Inflammatory Bowel Disease: New Insights into Therapy and Treatment Goal

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Conflict of Interest Declaration: Nothing to Disclose

Presenter: Alallam Alallam

Title of Presentation: Inflammatory Bowel Disease: New Insights into Therapy and Treatment Goal

I have no financial or personal relationships to disclose
Objectives

• Overview of treatment options
• Role of primary care providers in managing IBD patients
• Caring for a patient on biologics
Case 1

- 23-year-old male with 6 months history of 2-3 soft bowel movements, occasional rectal bleeding, tenesmus
- Otherwise healthy, no meds
- O/E: unremarkable
- BW: normal CBC, CRP and Albumin
Case 1

- Colonoscopy: mild proctitis
Case 2

- 19-year-old female with few months history of abdominal pain, wt loss and non-bloody diarrhea, along with anal pain
- O/E: tenderness in RLQ, perianal fistula
- BW: Hb 115, MCV 75, CRP 20, Albumin 35
Case 2

- Colonoscopy: terminal ileum ulceration, deep ulcers in the rectum
Case 3

- 31-year-old male with 1 month history of bloody diarrhea, Abdominal cramps, feeling unwell
- Recently quite smoking
- O/E: a febrile, HR 105, abdominal tendernessness
- BW: Hb 105, CRP 45, Albumin 32
Case 3

- Sigmoidoscopy: severe colitis
Some thoughts about the cases

• Severity of disease

• Urgency of the consultation, scope, therapy
Treatment Goal(s)

• “Old” goal
  • Clinical symptoms control (Patient feeling better)

• Ultimate goal of IBD management
  • Complete disease control
  • Stop disease progression
  • Altering the natural course of IBD
New Therapeutic Outcomes

- Clinical remission (Steroid-free remission)
- Biological remission (e.g. normal CRP)
- Endoscopic remission (mucosal healing)
Treatment phases

- Induction of remission
- Maintenance of remission

Response
## Treatment Options

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<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>5-ASA &amp; Sulfasalazine</strong></td>
<td>Mesalamine</td>
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<tr>
<td><strong>Steroids</strong></td>
<td>Prednisone, budesonide</td>
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<tr>
<td><strong>Immunomodulators</strong></td>
<td>6-MP, AZA, MTX</td>
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<tr>
<td><strong>Biologics</strong></td>
<td>Anti-TNFa</td>
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</table>
IBD Treatment Pyramid

- Surgery
- Biologic agents
- Immunosuppressants (AZA or 6-MP or MTX)
- Prednisone or budesonide
- 5-ASA or sulfasalazine

Step-up approach
Top-down approach
5-ASA

- Mesalamines
  - Salofalk, Asacol, Pentasa, Mezavant
- Ulcerative colitis
  - Induction and maintenance
- Crohn’s
  - Induction: ? Modest effect for mild to moderate disease
  - Maintenance: ? post op
Corticosteroids

- Commonly used steroids
  - Prednisone
  - Budesonide (Entocort)
    - Mainly for Rt side Crohn’s disease
    - Methylprednisolone
- Very effective for induction
- Not for maintenance
Immunomodulators

- Thiopurines
  - Azathioprine (Imuran)
  - 6 mercaptopurine (6-MP)
- Methotrexate
- Induction: not effective, mechanism of action
- Maintenance: yes, especially as steroid sparing
Biologics
Immunology 101

- T helper cell:
  - Th1, Th2

- Th1 (proinflammatory cell), produce cytokines: e.g.
  - TNF (tumor necrosis factor)
  - IL 12 (interleukin)
Immunology 101

• Principle of therapy
  • Down regulate Th1
  • Inhibit the effector functions of the cytokines
    • Monoclonal antibodies

• Nomenclature
  • ‘-mab’ indicates a monoclonal antibody (mAb)
  • ‘-ximab’ indicates a chimeric mAb
  • ‘-zumab’ indicates a humanized mAb
Monoclonal Antibodies (mAb)

- **Murine (0% human)**
- **Chimeric (65% human)**
- **Humanized (> 90% human)**
- **Fully Human (100% human)**

