Action of Thalidomide Drug on Female and Male E/Beta Thalassemia Patients

Shubhajit Roy

Postgraduate Student
SRM Institute of Science and Technology

***Abstract*- The idea of thalidomide drugs being effective in treating beta-thalassemia patients and in this case, beta-thalassemia was successfully treated. Thalidomide, sold under the brand names Contergan and Thalomide, is a medication used to treat cancers (including multiple myeloma) and graft-versus-host disease, as well as skin conditions including complications of leprosy. HIV-associated conditions have been treated with it, but such treatment has been associated with increased virus levels. It is taken orally. In addition to improving hemoglobin count, thalidomide also improved other important factors in patients. The use of this drug as per the data we got by implementing them in thalassemia patients has been recommended with proper dosage. Females generally respond better to this drug than males. Thalidomide, in its entirety, might not be a game-changer, but a temporary treatment for thalassemia that keeps patients on track with hemoglobin counts.**

Keywords: **Thalassemia Curing, Thalidomide Drug. Thalidomide. Hemoglobin. MCV. MCH. MCHC. HCT level comparison.**

Literature Review

Thalidomide drugs have been studied for many years as a treatment for Thalassemia. In order to find out how using it as medicine affects patients, I gathered some of the resources that gave me this idea. β-Thalassemia occurs when the β-globin chains of hemoglobin are not synthesized (β0) or are not synthesized sufficiently (β+). There are three hematological and clinical conditions of increasing severity: thalassemia minor, intermedial, and major (a transfusion-dependent anemia) [1]. The clinical severity of β-thalassemia syndromes is also influenced by genetic factors unlinked to globin genes as well as environmental conditions and management. At present, the only definitive cure is bone marrow transplantation, however, not all can afford such a cost-effective operation. Therefore, we observed that Thalidomide Drug which has been used for many diseases like HIV, previously can now be used to increase the important blood parameters. Three centers in southern China recruited thalassemia patients with non-transfusion-dependent or transfusion-dependent thalassemia (NTDT) who would not respond to conventional therapy with transfusions and chelation over a three years period [2]. In this research paper, Kun Yung shows that it has significant therapeutic effects on patients with beta thalassemia. Peripheral neuropathy is one of the most feared complications. This study indicates that thalidomide could become an effective long-term treatment for beta thalassemia, but several questions still need to be answered before its application in the clinic[2]. Three years ago, a center in Iraqi Kurdistan recruited 37 patients with symptomatic beta thalassemia syndrome [14 patients with transfusion-dependent thalassemia (TDT), and 23 patients with non-transfusion- dependent thalassemia (NTDT), who were unable to pursue conventional treatment with transfusion and chelation. Following informed consent, patients were given low-dose Thalidomide (2-10 mg/kg) and were followed up for at least eight months for a response [3]. From the paper of Radhakrishnan, Naga A, we get to see the impacts of E-beta Thalassemia patients responding to Hydroxyurea [4]. I have also taken helps of other journals and documents related to adverse health effects, and thereby proceeding to the safety and efficacy of thalidomide. Based on Chen J's paper, Thalidomide induces expression of *-globin in erythroid progenitor cells, but its efficacy on patients suffering from transfusion-dependent *-thalassemia (TDT) is unclear. In this phase 2, multi-center, randomized, double-blind clinical trial, we aimed to determine the safety and efficacy of thalidomide in TDT patients. A hundred patients of 14 years or older were randomly assigned to receive placebo or thalidomide for 12 weeks, followed by an extension phase of at least 36 weeks. The primary endpoint was the change of hemoglobin (Hb) level in the patients. The secondary endpoints included the red blood cell (RBC) units transfused and adverse effects. Adverse events of drowsiness, dizziness, fatigue, pyrexia, sore throat, and rash were more common with thalidomide than placebo. In the extension phase, treatment with thalidomide for 24 weeks resulted in a sustainable increase in Hb concentrations which reached 104.9 ± 19.0 g/L, without blood transfusion. Significant increase in Hb concentration and reduction in RBC transfusions were associated with non β0/β0 and HBS1L-MYB (rs9399137 C/T, C/C; rs4895441 A/G, G/G) genotypes. These results demonstrated that thalidomide is effective in patients with TDT [5]. Also, from the research of Xinyu Li et al, we have seen the efficacy and side effect managements of implementing this drug, they concluded that, the dose of thalidomide between 2.5 mg·kg-1·d-1 and 3.6 mg·kg-1·d-1 was effective in children with

TDT. Severe side effects were not found. HbF concentration of 47.298 g·L-1 at the third month is recommended as the predictor for further major responders [6]. Hemoglobin E-β-thalassemia is a common β-thalassemia that has a variable presentation from mild to severe life-threatening anemia. We describe such a case, who presented with severe anemia and multiple allo-antibodies. Our case illustrates the role of thalidomide in transfusion-sparing therapies in patients with transfusion-dependent thalassemia and challenges in the blood bank [7]. Chandra J et al also found that Thalidomide resulted in major/moderate response in majority of children with transfusion-dependent thalassemia with satisfactory adverse effect profile. Therefore, we, with all safety precautions, thereby took the data and supervised the thalidomide drug on the patients on our Thalassemia research Unit and Hospital.

