Objectives

Today’s discussion will address the following topics:

- Risks and benefits of medication, surgery, and integrative treatments in inflammatory bowel diseases (IBD)
- Impact of treatment adherence on disease management and quality of life
- Talking with your health care team about your treatment plan
Treatment Strategy

“Top-down” Strategy
• Early, aggressive use of biologic as initial treatment
• Induces rapid clinical response
• May enhance quality of life

“Bottom-up” Strategy
• Standard, sequential treatment for remission and maintenance
• Cost-effective
• Minimal side effects

The IBD “Medicine Cabinet”

- Over-the-Counter
- Antibiotics
- Aminosalicylates
- Corticosteroids
- Immunomodulators
- Biologics
Over-The-Counter (OTC) Medications

- Address symptoms only
  - Anti-diarrheal agents
  - Laxatives
  - Pain Relievers
- NSAIDs may cause or worsen GI irritation
- Important: talk with your physician before taking any OTC medications

Antibiotics

Benefits
- Effective in pouchitis, perianal fistulas, abscesses, and in some patients with inflammatory CD

Risks
- Bacterial resistance
- Associated with flares
- Side effects include abdominal cramping, Clostridium Difficile, and diarrhea
## Antibiotics (cont)
- Ciprofloxacin (Cipro®. Proquin®)
- Metronidazole (Flagyl®)

### Over-the-Counter
- Antibiotics
- Aminosalicylates
- Corticosteroids
- Immunomodulators
- Biologics

## Aminosalicylates (ASAs)

### Benefits
- Useful in preventing relapses and maintaining remission
- Generally well-tolerated
- Formulated to release medication to specific areas of the bowel
- Most effective in treating UC, but weak treatment for Crohn’s disease

### Risks
- Few serious side effects

### Over-the-Counter
- Antibiotics
- Aminosalicylates
- Corticosteroids
- Immunomodulators
- Biologics

### Over-the-Counter
- Antibiotics
- Aminosalicylates
- Corticosteroids
- Immunomodulators
- Biologics
Aminosalicylates (ASAs) (cont)

- Balsalazide (GIAZO®, Colazal®)
- Mesalamine formulations
  - Delayed/Extended release tablets (Lialda®, Asacol HD®, Apriso™, Delzicol®)
  - Controlled release tablets (Pentasa®)
  - Rectal suspension (Rowasa®)
  - Rectal suppository (Canasa®)
- Olsalazine (Dipentum®)
- Sulfasalazine (Azulfidine®)

Aminosalicylates and Crohn’s Disease

Guidelines

American College Gastroenterology
“Sulfasalazine and mesalamine have not had consistent maintenance benefits after medical inductive therapy”

American Gastroenterological Association
Not recommended at all.

Over-the-Counter
Antibiotics
Aminosalicylates
Corticosteroids
Immunomodulators
Biologics
Corticosteroids

Benefits
– Initially effective in inducing remission

Risks
– Numerous, including
  • Infection
  • Psychosocial impact: sleep disturbance, mood swings
  • Neurological changes
  • Physical appearance: weight gain, skin fragility
  • Growth delays and bone loss

Corticosteroids (cont)
– Budesonide (Entocort®, UCERIS®)
– Methylprednisolone (Medrol®)
– Prednisone (Deltasone®)
– Prednisolone

Over-the-Counter
Antibiotics
Aminosalicylates
Corticosteroids
Immunomodulators
Biologics
Immunomodulators

- Quiet down the immune system

Benefits
- Steroid-sparing agents, used in maintenance
- Usually taken along with another medication to get patients into remission
- Once achieved, about 70% of adult patients stay in remission for at least one year

Risks
- Early reactions: fever, pancreatitis
- Adverse events: low white blood cells, elevated liver tests, infection (viral), lymphoma

Immunomodulators (cont)

- Azathioprine (Imuran®, Azasan®)
- 6-Mercaptopurine (Purinethol®)
- Cyclosporine (Neoral®)
- Methotrexate
- Tacrolimus (Prograf®)
Biologics

- “Designer drugs” made to specifically block inflammation or stimulate anti-inflammatory processes
- Similar or identical to the actual biologic chemicals that our body makes

