Abstract: P2187

Title: STUDY OF SAFETY AND EFFICACY OF THALIDOMIDE IN COMBINATION WITH HYDROXYUREA IN PATIENTS OF SICKLE CELL ANAEMIA: A RANDOMISED CLINICAL TRIAL FROM EASTERN INDIA

Abstract Type: e-Poster Presentation

Topic: Sickle cell disease

Background:

Sickle Cell Disease (SCD) is a monogenic disorder characterized by the substitution of glutamic acid for valine at the sixth position of the beta globin chain of hemoglobin, resulting in the formation of sickle hemoglobin (HbS), The two hallmarks of the disease are occlusion of blood vessels in almost every organ, resulting in end organ damage, vaso-occlusive crisis (VOC) and chronic Hydroxyurea (HU) remains the mainstay of pharmacologic therapy; however, many patients still experience VOCs while on Hydroxyurea. Thalidomide (TH), an immunomodulator drug, has been shown to induce HbF and reduce the incidence of VOCs in mice models.

Aims:

To evaluate the safety and efficacy of combining HU with TH compared to HU alone in SCD patients. The objectives of this study were to compare a) the number of Vaso-Occlusion Crises, b) packed red blood cells (PRBC) transfusion requirements, c) change in Hb, HbF and HbS, d) evaluate the side effects of both the regimens.

Methods:

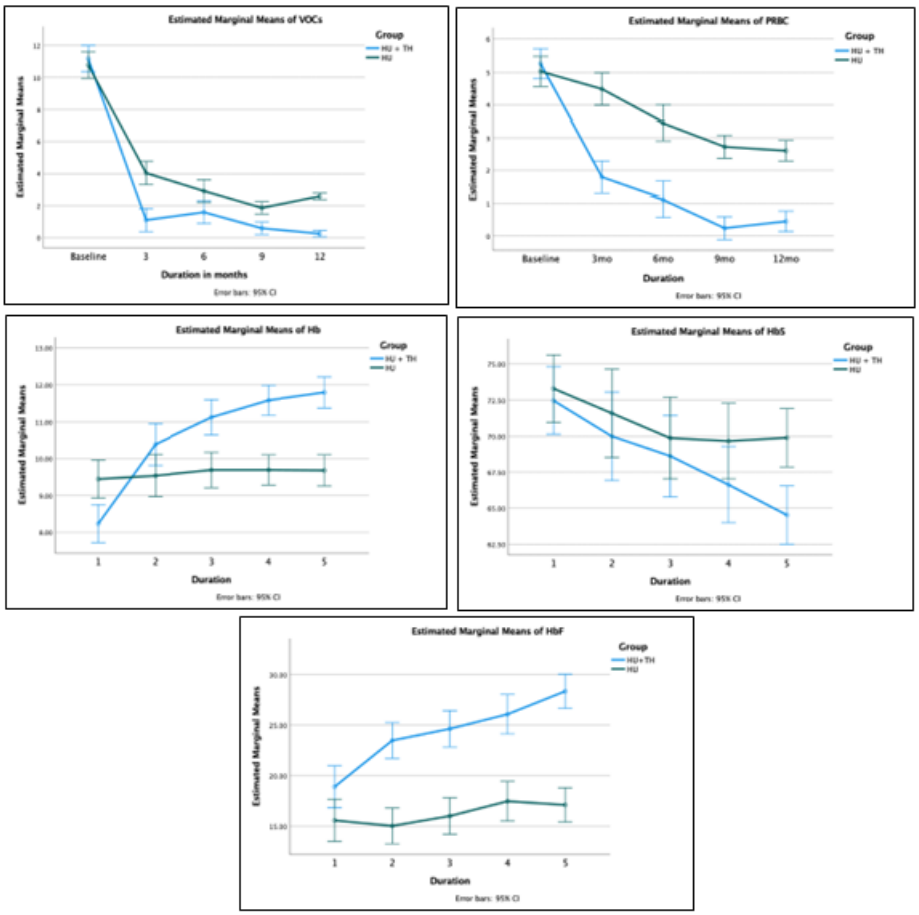
A randomised clinical trial was conducted on SCD patients from October 21 to May 23. Patients aged >12 years and post-menopausal females were randomised into two groups. Patients in group A received TH (50mg/day) + HU (20mg/kg/day) + Folic Acid (5mg/day). Group B patients received HU (20mg/kg/day) + Folic Acid (5mg/day) + a Multivitamin capsule. Outcome variables were compared between the groups using student's t-test, and the change in Hemoglobin, HbF and HbS levels over the 12 months was compared using repeated measures ANOVA testing. A p-value of < 0.05 was considered statistically significant.

Results:

A total of 66 patients diagnosed with SCD were included in the study. The mean age of patients was 32.9 ± 11.5 years. Most (56.1%) of the patients were 21-40 years old, and males constituted 57.6% of the study. The baseline PRBC requirement (5.27 vs 5.03) and VOC episodes (11.18 vs 10.79) between the groups in the preceding 12 months were comparable statistically ($p = 0.467$ and 0.501). Patients in Group A had significantly fewer episodes of VOCs (3.48 ± 2.81, SD) and the mean number of PRBC transfusions (3.61±2.19) over the period of 12 months compared to VOCs (11.36 ± 4.20) and PRBC transfusions (13.27±3.70) in Group B respectively ($p = 0.0001$ and 0.0001). There was a steady increase in the mean Hb level from the baseline value of 8.2 ± 1.8 gm/dl to 11.8 ± 1.2 gm/dl at 12 months in patients of Group A ($p < 0.0001$), with no significant improvement ($p = 0.726$) in group B. A steady decrease in mean HbS% from the baseline values of 72.5 ± 5.5 to 64.5 ± 5.4 at 12 months in Group A ($p < 0.0001$) was seen. Following treatment, HbF values in Group A patients steadily rose across the timeline from 18.9 ± 5.1 to 28.4 ± 5.6 ($p < 0.0001$) at 12 months, which was not observed at a statistically significant level among Group B patients ($p < 0.115$). A relatively higher proportion of patients (27/33 ~ 82%) in Group A experienced adverse events compared to Group B (61%); the difference was statistically not significant ($p > 0.5$). Constipation (grade 1) and somnolence (grade 1) were the significant side effects in group A, while nausea (grade 1) in group B. Only two patients in Group A had grade 1 peripheral neuropathy.

Summary/Conclusion: There was a significant decrease in VOCs and PRBC requirements in patients receiving TH and HU compared to HU alone. The reduction in HbS level and the increase in HbF in the combination arm

was more significant than the HU alone. The combination therapy was well tolerated with minimal adverse events and was managed symptomatically. Since the results are from a single institution, generalization could be a limitation of this study.



Keywords: Blood transfusion, Vasoocclusive crisis, Sickle cell disease, Hemoglobin