

Drugs used in treatment of anaemia

❖ Learning objectives

- ❖ Iron preparations
- ❖ indications of iron
- ❖ adverse effects
- ❖ folic acid
- ❖ Vitaminb12
- ❖ Haemopoietic growth factors.
- ❖ Classification:-

Drugs used in treatment of anaemia

❖ **Definition:** - blood Hb is below the normal.

❖ **Classification:-**

1-Microcytic anaemia: - low MCV; due to iron deficiency.

2- Normocytic anaemia: - normal MCV; either due to blood loss or chronic disease.

3- Macrocytic anaemia: - MCV larger than normal occur due to B12 or folate deficiency.

Pharmacokinetic of iron:-

- ❖ Total body iron 3-5gm (in male more than female)
- ❖ 66% of this iron is in Hb of blood ; iron cross the intestinal mucosal cell by active transport ;the rate of iron absorption is depend on storage form of iron (Ferritin) and rate of erythropoiesis ;transport from intestinal mucosal cell to the plasma via transferrin , Iron binds to a protein (apoferritin) and form a complex called (Ferritin)that stored in intestinal mucosal cells and in macrophages ,liver, spleen and bone .
- ❖ there is no mechanism for excretion of iron ,small amount of iron are lost by exfoliation of intestinal mucosal cell ,and trace amount excreted in bile ,urine and sweat (this represented 1 mg /day)
- ❖ Ascorbic acid and other acid increase absorption of iron while tea ,bran, Desferrioxamine and other chelating agents like Tetracycline ,Penicillamine ,Ciprofloxacin ,L-dopa , Carbidopa , are decrease absorption of iron .

Clinical indications of iron

❖ Iron deficiency anaemia is the only indication for iron therapy.

1- Dietary iron deficiency.

2- Chronic blood loss.

3- During pregnancy; where extra demand of iron is required from the 4th month of Gestation.

4- Premature baby ;(iron established at 36 weeks of gestation).

5- Various abnormalities of GIT as mal absorption syndrome.

6- Early treatment of severe pernicious anaemia with B12.

Adverse effects of oral iron therapy:-

- 1-Bad taste.
- 2- Black stool.
- 3- Irritation of gastric mucosa lead to nausea, vomiting and heartburn.
- 4- Irritation of intestinal mucosa lead to diarrhea or constipation.

These side effects are dose related may be overcome by:-

- 1-decrease the dose
- 2- Taking the tablets with or after the meals.
- 3- Trying different iron salt.

Parenteral iron therapy:-

❖ Parenteral iron therapy indicated only when:-

- 1-Oral iron is not tolerated (vomiting, epigastric pain, constipation or diarrhea ...)
- 2- Failure to absorb oral iron e.g. mal absorption syndrome.
- 3- Noncompliance.
- 4- Severe deficiency with chronic bleeding.

❖ There are 2 types of parenteral iron therapy:-

1-Iron dextran (Inferon)^R

2-Iron sorbitol –citrica (Jectofer)^R :-

Iron dextran (Inferon)^R

- 1-**high molecular weight
- 2-** Can give I.M., and I.V.
- 3-** If given I.M.10-30 %locally bound (not available to use.) .
- 4-** Its absorption through the lymphatic.
- 5-** Not bound to transferrin.
- 6-** Not excreted.
- 7-** Taken up by macrophages and stored in reticuloendothelial cells.

Iron sorbitol –citrica (Jectofer)^R :-

- 1-**low molecular weight.
- 2-** Given I.M.
- 3-** Not locally bound.
- 4-** Directly into circulation.
- 5-** Bind to transferrin and may saturate it.
- 6-** 30% excreted in urine.
- 7-** Directly available for erythropoiesis.

Adverse effects of I.V. preparation of iron:-

- 1-**Headache, nausea, vomiting with metallic taste.
- 2-** Allergic reaction as pyrexia, flushing; sweating and palpitation.
- 3-** May cause thrombophlebitis and embolism.
- 4-** Irritation at site of injection, but not like I.M.
- 5-** An anaphylactic reaction may lead to vascular collapse and death.

Adverse effects of I.M. preparation of iron

- 1-** Pain at site of injection.
- 2-** Very irritant and stain the skin
- 3-** Very rare reports of malignant tumor (skin sarcoma) .
- 4-** Non sorbitol-citrica complex is irritant to kidney tubules.