Benefits
- Often administered to patients who do not or no longer respond to standard therapies
- 60% of patients respond to within a few doses

Risks
- Risk of infections, infusion or injection site reactions, psoriasis-like reaction

Over-the-Counter
Antibiotics
Aminosalicylates
Corticosteroids
Immunomodulators

Biologics (cont)

Anti-TNF
- Adalimumab (Humira®)
- Certolizumab pegol (Cimzia®)
- Infliximab (Remicade®)
- Golimumab (Simponi®)

Integrin Antagonist Receptors
- Natalizumab (Tysabri®)
- Vedolizumab (Entyvio™)
anti-TNF-α Mechanism of Action

α4β7 Antibody Mechanism of Action
Risks of Anti-TNFs and Immunomodulators

If 10,000 patients were treated for 1 year

<table>
<thead>
<tr>
<th>Event</th>
<th>Estimated Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHL (baseline)</td>
<td>2/10,000</td>
</tr>
<tr>
<td>NHL (on IMs)</td>
<td>4-9/10,000</td>
</tr>
<tr>
<td>NHL (on anti-TNF with prior IMs)</td>
<td>4-9/10,000</td>
</tr>
<tr>
<td>Hepatosplenic T-cell lymphoma</td>
<td>Unknown</td>
</tr>
<tr>
<td>Death from sepsis (lower for younger patients)</td>
<td>4/1,000</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>5/10,000</td>
</tr>
</tbody>
</table>

Anti-TNF, anti-tumor necrosis factor; IMs, immunomodulators; NHL, non-Hodgkin lymphoma. Table adapted from Siegel CA. In *Inflammatory Bowel Disease: Translating Basic Science Into Clinical Practice*. Wiley, 2010.

Baseline Risk of Lymphoma
Risk of Lymphoma on Anti-TNFs

Overall Medication Side Effects

Medication Considerations in Special Populations

- Each medication presents benefits and risks
- Children require special considerations
  - 10% of people affected by CD or UC are under the age of 18 and require individualized treatment
  - Few clinical trials have addressed efficacy and dosage in children
  - As such, treatment approaches for children are largely based on adult experience
- Some medications, including methotrexate, may be contraindicated in pregnant women
- Talk with your health care provider about your concerns
  - Be sure you understand potential side effects, what benefits to expect, and how long it may take for benefits to appear

Chance of Needing Surgery

Crohn’s Disease: 66%-75%  Ulcerative Colitis: 25%-40%
Goals of Surgery

– Surgery and medication can combine for better quality of life
– Primary goals of surgery
  • Alleviate complications
  • Alleviate symptoms
  • Achieve best possible quality of life
  • Bowel conservation

Elective and Emergency Surgery

<table>
<thead>
<tr>
<th>Crohn’s Disease</th>
<th>Ulcerative Colitis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Elective</strong></td>
<td><strong>Elective</strong></td>
</tr>
<tr>
<td>• Excessive bleeding in the intestine</td>
<td>• Failure of medication to control disease</td>
</tr>
<tr>
<td>• Formation of a fistula or abscess</td>
<td>• Dysplasia</td>
</tr>
<tr>
<td>• Failure of medication to control disease</td>
<td><strong>Emergency</strong></td>
</tr>
<tr>
<td>• Dysplasia</td>
<td>• Perforation of the colon</td>
</tr>
<tr>
<td>• Stricture</td>
<td>• Intestinal obstruction</td>
</tr>
<tr>
<td><strong>Emergency</strong></td>
<td><strong>Emergency</strong></td>
</tr>
<tr>
<td>• Perforation of the bowel</td>
<td>• Toxic megacolon</td>
</tr>
<tr>
<td>• Intestinal obstruction or blockage</td>
<td>• Excessive bleeding</td>
</tr>
</tbody>
</table>
Types of Surgery in IBD

**Crohn’s Disease**
- Strictureplasty
- Resection of small intestinal segment
- Colectomy (partial or complete)
- Proctocolectomy
- Diverting colostomy or ileostomy
- Unlike UC, CD cannot be cured with surgery

