Abstract: P1504

Title: FACTORS LIMITING HYDROXYCARBAMIDE DOSING IN ADULTS WITH SCD. RESULTS FROM THE UK'S SICKLE NATURAL HISTORY STUDY

Abstract Type: Poster Presentation

Topic: Sickle cell disease

Background:

The UK's "Sickle Natural History Study" is a real-world multi-site study of adults with Sickle Cell Disease (SCD) collecting on standard of care clinical data. 543 patients with SCD have been recruited to the study with 481 having reportable data.

There remain very few disease modifying therapies for SCD. Hydroxyurea (HU), also known as hydroxycarbamide, is the only licensed, disease modifying drug treatment available in the UK. Given the lack of treatment choices; it is important to understand which factors may affect the dosing of HU. HU is dosed initially by weight, then titrated to a maximum tolerated dose according to neutrophil, platelet, reticulocyte, and haemoglobin counts. In our clinical practice we notice that there are a series of factors impacting HU dose escalation in adult patients.

Using these data, we have so far examined the relationships between HU and age, HU and serum creatinine and HU and sickle cell genotypes.

Aims:

To understand how Hydroxyurea dosing varies with age, genotype and serum creatinine in Sickle Cell Disease.

Methods:

Patients in the study who are on HU of all genotypes were identified. HU dosing was correlated with age and renal function. Correlations were examined using Pearson Correlation Coefficient

Dose was also examined by Genotype. Similar genotypes were grouped based on the typical phenotype they produce. HbSS and HbSB0 were grouped and HbSC and HbSB+thal were grouped. Mean HU doses were compared between groups using an unpaired T-Test

Results:

Of 543 patients in the study, 481 had full data for evaluation. From these 481 patients, 307 (63.8%) had HbSS, 152 (31.6%), HbSC, 21 (4.4%) had other genotypes (HbSB+, HbSB0, HbSHPFH). The age of the group ranged from 18-81 with a mean age of 40.1 years, females accounted for 59.7% of all patients.

239 (50.3%) of 481 were on disease modifying treatment (DMT), and 242 were not. Of the 239 DMT patients, 165 (69.0%) were on HU, and 78 (32.6%) on transfusion. 211 (68.3%) of HbSS patients were on DMT. Compared with 17 (11.1%) of HbSC patients. There were 2 patients with HbSB0 both of whom were on DMT.

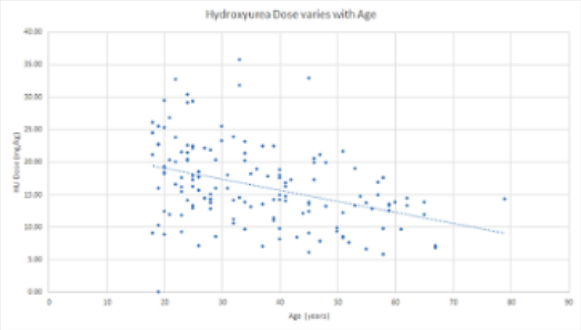
HU dosing was negatively correlated with age ($R=-0.381$, $P<0.0001$) with dosing decreasing with increasing age. Our data also show that HU dosing was negatively correlated with serum creatinine ($R=-0.242$, $P<0.0001$) with dose decreasing with rising serum creatinine.

There was not a significant difference in dose between genotypes ($P<0.1$). Average dose in HbSS + HbSB0 group was 16.7 mg/kg average dose in the HbSC + HbSB+thal group was 14.2mg/kg

Summary/Conclusion:

These data from 165 patients on HU show that dose decreased with age. This confirms the findings from our

initial analysis of 80 patients which we reported last year. Additionally, we are also able to show that there is a correlation between serum creatinine and the dose of HU. Understanding the relationship between HU dosing and age may affect how we choose to prescribe HU in the future. It is plausible that due to the dyserythropoiesis that occurs in SCD; bone marrow may become less resilient against the suppressive effects of HU. However, further work is required to establish this.



Keywords: Sickle, Sickle cell, Hydroxyurea