Affects of EPO on Dialysis patients with at least one lab Hgb > 13

Harlem Children Society
Research Project
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About the Program

This summer through the Harlem Children Society program I was able to work with a neurosurgeon and biomedical researcher (Anatole Beserab, and Stan Frinak) at Henry Ford Hospital on a research project about dialysis patients and the relationship between Erythropoietin and Hemoglobin. I am very glad I had this opportunity because it has widened my knowledge in the medical field. This will really help me later because I would like to become a pediatrician. Through this program I have developed many new skills in the computer field, a little calculus and some physics. I have acquired new friends that in the future will definitely write recommendation letters for me. I worked hard and determined to make sure I did the best on this project. I hope you enjoy my project as much as I have.

Introduction

This project was based on dialysis patients with at least one lab hemoglobin value greater than 13 and how Erythrpoietin affected their value, and why they are anemic. It was sponsored through the Harlem Children Society and mentored by Henry Ford Hospitals Nephrology Doctor Anatole Beserab and biomedical engineer Stan Frinak.

So why are Dialysis patients anemic?

When a patient has been diagnosed with Chronic Kidney Disease (CKD) the patients become anemic as they loose their kidney function. This results from the loss of the kidneys' ability to produce the red blood cell stimulating hormone Erythropoietin (EPO). In order to prevent anemia, EPO, normally produced in the kidney, is replaced, with "artificial" genetically engineered EPO. Anemia is measured as a reduction in Hemoglobin (Hgb), the substance in red blood cells that carries oxygen. However, maintaining a near constant Hgb is not easy for doctors and patients to do.

What is Dialysis?

Dialysis is a type of therapy used to provide an artificial replacement for lost kidney function due to kidney failure. It is a life maintaining treatment. It can be used for very sick patients who have suddenly lost their Kidney function or for quite stable patients who, (over time), have permanently lost their kidney function.

How a hemodialysis machine works

The hemodialysis machine has one tube (from the lower arm), which takes the un-cleansed blood out of the body to the hemodialyzer where the filtering takes place. Then another set of tubing takes the cleansed blood back to the body (again through the lower arm).

Hemoglobin

Hemoglobin is the oxygen-carrying protein in the red blood cells. In vertebrates, it transports oxygen from the lungs to the rest of the body. It also transports carbon dioxide to the lungs for removal.

EPO

Erythropoietin (EPO) is a glycoprotein hormone that is a growth factor for red blood cell precursors in the bone marrow. It is produced by the kidney, and is the hormone, which regulates red blood cell production. It is used in treating anemia resulting from chronic kidney disease or from cancer chemotherapy. EPO is generally injected under the skin of the patient. Several injections weekly are required for the original forms, but newer long-acting forms (Darbepoetin) may require injections only every 2 to 4 weeks. EPO can also be injected into the blood stream directly. Which is the preferred route of administration in dialysis patients.

When and how was EPO Developed?

EPO was first postulated in 1906 based on transfusion experiments in rabbits. In 1950, the still unidentified erythropoietic factor was found to be stimulated in rats breathing a low-oxygen atmosphere. In the 1960s it source was identified as the kidneys. T. Miyake, C.K. Kung and E. Goldwasser at the University of Chicago first purified human EPO from human urine in 1977.

EPO has now been identified with a molecular mass of about 30,000 Daltons. It has a 165 amino acid chain with 4 oligosaccharide side chains and circulates in the blood plasma at about 5 pmo/L.

What is Chronic Kidney Disease?

Chronic Kidney Disease (CKD) is a slowly progressive loss of kidney function over a period of months or years and quantitated as low Glomerular filtration rate.

The renal artery flows to the cortex (where the Glomerulus is) where the renal vein flows back from the cortex. The glomerulus filters the waste from the blood through the renal vein into the Bowman's capsule, which goes to the collecting tubule, which flows to the ureter, and the urine releases the waste. CKD that leads to sever illness and requires some form of renal replacement therapy (such as Dialysis) is called end-stage renal (Kidney) disease (ESRD).

