SP319

Variability in Individual Response to a Single Sickling Event for Normal, Sickle Cell, and Sickle-Trait Erythrocytes

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Background/Case Studies: Hemoglobin (Hb) S polymerization is the primary event in sickle cell disease, resulting, over repeated cycles of polymerization, in irreversible damage to red blood cell (RBC) membranes. A single polymerization triggered by a hypoxic environment was reported to result in a reversible, upon re-oxygenation, decrease in RBC deformability and increased mechanical fragility (MF). Individual responses, however, had not been reported, although it was shown that RBC fragility can vary even among healthy donors. This study evaluates individual variability in response to a single hypoxia-induced sickling event, through changes in RBC MF. **Study Design/Methods:** Blood was drawn from 10 normal (AA), 11 sickle cell (SS), and 7 sickle trait (AS) volunteers with Hb S fraction, osmotic fragility, and medical history also collected. Mechanical stress was applied by using a bead mill (oscillation at 50 Hz; durations 0.5-60 min) with MF profiles described in terms of % hemolysis following stress of a specified duration. MF was measured in AA, SS, and AS cells equilibrated with air, with nitrogen in an anaerobic chamber, and with air after the hypoxic event. Hypoxia was induced by gas exchange (N_2) in an anaerobic chamber. Statistical analysis was done by using descriptive statistics, the Kruskal-Wallis test, and a repeated-measures ANOVA with mixed-effects models. **Results/Findings:** For most AA samples, MF does not change upon de-oxygenation or re-oxygenation; however, in two AA samples, there was a statistically significant increase in hypoxia, with cells recovering to pre-hypoxia levels upon re-oxygenation. Fragility of oxygenated AS cells was similar to that for AA, and in most cases de-oxygenation resulted in a marked increase of MF, with the cells' MF reverting to original pre-hypoxia levels upon re-oxygenation. However, for some AS (3 of 7), hypoxia did not affect changes in MF. The majority of SS cells had higher MF than that in AA and AS; however, for 4 of 11, MF was not significantly different. No correlation was observed with HemS fraction, osmotic fragility, or hydroxyuria use. De-oxygenation resulted in increased MF in 9 of 11 SS samples, with the increase in the other 2 not being statistically significant. All SS samples except 1 recovered to a lower MF after de-oxygenation. **Conclusion:** There is significant variability between cells from individual SS patients, with some exhibiting "protection" against hypoxia-induced membrane changes, as shown by a lack of statistically significant changes in their MF. While the factors responsible for the effect remain to be elucidated, further study is warranted to determine the extent to which individual cell response to hypoxia may be indicative of patients' risk of sickling crisis. Also, caution may be warranted on the use of blood from AS donors for transfusions when hypoxia may occur.

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