**Ulcerative Colitis**
- Proctocolectomy (removal of the colon and rectum)
  - With ileostomy
  - Restorative (ileoanal or J pouch)
  - Disease is “cured” once the colon is removed

Risks of Surgery

**Crohn’s Disease**
- Complications, as with any surgery
- Recurrence of symptomatic disease
- Psychological implications for those with a stoma

**Ulcerative Colitis**
- Complications, as with any surgery
- Potential complications specific to IPAA include:
  - Pouchitis
  - Small bowel obstruction
  - Pouch failure (8%-10% of patients)
  - Difficulty getting pregnant
- Psychological implications for those with ileostomy
Complementary and Alternative Medicine (CAM)

- According to National Center for Complementary and Alternative Medicine, several categories of CAM (practices can fit into more than one category)
  - Natural products (e.g., supplements and probiotics)
  - Mind and body medicine (e.g., meditation and acupuncture)
  - Manipulation and body-based practices (e.g., massage and spinal manipulation)
- Particularly suited for IBD patients because
  - Inability of conventional medicines to perfectly control disease
  - Difficult symptoms of IBD
  - Chronic nature of illness with need for chronic therapy
  - Side effects of conventional medication, especially steroids

Smoking

- Ulcerative Colitis
  - Protective against smoking
    - Former smoker
      - odds ratio 1.79 (1.37-2.34)
    - Current smoker
      - odds ratio 0.58 (0.45-0.75)
- Crohn’s Disease
  - Current smokers
    - odds ratio 1.76 (1.4-2.22)
Smoking Continued

Because We Live in Montana

• “Cannabis induces a clinic response with Crohn’s disease: a prospective placebo-controlled study”
  – 21 patients
  – 5 of 11 improved vice 1 of 10

• THC verse CBD (delta-9-tetrahydrocannabinol verse cannabidiol)
  – This study evaluated THC rich cannabis
  – Clinical experience improvement with CBD rich

PMID - 23648372
Clinical Trials.gov - NCT01040910
What Forms of CAM Do IBD Patients Use? (N=1332)

- 28% Special Diets
- 41% Herbal Supplements
- 16% Other
- 15% Alt. Medical Practices

Probiotics and IBD

- “Good” bacteria that restore balance to the enteric microbiota-bacteria in the intestines
- Limited studies on effectiveness- shown to prevent and treat pouchitis, improve UC at high doses, prevent relapses of C Diff and prevent antibiotic associated diarrhea.
- May be helpful in aiding recovery of the intestine and maintaining remission
- Various strains
  - VSL#3® *Escherichia coli* Nissle 1917 (Mutaflor®), *Lactobacillus acidophilus* (Flora-O®)
- Important to discuss with physician before initiating treatment

Other Alternatives

- Helminthic therapy (worms)
  - Pig whipworm used to treat both UC and CD
  - Show promise for symptom control and healing inflamed tissue
  - Clinical trials being conducted with FDA oversight
- Curcumin, extract from turmeric
  - Pilot study with UC and CD patients: ASA dosage reduction in UC patients and symptomatic improvement in CD patients\(^1\)
  - Large trial in quiescent UC: 2 relapses in treated group versus 8 in ASA-only group within 6-month treatment period\(^2\)
  - Larger scale prospective studies needed
- Fish oil supplements containing omega-3 fatty acids\(^3\)
  - May reduce pain and inflammation when added to standard therapy
  - Clinical trial results are inconsistent, no clear recommendation


Weigh the Risks and Benefits

- Complementary and alternative therapies continue to be popular
  - Some have good data to show they work
  - Some have good data to show they don’t
  - “Work” = relieve symptoms
- Important to seek out good data to minimize potential risk
  - Choose well-researched options
  - Consider the qualifications of the information resource
- Alternative therapies should not replace prescription medications!
- Tell your doctor everything you are taking
The Critical Role of Nutrition

- Including good nutrition in your diet is essential to quality of life and improved long-term outcomes
  - “Diet” = the food you eat on a daily basis
  - “Nutrition” = how your body uses nutrients from your diet
- No known diet alters inflammation
- Certain foods for individual patients may exacerbate symptoms during a flare

