

#### وَأَمَا مَا يَنفَعُ النَّاسَ فَيَمَكُثُ فِي ٱلْأَرْضِ

but as for that which benefits the people, it remains on the earth.

Quran 13:17 (Surah ar-Ra'd)







- To impart evidence based research oriented medical education
- To provide best possible patient care
- To inculcate the values of mutual respect and ethical practice of medicine













### CNS, PSYCHIATRY & MSK MODULE 4th year MBBS

#### LGIS ANTI-GOUT DRUGS

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<u>Sources</u>

Bertram G. katzung Basic & Clinical Pharmacology 15th Edition Goodman and Gilman's The Pharmacological Basis of Therapeutics 13th edition



#### LEARNING OBJECTIVES



- Classify Drugs used in the treatment of Gout
- Describe the role of Corticosteroids in the treatment
- Describe the role of NSAIDs in the treatment of Gout















#### CAUSES OF HYPERURICEMIA DECREASED RENAL EXCRETION

- > RENAL FAILURE> DRUGS
  - ✤ DIURETICS
  - PYRIZINAMIDE
  - LOW DOSE ASPIRIN
- LACTIC ACIDOSIS
  - ALCOHOL
  - ✤ EXERISE
  - VOMITING
  - **STARVATION**

#### **INCREASED PRODUCTION OF URIC ACID**

- \* MYELOPROLIFERATIVE DISORDERS e.g. POLYCYTHEMIA
- LYMPHO- PROLIFERATIVE DISORDERS e.g. CLL
- \* PSORIASIS

#### URIC ACID LEVELS

 MALES:
 2.5–7.0 mg / dl

 FEMALES:
 1.5–6.0 mg/dL

Vertical Integration



#### High Purine Diet







#### COLCHICINE



- Alkaloid isolated from Colchium autumnale
- Absorbed readily after oral administration
- Peak plamsa levels in 2hrs
- Half life 9hrs
- Metabolites excreted in intestines and urine





#### **Mechanism of action**



- Acute attack of gout started by precipitation of urate crystals in synovial fluid
- Chemotactic factors produced
- Granulocyte migration which phagocytose crystals releasing glycoprotein increasing inflammation









- Increased lactic acid from inflammatory cells→↓ pH→ more crystals precipitated
- Lysosomal enzymes released causing more joint destruction







- Colchicine inhibits release of glycoproteins by binding to fibrillar protein tubulin→inhibiting granulocyte migration
- Causes metaphase arrest by binding to microtubules of mitotic spindles
- Increases gut motility through neural action



#### **Adverse effects**



- Diarrhea, nausea, vomiting, abdominal pain
- Hepatic necrosis
- Acute renal failure
- DIC
- Hair loss
- Bone marrow depression
- Overdose → bloody diarrhea, burning throat pain, shock, hematuria, oliguria









- First line of treatment in gout
- Inhibit prostaglandin synthesis
- Inhibit urate crystals phagocytosis
- Low dose aspirin is not used



#### **Uricosuric agents**



#### • <u>Probenecid:</u>

- Highly lipid soluble organic compound
- Inhibit tubular secretion of penicillin
- Competitively inhibits OATP (Organic anion transporting polypeptides) at all sites
- Uric acid largely reabsorbed by active transport, while less of it is secreted
- Only 1/10<sup>th</sup> is excreted in urine



#### **Adverse effects**



- GIT irritation(dyspepsia)
- Nephrotic syndrome
- Aplastic anemia







#### • <u>Sulfinpyrazone:</u>

- Pyrazolone derivative
- Neither analgesic nor anti-inflammatory action
- Inhibits tubular reabsorption of uric acid
- Smaller doses can decrease urate excretion
- Inhibits metabolism of sulfonylureas and warfarin



#### **Adverse effects**



- GIT irritation(dyspepsia)
- Nephrotic syndrome
- Aplastic anemia



#### **Xanthine oxidase inhibitor**



- Allopurinol
- Hypoxanthine analogue synthesized as purine antimetabolite for cancer chemotherapy
- No antineoplastic activity





#### **Pharmacokinetics**



- 80% absorbed by oral administration
- Half life 1-2hrs
- Metabolized by xanthine oxidase resulting compound alloxanthin, retains the capacity of inhibition so given once daily



spiral



#### Pharmacodynamics



- Purine ribonucleotides not incorporated in to nucleic acids and derived from nucleic acid degradation are converted to xanthine and hypoxanthine and oxidized to uric acid
- Allopurinol blocks the last step causing reduction in overall urate burden
- More soluble xanthine and hypoxanthine amount increased



#### **Drug interactions**



- Inhibits degradation of 6mercaptopurine, azathioprine, warfarin and theophylline
- Probenecid shortens the half-life of alloxanthin and allopurinol prolongs half life of probenecid
- Rashes in pts. Taking allopurinol if ampicillin is administered
- Iron therapy not recommended in pts.on allopurinol



#### **Adverse effects**



- GIT intolerance
- Peripheral neuritis
- Necrotizing vasculitis
- Bone marrow suppression
- Interstitial nephritis



#### Febuxostat



- Nonpurine xanthine oxidase inhibitor
- Halflife 4-8hrs
- Selective inhibitor of xanthine oxidase therefore do not affect other enzymes in purine and pyrimidine synthesis
- <u>Adverse effects</u>:
- Diarrhea, headache
- Risk of cardivascular events







spiral





#### Non-pharmacological Treatment for Chronic Gout:

1. Avoid high-purine foods 2. Avoid alcoholic, particularly beer 3. Avoid sodas and other beverages with high-fructose corn syrup 4. Use food that increase excretion of uric acid 5. Good hydration with water (≥8 glasses of liquids daily) 6. Weight reduction

#### LOW PURINE DIET:



CHEDDAR CHEESE: Enhances excretion of uric acid



BANANA: RICH IN POTASSIUM:



Integration with family medicine



## Glucocorticoids



- For severe symptomatic gout
- Intra-articular, sytemic and subcutaneously given in refractory pts.





# **Interleukin-1** inhibitors



- Anakinra
- Canakinumab,rilonacept

Acute gout, pts.resistant to traditional therapies



RESEARCH



 Lin, Z.; Gupta, J.K.; Maqbool, M.; Kumar, K.; Sharma, A.; Wahi, N. The Therapeutic Management of Chemical and Herbal Medications on Uric Acid Levels and Gout: Modern and Traditional Wisdom. *Pharmaceuticals* 2024, *17*, 1507. https://doi.org/10.3390/ph17111507





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Beneficence

The principle of beneficence is the obligation of physician to act for the **benefit of the patient** and supports a number of moral rules to protect and defend the right of others, prevent harm.



TAKE HOME MESSAGE

Vertical Integration





# جز ألم الله هير المحكم بي المحكم بي المحكم بحد منه العظيم معان الله المعظيم أحباب الله