



Lecture 5



Drugs used in inflammatory bowel disease

Learning objectives

★ not given

- Additional Notes
- Explanation –Extra-
- **Important**

before starting, please check our [GIT block correction](#)

For any correction, suggestion or any useful information do not hesitate to contact us: Pharmacology434@gmail.com

What is IBD ?

is a group of inflammatory conditions of small intestine & colon
e.g : **crohn's disease** , **ulcerative colitis**.

	crohn's disease	Ulcerative colitis
Location	affect any part of the GIT, from mouth to anus	Restricted to colon & rectum
Distribution	(Patchy areas of inflammation (<i>Skip lesions</i> •	Continuous area of inflammation
Depth of inflammation	May be transmural, deep into tissues	Shallow, mucosal
complication	Strictures, Obstruction , Abscess , Fistula	Toxic megacolon , colon cancer

Causes:

1-Unknown

2-autoimmune

3-genetic

Symptoms :

- Abdominal pain
- Vomiting
- Diarrhea
- Rectal bleeding
- Weight loss

Complication:

- Anemia
- Abdominal obstruction (crohn's disease)
- Mega colon
- Colon cancer

goals of therapy :

*No complete recovery

- 1- Achievement of remission
- 2- prevention of disease flares (maintenance)

Stepwise therapy : (if the 1st drug is not effective we move to the next)

1- Amino salicylic acid compounds(5-AsA) or aminosalicylate

2- Glucocorticoids

3- immunomodulators

4- Biological therapy (TNF- α inhibitors)

5- surgery in severe cases

1. 5-amino salicylic acid compounds (5-ASA) Aminosalicylates

M.O.A

Have **topical anti-inflammatory** * action due to:

- inhibition of prostaglandins and leukotrienes.
- decrease neutrophil chemotaxis.
- Antioxidant activity (scavenging free radical production).

* it has to be in contact with the inflamed area

Pharmacokinetic

- 5-ASA itself is absorbed from the proximal small intestine.
- Different formulations are used to overcome rapid absorption of 5-ASA from the proximal small intestine.
- All aminosalicylates are used for **induction** and **maintenance** (prophylaxis) of remission

Different formulations of aminosalicylates are:

The major differences are in **mechanism** and **site** of delivery

1- Azo compounds (5-ASA + amino acid connected by azo bond (N=N))

- A. Sulfasalazine : 5-ASA+ sulphapyridine
- B. Olsalazine : 5-ASA+ 5-ASA
- C. Balsalazide : 5-ASA+ inert carrier

- **Azo structure reduces absorption of 5-ASA in small intestine.**
- **Azoreductase enzyme produced by bacterial flora cleaves the azo bond and releases ASA in the terminal ileum and colon.**

2- Mesalamines (5-ASA but in another formulation)

- A. Asacol
- B. Pentasa
- C. Canasa
- D. Rowasa

1. Aminosalicylates

	1- Azo compounds	2- Mesalamines
drugs	Sulfasalazine (Azulfidine)	Asacol,Pentasa,canasa,Rowasa
P.C	<p>A combination of 5-ASA + sulfapyridine , pro-drug, given orally (enteric coated tablets) , little amount is absorbed(10%)</p> <p>In the terminal ileum and colon, sulfasalazine is broken by azoreductase into:</p> <ul style="list-style-type: none"> ● 5-ASA)not absorbed, active moiety acting locally) ● Sulphapyridine (absorbed, <u>causes most of side effects</u>). 	<p>oral formulations: secondary to PH</p> <ul style="list-style-type: none"> - Asacol : dissolve at PH 7 (controlled release) - Pentasa : microgranules that release 5-aSA throughout the S.I <p>Rectal formulations:</p> <ul style="list-style-type: none"> - Canasa (suppositories) تحاميل - Rowasa (enema) حقنه شرجيه
ADV	side effect of sulfasalazine : (crystalluria, BM depression, megaloblastic anemia, folic acid, impairment of male fertility (oligospermia) / side effect of 5-ASA : interstitial nephritis	Sulfa free : useful in patient sensitive to sulfa drugs well tolerated : less side effect
Uses	<p>1-induction & maintenance of remission in mild to moderate IBD(<u>1st line treatment</u>)</p> <p>2-rheumatoid arthritis (<u>Sulfasalazine</u> only) 3-rectal* formula used in U.proctitis & proctosigmoiditis</p> <p>*5-ASA will be released in distal colon</p>	

2. Glucocorticoids

preparation	drugs	pharmacokinetics	MOA	uses
oral	-prednisone -prednisolone - Budesonide*	Higher rate of absorption . more adverse effects compared to rectal administration. Budesonide* (A potent synthetic prednisolone analog-.Given orally (controlled release tablets) so release drug in ileum and colon. -Low oral bioavailability(10%) is subject to extensive first pass metabolism)	-Inhibits phospholipase A2. -inhibits gene transcription of No synthase, cyclo-oxygenase- 2 (cox-2). -Inhibit production of inflammatory cytokines.	-acute flares of disease (moderate & severe active IBD) not effective as prophylactic. oral glucocorticoids: is commonly used in active condition Rectal glucocorticoids: are preferred in IBD involving <u>rectum or sigmoid colon</u> Budesonide* : treatment of active mild to moderate crohn's disease involving ileum and proximal colon.
parenteral	-hydrocortisone -methyl prednisolone			Extra: -Asthma -rheumatoid arthritis -antiemetic during cancer chemotherapy -immunosuppressive drug for organ transplants
rectal	-Hydrocortisone	As enema or suppository. give topical. less absorption rate than oral. minimal side effects & maximum tissue effects.		

