranitidine vs Omeprazole

Jeppesen *et al*, 1998

13 patients, double blind, crossover trial

- Median SB length = 100cm
- 2 treatments with 2 day washout period
  - (IV ranitidine 150mg vs omeprazole 40mg BD)
- Assessing effect on wet weight absorption

Omeprazole more effective than ranitidine at increasing wet weight absorption
Nightingale et al, 1991

- 11 patients (7 secretors & 4 absorbers)
- SB length < 150cm
- Oral omeprazole for 3 days
Reduction in intestinal output not sufficient to stop parenteral fluid & electrolyte replacement
Antisecretory Drugs

- Only effective in net secretors

- Omeprazole
  - High dose often necessary (40mg BD)
  - Titrate against stomal pH
  - Oral omeprazole may be ineffective in patients <50cm jejunum
Antimotility drugs

Act on $\mu$-receptors
- $\downarrow$ peristalsis
- $\uparrow$ water absorption

Codeine phosphate
- 120-240mg daily

Loperamide
- 16-64mg daily
- Not addictive or sedating
- More favourable than codeine

Greater effect
- if used in combination$^1$

Effect of codeine & loperamide

King at al, 1982 Aust NZ Surg:52:121-124
# Loperamide preparations

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Absorption (hrs)</th>
<th>Onset of action (hr)</th>
<th>Half life (hrs)</th>
<th>Cost for 2mg dose (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loperamide syrup 1mg/5ml</td>
<td>2.4 +/- 0.7</td>
<td>1</td>
<td>11</td>
<td>0.12</td>
</tr>
<tr>
<td>Loperamide capsules</td>
<td>5.2 +/- 0.3</td>
<td>1</td>
<td>11</td>
<td>0.11</td>
</tr>
<tr>
<td>Loperamide tablets</td>
<td>No data</td>
<td>1</td>
<td>11</td>
<td>0.09</td>
</tr>
<tr>
<td>Loperamide melts</td>
<td>No data</td>
<td>1</td>
<td>11</td>
<td>0.33</td>
</tr>
</tbody>
</table>

Locally acting on the gut, only 1% systemically absorbed. All formulations bioequivalent. MI, Jonson & Jonson, Nov14
Octreotide

- Delays gastric & small bowel emptying

- ↓ salivary, gastric & pancreatic-biliary secretions

- Absorbers / secretors
  - Greatest effect in net secretors

- Effective for
  - ileostomy diarrhoea
  - large volume jejunostomy & Na losses

- No effect on energy/nitrogen absorption

1 O'Keefe et al, (1994) JPEN;18:26-34
## Side Effects

<table>
<thead>
<tr>
<th>Very common</th>
<th>Common</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperglycaemia</td>
<td>Thyroid dysfunction</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>Hypoglycaemia</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>Bradycardia</td>
</tr>
<tr>
<td>Nausea</td>
<td>Dyspnoea</td>
</tr>
<tr>
<td>Constipation</td>
<td>Dyspepsia</td>
</tr>
<tr>
<td>Headache</td>
<td>Vomiting</td>
</tr>
<tr>
<td>Cholelithiasis</td>
<td>Bloating</td>
</tr>
<tr>
<td>Injection site pain</td>
<td>Steatorrhoea</td>
</tr>
<tr>
<td></td>
<td>Dizziness</td>
</tr>
<tr>
<td></td>
<td>Cholecystitis</td>
</tr>
<tr>
<td></td>
<td>Rash</td>
</tr>
<tr>
<td></td>
<td>Alopecia</td>
</tr>
</tbody>
</table>
Octreotide

**Problems**
- Expensive
- Unlicensed
- Inhibits adaptation

**Suggested use**
- Trial use for 2-3 days
- Stop if no effect
- Long acting preparations if sustained effect
Racecadotril

- Enkephalinase inhibitor
- Enkephalins act on δ-opiate receptors – reducing hypersecretion of water and electrolytes
- Enkephalins are broken down by enkephalinases
- Licensed for acute diarrhoea, especially secretory
- Possible role in secretors?
Magnesium

**Mg deficiency**
- Common in SBS

**Causes of deficiency**
- Reduced area of absorption
- Fat malabsorption
- Na depletion
- Hyperaldosteronism
- PPI treatment

**Oral replacement**
- Mg oxide, Mg glycerophosphate, Mg aspartate
- Form used dependent on response
- Doses used: 12-24mmol/day
- Intestinal transit slowest at night

**Parenteral replacement**
- S/c: maximum of 8mmol in 1L 0.9% saline
- IV: higher doses can be given

## Drug administration: Tips

<table>
<thead>
<tr>
<th>Timing</th>
<th>Caution with liquids/syrups</th>
<th>Use capsules/tablets</th>
</tr>
</thead>
</table>
| • Give drugs **30mins to 1hour** before food | • High osmolality  
• May contain sorbitol  
• Will increase stomal output | • If comes out of stoma bag then crush tablet or open capsules |
Glucagon-like Peptide 2

Naturally occurring 33 AA peptide

<table>
<thead>
<tr>
<th>Production</th>
<th>Intestinal L cells (ileum &amp; colon)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Release</td>
<td>stimulated by luminal nutrition</td>
</tr>
<tr>
<td>Receptors</td>
<td>Mainly in jejunum &amp; proximal ileum</td>
</tr>
<tr>
<td>Action</td>
<td>Strong intestinotrophic properties</td>
</tr>
</tbody>
</table>

- ↑ Mucosal proliferation
- ↑ Nutrient absorption
- ↑ Intestinal perfusion
- ↑ Cytoprotection
- ↑ Bone density
Teduglutide: [gly2]-hGLP-2

- Novel recombinant analogue of GLP-2 (orphan drug)
- 33 AA peptide that differs from GLP-2
  - Substitution of ALA by GLY at 2<sup>nd</sup> position (from N-terminus)
  - Resistance to <i>in vivo</i> degradation by dipeptidyl peptidase-IV

Revestive

<table>
<thead>
<tr>
<th></th>
<th>GLP-2</th>
<th>Teduglutide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Half life</td>
<td>7 minutes</td>
<td>2 hours</td>
</tr>
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</table>
Teduglutide in SBS with IF

**Jeppesen PB et al Gut 2011;60:902-14**
Teduglutide: 24 week RCT

% responders (>20% PN reduction)

<table>
<thead>
<tr>
<th>Placebo</th>
<th>Teduglutide</th>
</tr>
</thead>
<tbody>
<tr>
<td>13/43</td>
<td>27/43</td>
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</table>

Jeppesen PB et al, Gastroenterology 2012;143(6):1473-1481
STEPS2: sustained response (TED/TED completers)

Sustained reductions in PS volume requirements were observed over 30 months (TED/TED group)
Remnant SB length & discontinuing PN with teduglutide

![Bar chart showing the number of patients stopping PN based on remaining SB length in patients, cm.](Jeppesen et al. Poster ESPEN 2014 (PP131-SUN))
Identifying suitable patients

Probably all adult patients with SBS could benefit

- Patients should be stable following adaptation

Reasonable to start with

- Patients with smaller PS requirements (A–D1)
- Patients with high PS volume requirements (A–D4)

Remember it is a growth factor

Contra-indications
- Active or suspected malignancy
- Patients with a history of a GI malignancy within the last 5 years
Conclusion

Drug management in IF

- Electrolyte mix
- New therapies?
- Loperamide
- Octreotide
- Codeine phosphate
- Omeprazole
- Mg supplements