

دفععة يقين 2025

HLS

PHARMACOLOGY

LECTURE

2

BY

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EDITED

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تعديل



#معكم_خطوة_بخطوة

Pharmacology-lecture 2- Drugs for Anemia:

3) vit B12 deficiency anemia :

-vit B12 plays a vital role in folic acid functions so it's deficiency will keep folic acid at inactive (methylated) form and can't be used in DNA synthesis (by decreasing purine and pyrimidine synthesis), so RBCs will decrease and Hb also so anemia will develop.

• Causes of vitamin B 12 deficiency:

1. Low dietary intake

2. Malabsorption (e.g., pernicious anemia: ↓ intrinsic factor)

3. Loss of activity of intestinal B 12 receptor

4. Gastric resection

فيتامين B12 يدخل في تحويل الـ folic acid لشكله الفعال والتي يمكن انه تستخدمه لتكوين النيوكليوتيدات للـ DNA ولكن في حال نقص الـ B12 راح يضل الـ folic acid في شكله الخامل او الغير فعال وما راح يستخدم لتكوين الـ DNA وبالتالي يقل الـ proliferation للخلايا ومنها الـ RBCs ويحصل انيميا .

-أسباب نقص vitB12 :

- 1)نقصه بسبب عدم تناول طعام يحتوي عليه بكمية كافية يكون عالي باللحوم الحمراء.
- 2)او خلل في عملية امتصاصه من الجسم حيث يتم امتصاصه في الـ ileum وعملية امتصاصه معقدة شوي حيث انه يحتاج بروتين يفرز من المعدة يسمى intrinsic factor حتى يتم امتصاصه ونقص هذا الـ factor يقلل امتصاص الـ vit B12 ويعمل ما يسمى الانيميا الخبيثة او حتى من الاسباب التي تقلل امتصاص الـ vit B12 استئصال او ازالة الجزء المسؤول عن امتصاصه بالجسم الـ ileum بواسطة عملية جراحية.

Loss of activity of intestinal B 12 receptor (3

4)استئصال المعدة مثل في حالة سرطان المعدة راح يقلل من افراز الـ intrinsic factor

وبالتالي يقل الvit B12 .

-نقص الfolic acid ونقص الvit B12 الاثنين يعملوا نفس النوع من الانيميا وهو
الmegaloblastic anemia

لكن ممكن نميز بينهم بواسطة علامات معينة تظهر في حالة نقص الvit B12 مثل
الmental problems مثل brain fog التشوش وقلة التركيز او حتى علامات psychotic
مثل الilusion الوهم والhallucination الهلوسة ويعمل مشاكل بالشعر مثل خسارة الشعر
ويعمل كمان peripheral neuropathy (وهو شائع عند مرضى السكري) ويعمل
fatigue and chronic pain واكيد الانيميا.

-شو بصير لو استخدمنا الfolic acid لعلاج الانيميا الي سببها نقص الvit B12 بما انه نفس
نوع الانيميا والاثنين عملهم اله علاقة ببعض؟ الي بصير انه الfolic acid بعالج الانيميا
ولكن الاعراض الي من نقص الvit B12 راح تضل موجودة
.Reverse the hematologic problem but masks vitamin B deficiency

-Ttt: Cyanocobalamin and Hydroxocobalamin (vit B12):

Orally: for dietary deficiencies.

IM, or deep subcutaneously: pernicious anemia, malabsorption, ileal
Resection.

1)Hydroxocobalamin (IM): rapid response.

2)Cyanocobalamin: daily (high oral doses) or monthly (parenteral).

**Most of megaloblastic anemia ttt is combination of folic acid and vit
B12.

4)Erythropoietin and Darbepoetin:

- cells secret erythropoietin called : Peritubular cells in the kidney

-Functions of erythropoietin :

1. Stimulates the differentiation of proerythroblasts.
2. Promotes the release of reticulocytes.
3. Initiates hemoglobin formation.

- Darbepoetin has :

- 1) long acting
- 2) Half-life: 3 times > epoetin alpha

Q:Both epoetin alpha and darbepoetin are NOT useful for the treatment of acute anemia. Why?

Bec they need long time to generate RBCs in bone marrow (120 days), and due to their adverse effects.

- Adverse effects for both (epoetin alpha and darbepoetin):

- Edema
- Hypertension
- Arthralgia
- Thrombosis/increased risk of death (if used to target hemoglobin levels over 11 g/dL).