Iron toxicity

1-Acute overdose

mainly occur in children; Desferrioxamine (dysferal)^R half-life is 6hs. ; it is iron chelating agent ; its straight chain twins around iron and form a non toxic complex of great stability ((ferrioxamine)) which is excreted in urine and give red-orange color .

Side effects:-

Rare, but chronic use may cause cataract, retinal damage, deafness, anaphylactic reaction.

2- Chronic iron overload occur due to-

A-Excessive Parenteral iron therapy.

B- Repeated blood transfusion as in treatment of Thalassemia.

C- Could be inherited as excessive absorption syndrome of iron called hemochromatosis.

Treatment:

1- Venesection (phlebotomy), in absence of anaemia (450ml/wk.)

2- Desferrioxamine; S.C. infusion

Vitamin B12

- The normal daily requirement of vit.B12 are only 2 microgram ; it would take about 5 years for all of stored vit.B12 to be exhausted
- there are 2 factors necessary for absorption vitB12 ;Extrinsic factor (in food) and intrinsic factor (glycoprotein) secreted by parietal cells of stomach ; absorption of vitB12 only when it combined with intrinsic factor ,this complex absorbed in the distal ileum .
- The cobalamin is active cellular coenzyme is necessary for demethylation of tetrahydrofolate (THF) and thus for DNA synthesis .

Deficiency and indications Vit B12

- Deficiency extrinsic ,intrinsic factors or their receptors defect lead to B12 deficiency and this lead to :-
- 1-Megaloblastic anaemia .
- 2- Degeneration of brain ,spinal cord , and peripheral nerves .
- 3- Abnormalities of epithelial tissue especially in GIT .
- Indications :-
- 1-Pernicious anaemia (Atrophic gastric mucosa) .
- 2- Mal absorption syndrome due to disease or drugs
Neomycin ,Colchicine' .

Folic acid

Folic acid reductase

DHFA reductase

- ❖ Folic acid $\rightarrow \rightarrow \rightarrow \rightarrow \rightarrow \rightarrow \rightarrow \rightarrow \rightarrow$ Di hydro folic acid(DHFA) $\rightarrow \rightarrow \rightarrow \rightarrow \rightarrow \rightarrow \rightarrow \rightarrow \rightarrow$ Tetra hydro folic acid(THFA)
- ❖ THFA is important in nucleotide bases synthesis ; deficiency of THFA lead to decrease synthesis of amino acid, purine , pyrimidine and lead to decrease DNA and RNA and lead to megaloblastic anaemia .

❖ Indications :-

- 1-Megaloblastic anaemia that occur due to pernicious anaemia ,increase body requirement for folic acid during pregnancy or due to dietary folic acid deficiency ; Folic acid should not be used alone because vitB12 is needed for the conversion of folic acid to tetrahydrofolate .
- 2- Malabsorption syndrome .
- 3- Prevention of neural tube defect (spina bifida) .
- 4- With antiepileptic drugs e.g. Phenytoin .
- 5- Methotrexate toxicity .
- 6- High doses of Methotrexate with folinic acid in certain malignancies .

Haemopoietic growth factors

1-Epoetin alpha :-

- recombinant derived of human erythropoietin that secreted mainly from kidney lead to increase proliferation and differentiation of erythrocyte precursors ;it's used for treatment of anaemia of chronic renal failure .
- **Side effects**
 - 1) dose dependent hypertension and hypertensive encephalopathy, may occur due to increase peripheral vascular resistance or due to increase blood viscosity .
 - 2) Iron deficiency anaemia .

2- Colony stimulating factors include

- **A)** Recombinant of human granulocyte stimulating factor (G-CSF) e.g. Filgrastin and Lonograstin
- **Indications :-**
 - 1- Neutropenia from cytotoxic drugs .
 - 2- Bone marrow transplant to decrease infection .
 - 3- Aplastic anaemia .
 - 4- Acquired immune deficiency syndrome (AIDS) .
- **Side effects :-** dysuria and splenomegaly .

B) Recombinant of human granulocyte – macrophage –colony stimulating factors

- **B) Recombinant of human granulocyte –macrophage – colony stimulating factors (G M-CSF) e.g. molgramostim Sargramostim .**
- **Indications :-**
 - 1-Neutropenia from cytotoxic drugs .
 - 2- Bone marrow transplant to decrease infection .
 - 3- Aplastic anaemia .
 - 4- Acquired immune deficiency syndrome (AIDS) .
- **Side effects :-** Pleural and pericardial effusion in high dose .