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Convirtional therapy in IBD

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## Anti-inflammatory drugs

<table>
<thead>
<tr>
<th><strong>Aminosalicylates</strong></th>
<th><strong>Corticosteroids</strong></th>
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<tbody>
<tr>
<td>5-ASA active moiety</td>
<td>natural hormones or their derivates</td>
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<tr>
<td>inhibit proinflammatory cytokine production</td>
<td>potent non-specific anti-inflammatory effect</td>
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<tr>
<td>first line in UC</td>
<td>multiple side effects</td>
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<tr>
<td>dose-dependent efficacy and adverse events</td>
<td>oral (high or low systemic bioavailability)</td>
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<tr>
<td>oral, topical</td>
<td>intravenous, topical</td>
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Conventional immunomodulators

Thiopurines
interfere with nucleic acid synthesis/ cell division and growth

Methotrexate
interfere with nucleic acid and protein synthesis / cell division
promotes cells apoptosis (death)

Calcineurin inhibitors
lower the activity of T lymphocytes and their immune response
## Induction of remission

### Ulcerative colitis
- +
- +
- +/- (few data)
- +/- (few data)
  - +
  - +
  - +

### Crohn’s disease
- +/- (colon)
  - +
  - -
  - +
  - ?
  - +
  - +

### Medications
- **Aminosalicylates**
- **Corticosteroids**
- **Thiopurines**
- **Methotrexate**
- **Calcineurin inhibitors**
- **Anti-TNF agents**
- **Anti-integrin agents**
Maintenance of remission

**Ulcerative colitis**

- Aminosalicylates
- Corticosteroids
- Thiopurine
- Methotrexate
- Calcineurin inhibitors
- Anti-TNF agents
- Anti-integrin agents

**Crohn’s disease**

+/- (post-op)

- Aminosalicylates
- Corticosteroids
- Thiopurine
- Methotrexate
- Calcineurin inhibitors
- Anti-TNF agents
- Anti-integrin agents
92% in remission at 7 weeks with prednisolone

Prednisolone 1mg/kg until in clinical remission

- Week 4: 63%
- Week 5: 80%
- Week 6: 88%
- Week 7: 92%
Induction of remission in UC

Mesalazine: strong effect
Steroids: strong effect (systemic or topical steroids)
Cyclosporin: strong effect in acute severe colitis
Meta-analysis of mesalazine for induction of remission in UC

Remission failure rate

48 studies
7776 patients
RR: 0.86 (0.81-0.91)

Maintenance of remission in Crohn

No treatment in mild cases
Mesalazine in mild cases
Purines:
- Tolerated by 80% of patients
- Steroid sparing in 50% of patients
- Remission without steroids in 25%
- Tissue healing in 20%
- Safety issues (lymphoma, skin cancers, liver toxicity)

Methotrexate:
- Similar to purines (but less data and finally apparently less toxicity)
Azathioprine withdrawal trial in CD

Azathioprine (n=40)

Placebo (n=43)

$p = 0.015$
Maintenance of remission in UC

Mesalazine: strong effect

Purine: probably similar to Crohn (but less data)

Methotrexate: ?
Meta-analysis of mesalazine for maintenance of UC

Relapse rate

7 studies
1298 patients
RR: 0.69 (0.62-0.77)

12 studies
1655 patients
RR: 1.14 (1.03-1.27)

Crohn: surgery is not always bad…
and should be part of the strategy in some cases

Sometimes best option for very damaged tissue (fibrosis-fistula-abcesses)
Must be limited in extent and number (short resection) and should preserve intestinal function
Allows to « restart on a clean base » with optimal treatment strategy and monitoring
How would you treat this?
Surgery may induce longstanding remission

UC: surgery is sometimes the best option…
but should not be seen as a cure.

Best option in:
- Refractory acute severe colitis (potentially lethal disease)
- Chronic untractable disease (situation should be compared to the predicted results of surgery and also integrate potential new drugs)

Average function includes:
- 5-6 stools/d including 1 at night
- Some incontinence episodes

Risk of pouchitis is significant (10-15% of chronic inflammation)
Tailored therapeutic algorithm for IBD

Diagnosis of IBD

- **Mild disease**
  - 40% CD
  - 60% UC
  - **Step up**
    - 5ASA, topical steroids, occasional systemic steroids
  - **No need for Biologics**

- **Moderate disease**
  - 40% CD
  - 30% UC
  - **accelerated step-up**
    - Close monitoring (clinical, biomarkers, imaging)
  - **Secondary non-severe disease**
    - **No need for Biologics**
  - **Secondary severe disease**
    - Biologics+/-IS

- **Directly severe disease**
  - 20% CD
  - 10% UC
  - **Targeted top down**
    - Biologics+/-IS

Numbers give in this slides represent an approximate estimation from several cohorts and population-based data:

Thank you for your attention