Generic suffix:
- omab
- ximab
- zumab
- umab

High Potential for immunogenicity

Low
# IBD-Biologics

<table>
<thead>
<tr>
<th>Anti-TNFa therapies</th>
<th>Anti-integrin antibodies</th>
<th>IL 12 &amp; IL23 inhibitors</th>
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<tbody>
<tr>
<td>Neutralize TNFα</td>
<td>Block leukocyte migration to the sites of inflammation</td>
<td>Block IL12&amp;IL23 receptors on Th</td>
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<tr>
<td>Examples:</td>
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<tr>
<td>Infliximab (Remicade)</td>
<td>Natalizumab (Tysabri)</td>
<td>Ustekinumab (Stelara)</td>
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<tr>
<td>Adalimumab (Humira)</td>
<td>Vedolizumab (Entyvio)</td>
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<td>Golimumab (Simponi)</td>
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<td>Certolizumab (Cimzia)</td>
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Biologics

- Anti-TNFα
  - Infliximab (Remicade)
  - Adalimumab (Humira)
  - Golimumab (Simponi)

- Anti-Integrin (new)
  - Entyvio (Vedolizumab)

- Effective for both induction and maintenance
When to use Biologics

• Examples:
  • Refractory disease (to conventional therapy)
  • Severe disease (acute severe UC)
  • Steroid dependent
  • High disease burden
  • Fistulizing Crohn’s
## Dosing and regimen

<table>
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<tr>
<th></th>
<th>Remicade</th>
<th>Humira</th>
<th>Simponi</th>
<th>Entyvio</th>
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<tr>
<td><strong>Route of administration</strong></td>
<td>IV infusion</td>
<td>S/C</td>
<td>S/C</td>
<td>IV infusion</td>
</tr>
<tr>
<td><strong>Induction dose</strong></td>
<td>5 mg/kg @ 0,2,6 wks</td>
<td>160 mg @0,2wks</td>
<td>200mg @0,2wks</td>
<td>300mg @0,2,6 wks</td>
</tr>
<tr>
<td><strong>Maintenance dose</strong></td>
<td>5mg/kg q 8 wks</td>
<td>40mg q2wks</td>
<td>50 mg q4wks</td>
<td>300mg q8wks</td>
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</tbody>
</table>
Cautions/Adverse events

- Infection
- Reactivation of HBV infection
- Reactivation of Tuberculosis
- Demyelinating disease
- Autoimmune disease: lupus like
- Psoriasis like
- Worsening severe CHF
Anti-TNF and Malignancy

- Malignancies
- Lymphoma
- Hepatosplenic T cell lymphoma
  - Rare
  - Fatal
  - Young male
  - Concomitant use of thiopurines
Things to do before starting biologics

- Check for Hepatitis B virus (HbsAg)
- T.B skin test
- Chest x-ray
Immunosuppression & Vaccination

- Routine inactivated vaccines should be brought up to date
  - Including HAV, HBV, HPV
- Pneumococcal polysaccharide vaccine
- Live Vaccines are contraindicated once started high-level immunosuppression
  - (varicella, measles, rubella, yellow fever)
  - Check VZV immunity, give Zoster vaccine 4 wks before starting therapy if older than 50
Monitoring IBD patient

- Clinically
  - Remission, general well being, psychology, quality of life
- Examine: skin ? annually
- Blood work
  - No routine tests for pts on biologics
  - CRP
  - Routine CBC/ liver profile if on thiopurines or MTX
- Need for: Vit D, Ca, Vit B12, Iron
IBD Treatment Pyramid

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- Biologic agents
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Step-up approach
Top-down approach
Combo therapy

Points to mention

- Antibody formation against mAb
- Therapeutic drug monitoring
- Dose escalation
- Pregnancy
- New drugs are in the pipe line
Conclusion

• IBD have wide spectrum of presentation.
• New treatment goals including mucosal healing.
• Biologics have changed the natural history of IBD.
• Primary care providers play integral role in managing IBD patients.
• Future is brighter for IBD patients.