A NOVEL APPROACH FOR SICKLE CELL TREATMENT

William Heppenstall, DO[1], williamhep@pcom.edu, Kenneth Hoellein, MD[2]
1. Department of Internal Medicine, (Philadelphia College of Osteopathic Medicine, Philadelphia, PA)
2. Division of Internal Medicine, (Philadelphia College of Osteopathic Medicine, Philadelphia, PA)

BACKGROUND

Sickle cell disease has been studied for decades because of the devastating effects it causes for those suffering from it. The genes have been identified, the pathophysiology explained it detail, and proposed reasons as to why the mutation exist in the first place. Treatment has always consisted of pain management as this is primarily a PAIN MANAGEMENT disease. Developments have been discovered to target the root of the disease, so that hopefully pain may be secondary thought, and sickle cell disease can be controlled.

Any astute biology student knows the basic mechanism of the disease. Chromosome 11 that codes for the Glutamate (GAG codon) has a point mutation to translate to Valine (GTG codon). This allows for the tetramer hemoglobin molecule to mis-fold. The conglomeration of all the misshapen hemoglobin molecules will cause the erythrocyte to take on a sickling appearance under microscopic observation (hence the name).

These now sickled cells create chaos at the microscopic environment. The capillary beds are constantly becoming clogged and preventing perfusion to the subsequent tissues. The areas of the body that have the highest amount of capillary beds are skeletal muscle, brain, heart, lung, liver, spleen and kidney. Knowing this factoid, the complications are then easily explainable. Skeletal muscle not being perfused creates pain from lack of oxygenation. The brain starving for oxygen leads to a decreased seizure threshold. The heart with decreased blood flow creates the “acute chest syndrome”. The lungs can suffer from pulmonary infarct in situ. The liver eventually becomes cirrhotic. These patient’s are functionally asplenic by the time they are teenagers (hence they need their encapsulated bacteria vaccines). And finally, under decreased oxygenation, acidic and hyperosmolar environment, the renal papillae will necrose creating gross hematuria.

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PATIENT PRESENTATION

Patient is a 25 year old male with sickle cell disease. He has recurrent sickle cell crisis events in which he is hospitalized about 1-3 times a month for management. His typical hospital management therapies consist of IV narcotics, hypotonic fluids (as to not worsen the sickling of cells), and the American Red Cross performing an exchange transfusion to keep his HgbS to less than 55%.

PMH: Hgb SC Disease, Obesity, MDD, Opiate Dependence, Pulmonary Embolism, Syringoma

PSH: priapism decompression

MED: carvedilol 3.125mg BID, duloxetine 60mg, LMWH 150units, fentanyl TD 75mcg TD, gabapentin 600mg TID, hydromorphone 8mg q6hr, hydroxyurea 1000mg, hydroxyzine 20mg QID, ibuprofen 800mg TID, narcan 0.4mg PRN, topiramate 200mg BID, tramadol 100mg q6hr

ALL: nuts

FAM: mother (deceased from bariatric surgery, DMT2)
brother (GSW)
sister (deceased from polysubstance abuse, Bipolar)
sister (sickle cell anemia)

SOC: denies tobacco, denies etoh, denies illicit drug use

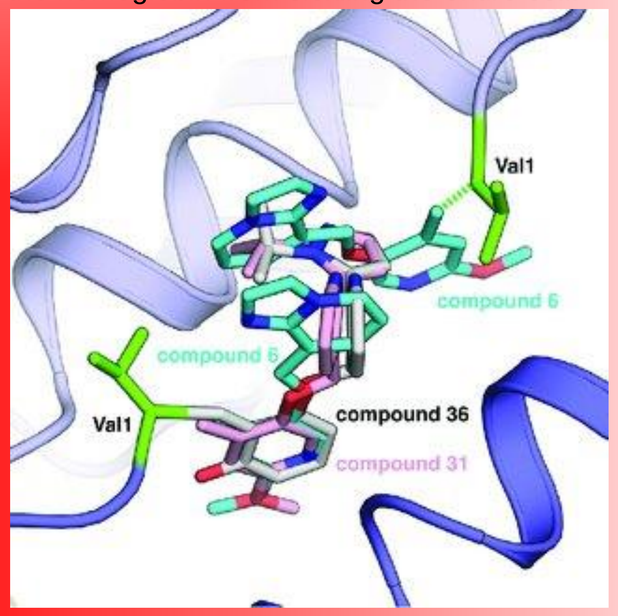
VITALS: 130s/60s mmHg – 90s bpm – 20 rpm – 95% RA

PE: pertinent positive of webbed fingers

Baseline Hgb in the 9’s
Baseline Retic Count 2’s

NEW FORM OF TREATMENT

Voxelotor is a novel approach for sickle cell disease treatment. It is a molecule allosterically binds to the site where the hemoglobin molecule inappropriately folds. This binding prevents the hemoglobin from sickling the entire cell.



The drug has been objectively studied for the effects of bone marrow turnover (aka reticulocyte count), hemoglobin levels, and hemolysis markers (ex. LDH and bilirubin). This patient had the expected results of his reticulocyte count increasing from his baseline 2 to 6 and his hemoglobin increasing from his baseline 9’s to 12’s.

But from a humane perspective, how is the patient clinically? He is still on his current doses of his narcotics BUT his hospitalizations have DECREASED from 1-3 times a month to about once every 3 months!!! This is not the cure for sickle cell disease yet, but it is definitely a step in the right direction.

REFERENCES

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