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113.SICKLE CELL DISEASE, SICKLE CELL TRAIT AND OTHER HEMOGLOBINOPATHIES, EXCLUDING THALASSEMIAS: BASIC AND TRANSLATIONAL

Fucosyltransferase VII (FUT7) Activity in Patients with Sickle Cell Disease and Healthy Controls

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Background: Sickle cell disease (SCD) is a severe monogenic disorder with a majority of the affected individuals living in Africa. Vaso-occlusion is a significant cause of morbidity and mortality in SCD, and selectin mediated intercellular adhesion is recognized as an important target for therapy. As such Anti-P-selectin agents are in clinical use to reduce the frequency of vaso-occlusive crises (VOCs) in SCD patients. Sialyl lewis x is a crucial ligand common to all members of the selectin family and the final step in the biosynthesis of sialyl lewis X antigen (fucosylation), is catalysed by Fucosyltransferase VII (FUT7). This enzyme is most expressed in leukocytes and endothelial cells. We hypothesized that FUT7 enzyme activity is abnormal in SCD patients and differs by VOC severity. We sought to measure plasma levels of FUT7 in SCD patients and healthy controls, and investigate their association with clinical and laboratory features, such as the frequency of VOCs.
Methods: This wasa single centre cross-sectional analytical study at the University of Nigeria Teaching Hospital, Enugu. 38 steady state adult SCD patients and 40 HbAA age- and sex-matched healthy control subjects were enrolled. SCD patients were stratified by clinical severity into: Group A- 19 subjects with mild disease (0-1 crises and no disease complication such as stroke, chronic leg ulcers, nephropathy, or avascular necrosis in the previous year), and Group B- 19 patients with moderate to severe disease (2 or more crises in the previous year, with or without complications). We excluded patients with red cell transfusion within 4 months, on hydroxyurea, or other agents that may affect vaso-occlusive crisis frequency, and co-existing

chronic disorders unrelated to SCD, such as asthma and diabetes mellitus. We performed a CBC and plasma FUT7 enzyme concentration measurements (ELISA kit, MyBiosource Inc, USA).
Statistical analysis was performed with SPSS version 22.0 for Windows. A 2-tailed P value of <0.05 was used.
Results: Our subjects were predominantly female (SCD 52.5%, HbAA 55%), with median age 28 years (range 19-46 and 19-45 for SCD and HbAA, respectively). Median frequency of VOCs in patients was 1 (range 0-5). Avascular necrosis (32.5%) was the most common complication, while stroke, acute chest syndrome, and eye disease were the least common. As expected, SCD patients had lower haemoglobin levels than HbAA (7.9±1.3g/dL vs. 12.6±1.4g/dL, P<0.001). Significantly higher WBC, ANC, and platelet counts were observed in SCD patients compared with HbAA controls (P<0.001). No significant correlations were found between FUT7 and haematocrit (r =0.06), WBC count (r = -0.08), neutrophil count (r = -0.12), and platelet count (r =0.1), with P values of 0.7, 0.6, 0.5, and 0.6, respectively.
We found no difference between the median and IQR values of plasma FUT7 of SCD (2.1; 1.8-2.5) and controls (2.2; 1.8-2.8), P = 0.7. FUT7 activity was higher in SCD subjects in Group A (2.2; 1.9-2.9) than in Group B (2.0; 1.2- 2.4), with a trend towards significance P = 0.1.
Discussion: In this study, FUT7 activity did not differ between SCD patients and controls. We also did not find correlations between FUT7 and blood cell counts, suggesting that plasma FUT7 activity is not increased at baseline in SCD and that the degrees of anemia or leukocytosis are not associated with changes in FUT7. Nonetheless, a mild decrease in FUT7 levels was found in more severe SCD patients and should be confirmed in a larger study. Our study did not evaluate patients in crises or who received hydroxyurea and/or other SCD-modifying therapies. Since FUT7 catalyses selectin expression, variation in its activity may be more relevant in subgroups of SCD patients on anti-selectin therapies. Future studies should be carried out in such patients to explore FUT7 activity as a marker of acute vaso-occlusion and as a modifier of response to therapy.

Disclosures Panch: *Sanofi:* Consultancy, Other: Advisory Board; *Sobi:* Consultancy, Speakers Bureau.

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