Immunomodulators

Are used to induce remission in IBD in **active or severe conditions** or **steroid dependent** or **steroid resistant** Patients and to **maintain remission**

drugs	Purine analogs (azathioprine & 6-mercaptopurine)	Methotrexate Orally, S.C., I.M
MOA	Azathioprine is pro-drug of 6-mercaptopurine -Inhibit purine synthesis of DNA, RNA, and proteins. -It may decrease proliferation of immune cells, which lowers autoimmune activity.	(a folic acid antagonist) Inhibits dihydrofolate reductase required for folic acid activation (tetrahydrofolate)
Uses	Induction and maintenance remission in IBD	Used to induce and maintain remission. *Inflammatory bowel disease . *Rheumatoid arthritis. *Cancer.
ADV	- Bone marrow depression :(leucopenia, thrombocytopenia) - Gastrointestinal toxicity. - Hepatic dysfunction. - Complete blood count & liver function tests are required in all patients (the best advance to the patient)	- Megaloblastic anemia - Bone marrow depression

Monoclonal antibodies used in IBD (TNF- α inhibitors) (suffix mab)

Infliximab

Pharmacokinetics

- a chimeric mouse-human monoclonal antibody
- 25% murine – 75% human.
- TNF- α inhibitors
- Inhibits soluble or membrane –bound TNF- α located on activated T lymphocytes.
- Given **intravenously** as infusion (5-10 mg/kg).
- has long half life (8-10 days)
- 2 weeks to give clinical response.

Uses

- In moderate to severe active Crohn's disease and ulcerative colitis.
- Patients not responding to immunomodulators or glucocorticoids.
- Treatment of rheumatoid arthritis
- Psoriasis الصدفية

<p>ADV</p>	<ul style="list-style-type: none"> - Acute or early adverse infusion reactions (Allergic reactions or anaphylaxis in 10% of patients). - Delayed infusion reaction (serum sicknesslike reaction, in 5% of patients). - This reaction can be reduced by Pretreatment with diphenhydramine, acetaminophen, corticosteroids is recommended. - Infection complication (Latent tuberculosis, sepsis, hepatitis B) all of these disease will show because the drugs is suppressent for immunity. - Loss of response to infliximab over time due to the development of antibodies to infliximab. - Severe hepatic failure. - Rare risk of lymphoma (all Immunosuppressive Agents have this effect) 	
	<p>Adalimumab (HUMIRA)</p>	<p>Certolizumab pegol (Cimzia)</p>
<p>Pharmacokinetics</p>	<ul style="list-style-type: none"> •Fully humanized IgG antibody to TNF-α •Adalimumab is TNFα inhibitor •It binds to TNFα, preventing it from activating TNF receptors. •Has an advantage that it is given by subcutaneous injection 	<ul style="list-style-type: none"> – Fab fragment of a humanized antibody directed against TNF-α – Certolizumab is attached to polyethylene glycol to increase its half-life in circulation.
<p>uses</p>	<p>is approved for treatment of, moderate to severe Crohn’s disease, rheumatoid arthritis, psoriasis.</p>	<ul style="list-style-type: none"> - Given subcutaneously for the treatment of Crohn's disease - rheumatoid arthritis

MCQs

1: B
2: A
3: C
4: A
5: B

1-what is the first line treatment of IBD?

- A-Methotrexate
- B-Asacol
- C-Budesonide
- D-azathioprine

2-A patient suffering from prostate cancer and he is also having IBD which one of the following is drug of choice?

- A-Methotrexate
- B- Infliximab
- C- azathioprine

3-A patient comes with IBD that involving the ileum and proximal colon. What is the drug of choice?

- A-Sulfasalazine
- B-infliximab
- C-Budesonide
- D-Hydrocortison

4-patient on treatment of IBD comes with oligospermia which drug he use?

- A-Sulfasalazine
- B-canasa
- C-Methotrexate

5-Which one of the following is a Clinical use of infliximab?

- A-Asthma
- B-Crohn's disease
- C- IBD with diarrhea
- D- IBD with constipation

Good luck!

Done by Pharmacology team

Asmaa Rusaies
Elham Alghamdi



For any correction, suggestion or any useful information do not
hesitate to contact us: Pharmacology434@gmail.com