ال erythropoietin يتم تصنيعه دوائياً بواسطة بكتيريا معينة ويسمى Human recombinant erythropoietin

((epoietin alpha : ويستخدم بالحالات :

1) Anemia due to end-stage renal disease

2) Anemia due to HIV infection

3) Anemia due to bone marrow suppression

4) Anemia due to malignancy وفي حالة العلاج الكيماوي حيث يدمر خلايا نخاع العظم فيقل تكوين خلايا الدم.

ويتم اعطائه IV ويعطى ايضاً in combination with iron supplements

Recommendations for patients receiving epoetin alpha or darbepoetin :

1 ,2 and 3 all are to avoid thrombosis

- Minimum effective dose that does not exceed hemoglobin level of 12g/dL.

- Minimum effective dose that does not rise hemoglobin level of 1g/dL over a 2-week period.

- If hemoglobin levels rise above 10 g/dL dose must be reduced.

Neutropenia:

-case in which neutrophils are reduced to less than normal , so leading to increase risk to infections especially bacterial ones.

Agents Used to Treat Neutropenia:

- Filgrastim, tbo-filgrastim and pegfilgrastim: granulocyte colony-

stimulating factors (G-CSF)

- Sargramostim: granulocyte-macrophage colony-stimulating factors

(GM-CSF)

- ❖ Stimulate granulocyte production in the bone marrow.

- Pharmacokinetics:

- Filgrastim and sargramostim: subcutaneous, IV

- tbo-filgrastim and pegfilgrastim: subcutaneous ONLY

- Filgrastim, tbo-filgrastim and sargramostim: once daily 24-72 hours for 3 days after chemotherapy until ANC is 5000-10000/ μ L.

- Pegfilgrastim: single dose 24 hours after chemotherapy (long-acting).

Adverse effects: Bone pain.

**ANC= absolute neutrophil count.

هناك نسبة من المرضى بعد العلاج الكيماوي يحدث عندهم ما يسمى " post chemotherapy neutropenia" ومن اعراضه fever , infections , neutropenia .

5) Hydroxyurea :

-specific to treat sickle cell anemia .

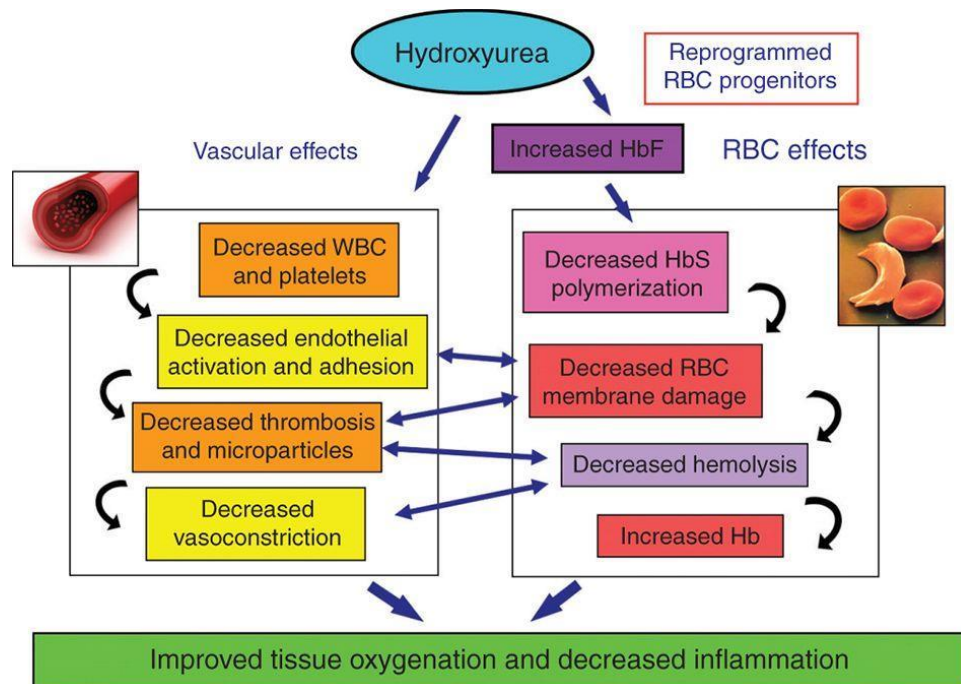
-its given orally.