Introduction

Thalassemia (thal-uh-SEE-mee-uh) is a blood disorder that is inherited. This means it is passed down from one or both parents through their genes. When you have thalassemia, your body makes less hemoglobin than normal. Hemoglobin is an iron-rich protein in red blood cells. It carries oxygen to all parts of the body. There are 2 main types of thalassemia: alpha and beta. Different genes are affected for each type. Thalassemia can cause mild or severe anemia. Anemia occurs when your body does not have enough red blood cells or hemoglobin. The severity and type of anemia depends on how many genes are affected. Alpha thalassemia occurs when some or all the 4 genes that make hemoglobin (the alpha-globin genes) are missing or damaged. There are 4 types of alpha thalassemia:

Alpha thalassemia silent carrier - One gene is missing or damaged, and the other 3 are normal. Blood tests are usually normal. Your red blood cells may be smaller than normal. Being a silent carrier means you don't have signs of the disease, but you can pass the damaged gene on to your child. This is confirmed by DNA tests.

Alpha thalassemia carrier - Two genes are missing. You may have mild anemia.

Hemoglobin H disease - Three genes are missing. This leaves just 1 working gene. You may have moderate to severe anemia. Symptoms can worsen with fever. They can also get worse if you are exposed to certain medicines, chemicals, or infectious agents. Blood transfusions are often needed. You have a greater risk of having a child with alpha thalassemia major.

Alpha thalassemia major - All 4 genes are missing. This causes severe anemia. In most cases, a baby with this condition will die before birth.

This is a genetic disease inherited from one or both parents. The only risk factor is having a family history of the disease. Different people will have different symptoms, based on which type of alpha thalassemia is inherited. Common symptoms for each type may include:

Silent alpha thalassemia carrier - This type has no symptoms.

Alpha thalassemia carrier - You may have mild anemia. You may have no symptoms. Or you may have mild symptoms such as mild fatigue or exercise intolerance.

Hemoglobin H disease - This type causes moderate to severe symptoms. These include lack of energy (fatigue) and exercise intolerance. You may also have an enlarged liver or spleen, yellowish skin, and leg ulcers. You have a greater risk of having a child with the most severe type, alpha thalassemia major.

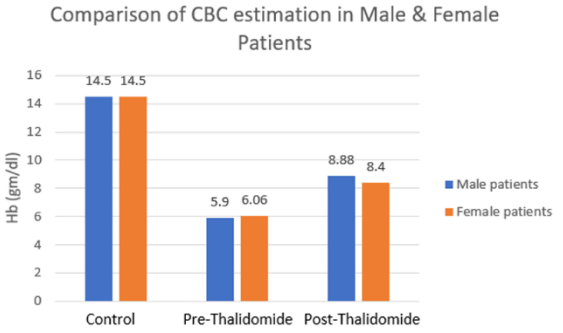
Alpha thalassemia major - Babies with this type usually die before they are born. Alpha thalassemia is most found in these parts of the world:

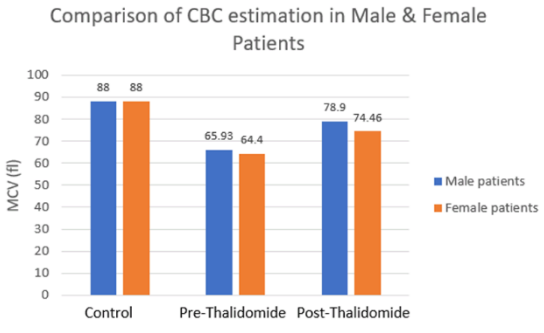
Africa
Middle East
India
Southeast Asia
Southern China
Mediterranean region

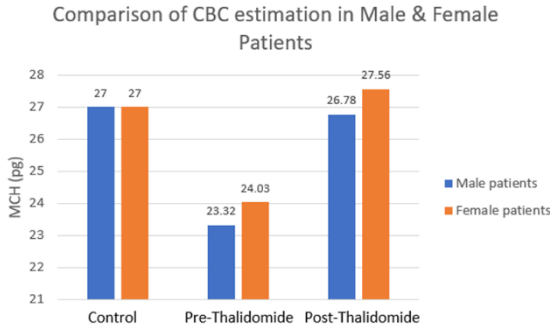
The following tests may help to tell if you are a carrier and can pass the disorder on to your children: Complete blood count (CBC). This test checks the size, number, and maturity of different blood cells in a set volume of blood. Hemoglobin electrophoresis with A2 and F quantitation. A lab test that tells what type of hemoglobin is present. FEP (free erythrocyte protoporphyrin) and ferritin. This test is done to rule out iron-deficiency anemia. All these tests can be done using a single blood sample. In a pregnant woman, the baby is diagnosed using CVS (chorionic villus sampling) or amniocentesis. A DNA test is needed to make a diagnosis of alpha thalassemia. How is alpha thalassemia treated? Your healthcare provider will figure out the best treatment for you based on your age, overall health, and medical history, how sick you are, how well you can handle certain medicines, procedures, or therapies, how long the condition is expected to last, your opinion or preference. Treatment may include daily doses of folic acid, blood transfusions (as needed), surgery to remove your spleen, medicines to reduce extra iron from your body (called iron chelation therapy), avoidance of certain oxidant drugs in hemoglobin H disease People with alpha thalassemia may have no symptoms. Or they may have many symptoms. If you don't have symptoms, you may still want to see a specialist. He or she can help you understand the risks of passing the disease to your children. If you have symptoms, work with your healthcare provider. He or she can help you find the best treatment to reduce anemia symptoms. The protein hemoglobin transports

