Oxysterols may contribute to hemolysis in sickle cell disease

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Sickle cell disease (SCD) causes severe anemia, oxidative stress and chronic inflammation in addition to various lipid abnormalities including reduced cholesterol levels. Oxysterols are oxidized derivatives of cholesterol. They are known to affect cholesterol metabolism and have been shown to increase eryptosis. Our aim was to determine whether the levels of 7-ketocholesterol (7-KC) and cholestane-3β,5α,6β-triol (C-triol) were associated with hemolysis and lipid profile in patients with SCD. A total of 32 steady-state pediatric patients with SCD (22 HbSS and 10 HbSß$^{+}$) and 25 healthy controls were included in the study. The hemoglobin, LDH, bilirubins, ferritin, serum iron, lipid profile, 7-KC and C-triol levels of all subjects were measured. Oxysterols were quantified with N,N-dimethylglycine derivatization via LC-MS/MS. Patients' 7-KC and C-triol levels were found to be significantly increased compared to controls (45.39±3.89 vs. 27.86±11.61 and 20.31±1.78 vs. 13.86±9.23, respectively), while there was no difference between the HbSS and HbSβ^{+} subgroups. 7-KC levels were found to be correlated negatively with hemoglobin (r=-0.539, p=0.007) and positively with lactate dehydrogenase levels (r=0.518, p=0.002), while C-triol levels were correlated negatively with HDL cholesterol (r=-0.439, p=0.022) . However, there were no correlations between oxysterol levels and direct/total bilirubin levels. Additionally, while 7-KC and C-triol levels were highly correlated among controls (r=0.620, p=0.001), there was no correlation in patients. The findings of our study suggest that 7-KC and C-triol may have a role in SCD pathophysiology. Particularly 7-KC may contribute to hemolysis by affecting the erythrocyte membrane and activating eryptosis. The lack of correlation in patients' 7-KC and C-triol levels suggest alterations in the mechanism of non-enzymatic oxysterol production in patients with SCD.