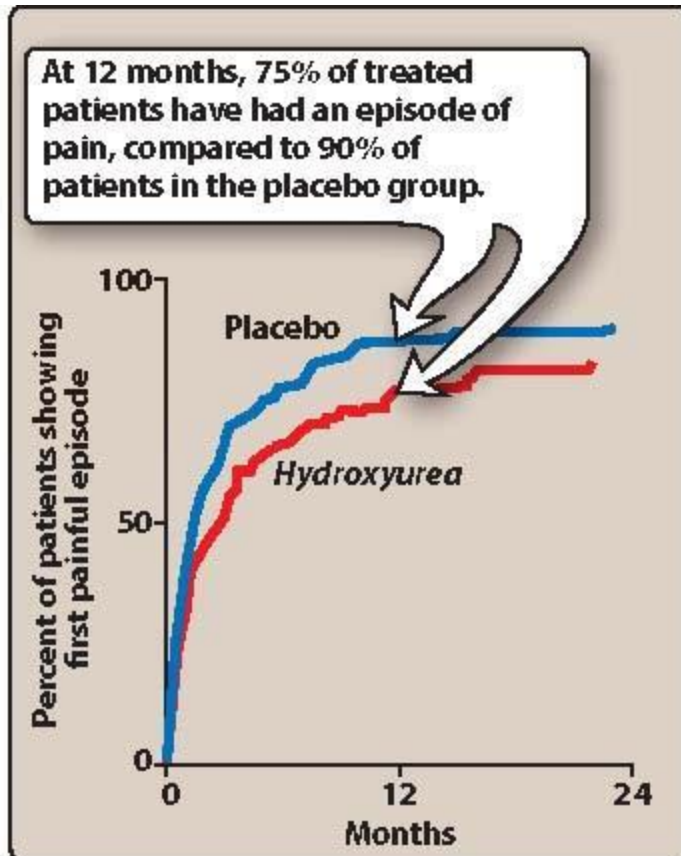
-it works as Ribonucleotide reductase inhibitor(in which it inhibits Ribonucleotide reductase which is used in nucleotides synthesis) and

interferes with DNA synthesis and it was used at ttt to cancer.

-MOA:

Increases HbF levels → dilutes HbS → reduces polymerization of HbS
→ reduce sickling and painful crises, it needs 3 to 6 months .





Hydroxyurea is usually prescribed by a hematologist, using rigorous selection criteria. Indications for hydroxyurea include the following:

- Frequent painful episodes (six or more per year)
- History of acute chest syndrome
- History of other severe vaso-occlusive events
- Severe symptomatic anemia
- Severe unremitting chronic pain that cannot be controlled with conservative measures

- History of stroke or a high risk for stroke

- Adverse effects: Myelosuppression, Cutaneous vasculitis.

MEDICATION	ADVERSE EFFECTS	DRUG INTERACTIONS	MONITORING PARAMETERS
TREATMENT OF ANEMIA			
<i>Cyanocobalamin/B₁₂</i>	Injection site pain Arthralgia Dizziness Headache Nasopharyngitis Anaphylaxis	Proton pump inhibitors—may decrease oral absorption of vitamin B ₁₂	Vitamin B ₁₂ Folate Iron
<i>Erythropoietin/epoetin alfa</i>	Edema Pruritus Nausea/Vomiting Hypertension CVA Thrombosis	<i>Darbepoietin alfa</i> —duplication of therapy can lead to increase adverse events	H/H Serum ferritin Blood pressure
<i>Darbepoietin alfa</i>	Edema Dyspnea Hypertension CVA Thrombosis	<i>Epoetin alfa</i> —duplication of therapy can lead to increase adverse events	H/H Serum ferritin Blood pressure
<i>Folic acid</i>	Bad taste in mouth Nausea Confusion Irritability	<i>Cholestyramine</i> —may interfere with absorption	CBC Serum folate
<i>Iron</i>	Pruritus N/V/D Headache Anaphylaxis	<i>Deferoxamine</i> —chelates iron <i>Dimercaprol</i> —chelates iron	H/H Serum iron TIBC Transferrin Reticulocyte count
TREATMENT OF SICKLE CELL ANEMIA			
<i>Hydroxyurea</i>	Myelosuppression Skin ulcer Secondary leukemia	HIV medications— <i>hydroxyurea</i> can decrease CD4 counts Salicylates—increased bleeding risk <i>Probenecid</i> —↑ uric acid	CBC
<i>Pentoxifylline</i>	Nausea/Vomiting Thrombocytopenia Jaundice Anaphylaxis	<i>Ketorolac</i> (contraindicated)—increased bleeding risk <i>Ginkgo biloba</i> —increased antiplatelet effect	CBC

CVA=cerebrovascular accident, H/H=hemoglobin and hematocrit, CBC=complete blood count, N/V/D=nausea/vomiting/diarrhea, TIBC=total iron binding capacity

*This table summarizes all anemia ttt.