Recommended Foods

| Carbohydrates with more soluble fiber (oat brans, legumes, barley) | A daily multivitamin |
| Protein (eggs, lean meats, smooth nut butters) | Vitamin B12 (monthly injection may be given to patients with ileitis) |
| Well-cooked fruits and vegetables | Calcium, Vitamin D |
| Healthful fats (canola or olive oil) | Folic acid |

Good Nutritional Choices

- Good nutrition is key to:
  - Medications being more effective
  - Healing, immunity, and energy levels
  - Preventing or minimizing GI symptoms
Diet During a Flare

- A low-residue diet often prescribed
- Keep hydrated
- Eat smaller, more frequent meals
- Add nutrition supplements if appetite is poor
- Keep food diary: [www.ccfacommunity.org/ResourceCenter.aspx](http://www.ccfacommunity.org/ResourceCenter.aspx)

<table>
<thead>
<tr>
<th>Low-Residue Foods</th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>Grains</strong></td>
<td><strong>Fruits</strong></td>
</tr>
<tr>
<td>Plain cereals</td>
<td>Fruit juices (except prune)</td>
</tr>
<tr>
<td>White rice</td>
<td>Apple sauce</td>
</tr>
<tr>
<td>Refined pasta</td>
<td>Bananas</td>
</tr>
<tr>
<td>Avoid whole grains</td>
<td></td>
</tr>
<tr>
<td><strong>Vegetables</strong></td>
<td><strong>Meat and protein</strong></td>
</tr>
<tr>
<td>Potatoes (no skin)</td>
<td>Well cooked</td>
</tr>
<tr>
<td>Well cooked</td>
<td>Avoid beans, nuts, seeds</td>
</tr>
<tr>
<td><strong>Dairy</strong></td>
<td></td>
</tr>
<tr>
<td>As tolerated or additional sources</td>
<td></td>
</tr>
</tbody>
</table>

Diet During Flare
“Drugs don’t work in patients who don’t take them” – C. Everett Koop, MD

Adherence generally associated with improved outcomes

- Decreased risk of disease progression
- Reduced inflammation and increased healing of GI lining
- Possible decreased risk of colorectal cancer
- Evidence demonstrates patients who continue their maintenance medications are less likely to experience flares

Compliance

Big Brother is Watching
Recently had a patient denied Hep C treatment
Adherence is Complex and Multifactorial

- Missed appointments
- Barriers to care or medications
- Complexity of treatment
- Cost of medication, co-payment, or both
- Poor provider-patient relationship
- Patient's lack of belief in benefit of treatment
- Medication side effects
- Treatment of asymptomatic disease
- Inadequate follow-up or discharge planning
- Cognitive problems, especially depression

To Increase Treatment Adherence

- Remain informed and educated
- Simplify the treatment regimen if possible
- Continue taking the medications
- Find support for emotional and social issues
  - CCFA support groups, Community site: www.ccfacomunity.org
  - Medical social workers
  - Religious leaders
Treatment Options in IBD: Key Points

- Disease modifying drugs improve the quality of life in IBD
  - Very rare serious side effects
  - Benefits most likely outweigh the risks
  - Adherence is importance in maintaining remission
- Over-the-counter medications offer symptom relief
- CAM treatments used in combination with prescribed medications can offer symptom relief
  - Always tell your doctor everything you are taking
- Surgery can be a very good alternative for some patients
- Clearly understand the pros and cons so that you can make a decision that is right for you

References and Resources

References

CCFA website: www.ccfa.org/info/treatment

National Center for Complementary and Alternative Medicine:
  http://nccam.nih.gov

Regueiro MD. Managing IBD: Taking Charge of Your Disease webcast:
  http://programs.rmei.com/CCFAnagelIBDVL/

Siegel CA. Balancing the Risks and Benefits of Treatment webcast:
  http://programs.rmei.com/CCFA139VL/


Additional Resources

Treatment and Self-Management: http://www.ibdetermined.org/
Community Site: http://www.ccfacommunity.org/
Information Resource Center: 888.694.8872 or info@ccfa.org
Question-and-Answer Session