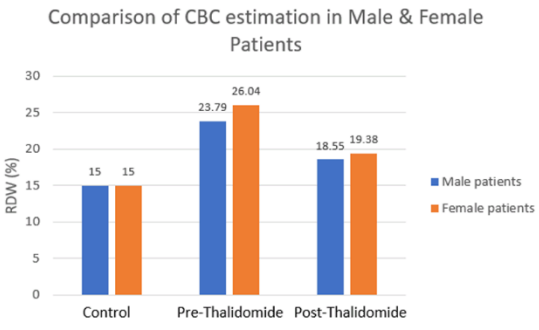
oxygen around the body in blood cells. Bone marrow uses the iron a person gets from food to make hemoglobin. In those with thalassemia, the bone marrow does not produce enough healthy hemoglobin or red blood cells. The body can also break down red blood cells with abnormal hemoglobin. Further, those red blood cells may not be flexible enough to squeeze through capillaries to reach necessary parts of the body. In some cases, these issues can lead to a lack of oxygen, resulting in anemia and fatigue. People with mild thalassemia may not require any treatment, but more severe forms will necessitate regular blood transfusions. [9].

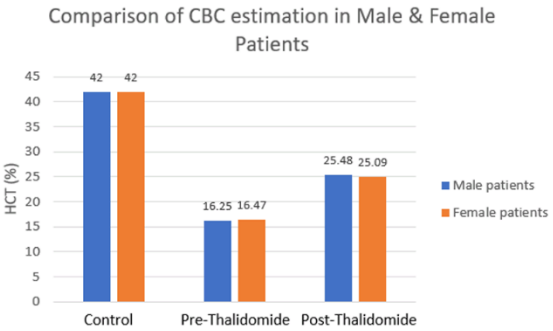
Results











Discussion

Thalidomide had significant therapeutic effects on patients with β-thalassemia with a sustained response. There is potential for thalidomide to be an effective long-term treatment for β-thalassemia based on these preliminary results, although several issues must be addressed before its use in patients. From the data bar charts we can compare the data following the parameters as follows: 1) Hemoglobin: When the patients came, their Hb was really low, and after Thalidomide drug implementation, the progress was observable. In the males, we can see, it was 8.88 compared to the control 14.5 and pre-Thalidomide: 5.9. In the females, the control was 14.5 with pre-Thalidomide: 6.06 and a notable change post-Thalidomide of 8.4 gm/dl respectively. 2) MCV: Analysing the data, we can see that the Males Pre-Thalidomide implementation was 65.93 fl and after the drugs when the patients came back, we can see the average to be 78.9 fl. The standard is 88.0 fl. In females, the pre-thalidomide data was 64.4 and after dosage it is found to be 74.46, which is really a notable change to the increase in the mean corpuscular volume data. It is incredible and proved to be really working. 3) MCH: The male and female have both the standard value of 27.0 pg. Now, the interesting fact is here. The Pre-Thalidomide Data Average was found in males to be 23.32 pg, and quite disappointingly the MCH value increased in a very small amount in male after the implementation of thalidomide. But progressive results were seen in the females as the post-Thalidomide data exceeded the control and resulted in 27.56 pg. Which was more than normal. 4) RDW: The standard count for male and female is 15%. The male pre-Thalidomide data was 23.79% which is normal for thalassemia patients. And in both the graphs, clearly observable that, the drug effected positively with decrease in RDW value. The male count decreased to 18.55 gm/dl and female to 19.38 gm/dl respectively. 5) HCT: While the

standard value of normal male is 42.0% for both male and female. In thalassemia, the male count before the implementation of thalidomide was 16.25% and female 16.47%. Now, after the drug implemented, the average value for males were found 25.48% and female was 25.09%. Again, a better impact to the females, although negligible.

Conclusion

Therefore, through this project we can get an idea of the effectiveness of the thalidomide drugs on the Thalassemia Patients and in this case, beta-thalassemia. The thalidomide drug helped patients improve hemoglobin count and other indexes. So, I can recommend this drug for the treatment. The overall females have shown better response than what males did. At, a whole, the thalidomide drug might not be a game changer but a sure impact factor to the thalassemic treatments.

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