What is Anemia?

Anemia is the diminution of red blood cells that contain hemoglobin. This reduces the ability of blood to carry oxygen to the tissues. Severity of anemia is measured as a decreased Hgb level below the normal range male: 13-18 gm/dL Female: 12-16 gm/dL

The Aims of this study are

To determine how well doctors regulate the Hgb of Dialysis patient's, to examine the trends between EPO dose and Hgb in dialysis patients. Can the data teach us how to do a better job of managing anemia?

Problems of Using EPO

The effect of a given EPO dose can persist for up to 3 months. Therefore, a change in EPO dosage may not alter the Hgb level to the desired level for up to several months.

There are many factors doctors must consider when dealing with EPO dosage. They must also look at the patients Ferritin (iron stored), Fesat (iron being used), and their CHR (amount of immature red blood cells) values. For these also alter Hgb levels. If a patient is low on Ferritin then the patients Hgb will be on the rise because they will be using the iron. Also if they are high on Fesat and CHR then their Hgb will begin to rise.

Another important factor is that the red blood cells live up to 120 days. EPO can be significantly reduced without causing a reduction in Hgb, making it hard to determine the right amount of EPO to give.

Defining the Project

Physicians respond to Hgb levels only when limits are exceeded. Low Hgb occur for many reasons, most of which are not under the control of the physician. High Hgb, however, results from dosing by doctors and medical staff and are potentially modifiable.

The methods we used were

- To first extract the data from the Greenfield Health System Database.
- Then import the data into Microsoft access and sort.
- Calculate the information in Excel
- Then we analyzed the data in Stat View and develop graphs and analyzed trends in the data.
- Last but not least, to suggest Improvements in dosing strategies.

Data

50% of the total Hgb's for all patients are between 11 and 13. 23% are less than 11. 24% are between 13 and 15. 3% are greater than 15.

The change in Hgb ranges form about -4 g/dL to + 4 g/dL. The mean change between measurements was 0.0 ± 1.12. The standard deviation is plus or minus 1.12.

Patient Data for Hgb less than or equal to 13 Vs. Hgb greater than 13.

For Hgb less than or equal to 13 the mean was 11.3, for Hgb greater than 13 the mean was 14.0. EPO dose for Hgb less than or equal to 13 the mean was 6445 and for the EPO dose with Hgb greater than 13 the mean was 5824…the mean difference was about 621.

For FESAT for Hgb less than or equal to 13 the mean was 25.9 and for FESAT for Hgb greater than 13 was 28.3. For FERR for Hgb less than or equal to 13 was 448 and for FERR for Hgb greater than 13 the mean was 412. For CHR for Hgb less than or equal to 13 the mean was 31.5 and for CHR for Hgb greater than 13 the mean was 31.9.

Individual Dialysis Patient data

It took 150 day before the Hgb increased above 13. The patient remained above 13 for 42 days before the Hgb decreased and then increased above 13 for another 77days. Dose.

Hemoglobin Distribution EPO vs. Darbepoetin Using Computerized Anemia Management Program

The Computerized Anemia Management Program has more patients in the right range (no one has a Hgb greater than 14 and no one lower than about 8) then the Dialysis patients

Suggest Improvements in Dosing Strategies

- A patients EPO dose should not be changed every month, because EPO effects can last up to 3 months or more.
- A trend analysis (graph) of the patient's data may be very useful in making dosing decisions.

Conclusions

- The study showed that an individual patient's Hgb can change over a wide range and the Hgb level did not always correspond to the patients EPO dose.
- There are many things other than just the Hgb in which the doctors must look at to decide the amount of EPO that might be right for the patient. The current Hgb level, the current EPO dose, and the patients iron status (measure by FERR, TSAT and CHR levels) must be taken into consideration.
- A trend analysis (graph) of the patient's data may be very useful in making dosing decisions.
- A computerized anemia management program that uses a database to track changes in Hgb and EPO dose may help regulate Hgb levels in dialysis patients.

References

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