

Alpha-thalassemia protects against cerebrovascular disease in children with sickle cell anemia

Alfa-talassemia protege crianças com anemia falciforme contra doença cerebrovascular

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Dear Editors,

Cerebrovascular disease (CVD) is a severe complication in children with sickle cell anemia (SCA). Currently, transcranial Doppler (TCD) ultrasonography is the only clinical tool available to detect increased risk of occurrence of CVD in these children. TCD is a very sensitive, but moderately specific test: 60% of untreated children with abnormal velocities did not develop a stroke at 40 months¹, and it would be unnecessarily subjected them to prophylactic blood transfusions. The identification of more specific biomarkers is clearly needed. Recently, Filho et al. found that Bantu/Atypical β^S -globin gene cluster haplotype (β^S -haplotype) was associated with the occurrence of CVD, and alpha-thalassemia (α -thal) was not².

We also have studied the influence of β^S -haplotype and α -thal on CVD in a cohort of 208 children with SCA from Minas Gerais state, Brazil, and published it in 2010^{3,4}. In our experience, α -thal genotypes were significantly associated with reduction in CVD risk⁴. This association has been previously described. Although the prevalence of α -thal was lower in patients with CVD in the study published by the Arquivos², the association was not statistically significant probably because the sample was too small (n=86) to detect the difference.

In our study, the data regarding β^S -haplotypes were analyzed in several ways, and none showed a significant

association between haplotypes and CVD³. The only current evidence on the association between β^S -haplotypes and SCA phenotype is their relationship to the level of Hb F. However, the Hb F concentration seems to have no association with CVD⁵.

We would like to know whether some analyses were done for this population and were not shown in the study:

- Were the patients molecularly tested to confirm sickle cell genotypes? Maybe some β^0 -thalassemic chromosomes were misclassified as atypical β^S -haplotypes.
- Were the atypical chromosomes as a group completely homogeneous to eventually justify its association with an increased risk of CVD? It seems that they are heterogeneous in sickle cell patients from Brazil⁶.
- Have the authors analyzed the association between hematological features and CVD? Logistic regression showed that reticulocyte count was the main factor for CVD in our experience⁵.

It is likely that the discrepancies between the two study results are due to differences in methodological design, CVD definition and relative prevalence of α -thal and β^S -haplotypes. Anyway, we congratulate the authors for the published data and we are sure that they contribute to foster debate and increase knowledge about this important topic.

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