Doctor.021

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HLS

PHARMACOLOGY

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Hematopoietic Growth Factors

- **The hematopoietic growth factors are glycoprotein hormones that regulate the proliferation and differentiation of hematopoietic progenitor cells in the bone marrow.**

Erythropoietin

We give the patients the

- Formed by the kidney in response to tissue hypoxia (severe anemia).
- Recombinant human Erythropoietin is available for use (epoetin alpha).

Pharmacodynamics:

1. It stimulates erythroid proliferation and differentiation by interacting with specific receptors on red cell progenitors.
2. It induces release of reticulocytes from bone marrow.

We can't give the patient EPO , if we have iron deficiency (we can't synthesize RBC without iron) , also if the disorder is in the factory itself (the bone marrow)

Erythropoietin

3. It corrects the anemia (provided that bone marrow response is not impaired by iron deficiency, primary bone marrow disorders, or bone marrow suppression from drugs or chronic diseases).
4. Normally, an inverse relationship exists between the hematocrit and erythropoietin level. This is NOT true in anemia of chronic renal failure.

A lot of chemotherapeutic agents have a side effect of bon marrow suppression.

Serum EPO(erythropoietin) :

- Non-anemic individuals usually have serum EPO less than = 20 IU/L.

- Anemic individuals usually have increase in EPO levels, due to the need of production of more RBC , so in moderate anemia the serum EPO = 100-500 IU/L , and in severe anemia serum EPO can reach 1000 IU/L .

With an exception of Renal disease patients , they have low EPO levels.

Erythropoietin

Clinical Pharmacology:

- Used for anemia of chronic renal failure, NOT other types of anemia where endogenous erythropoietin is usually high.
- Iron and folate supplementation may be required in cases of inadequate response.

Or to accommodate the high synthesis of RBCs after giving EPO

Erythropoietin

Adverse Effects:

1. Most common are those associated with rapid rise of hemoglobin and hematocrit: hypertension and thromboembolic complications.

Viscosity will increase, so the blood have higher chance to coagulate, leading to thrombus formation

- Hemoglobin levels should not be increased > 11 g/dL because of risk of serious cardiovascular events, thromboembolic events, stroke, and mortality.

2. Infrequent and mild allergic reactions.

Before we were using EPO extracted from animals , that may cause allergic reaction. Now with recombinant form we don't have these allergic reactions.

Remember
Thrombus:
formation of a blood clot in situ within the vessels.
Embolus:
Once it moves from its place.

Myeloid Growth Factors

- Granulocyte colony-stimulating factor (G-CSF), granulocyte-macrophage colony-stimulating factor (GM-CSF).
- Recombinant human G-CSF (rHuG-CSF): Filgrastim
- Recombinant human GM-CSF (rHuGM-CSF): Sargramostim

Myeloid Growth Factors

Pharmacodynamics:

- They stimulate proliferation and differentiation by interacting with specific receptors found on myeloid progenitor cells.

1. G-CSF stimulates proliferation and differentiation of progenitors committed to the neutrophil lineage. It also activates the phagocytic activity of mature neutrophils and prolongs their survival in the circulation.

Myeloid Growth Factors

2. **GM-CSF has broader biologic actions than G-CSF.**

- **It is a multipotential hematopoietic growth factor that stimulates proliferation and differentiation of early and late granulocytic, erythroid and megakaryocyte progenitors.**

Myeloid Growth Factors

They are used in case of neutropenia

Clinical Pharmacology:

1.Cancer Chemotherapy-Induced Neutropenia.

- **G-CSF and GM-CSF accelerate the rate of neutrophil recovery and reduces the duration of neutropenia after dose-intensive myelosuppressive chemotherapy.**

Myeloid Growth Factors

Adverse effects:

1. Bone pain. Because we stimulate the production process in bone marrow
2. Fever, arthralgias, myalgias.
3. Capillary leak syndrome characterized by peripheral edema, and pleural or pericardial effusions.
4. Allergic reactions.
5. Splenic rupture. In severe cases

Megakaryocyte Growth Factors

- Thrombopoietin and interleukin-11 (IL-11) are endogenous regulators of platelet production.
- Thrombopoietin agonists: Romiplostim and Eltrombopag.
- Recombinant form of IL-11: Oprelvekin.

Megakaryocyte Growth Factors

Eltrombopag:

- **It is an orally active small nonpeptide thrombopoietin agonist used for therapy of patients with chronic immune thrombocytopenia who have had an inadequate response to other therapies (steroids, immunoglobulins, or splenectomy).**

Therapies for immune system first , then if it didn't work , we give them a growth factor recombinant.

Megakaryocyte Growth Factors

- It is also used for treatment of thrombocytopenia in patients with hepatitis C to allow initiation of interferon therapy.

Romiplostim:

- It is used for therapy of patients with chronic immune thrombocytopenia.

Megakaryocyte Growth Factors

Adverse effects:

Eltrombopag:

1. Hepatotoxicity.
2. Portal vein thrombosis.

Megakaryocyte Growth Factors

Romiplostim:

1. Portal vein thrombosis.
2. In patients with myelodysplastic syndromes, it increases the blast count and risk of progression to acute myeloid leukemia.
3. Bone marrow fibrosis.
4. Rebound thrombocytopenia.

Megakaryocyte Growth Factors

Oprelvekin:

1. Fatigue,
2. Transient atrial arrhythmias.
3. Anemia (due to hemodilution).
4. Dyspnea (due to fluid accumulation in the lungs).
5. Hypokalemia.