

Reply – Genetic polymorphisms and cerebrovascular disease in children with sickle cell anemia from Rio de Janeiro, Brazil

Resposta – Polimorfismos genéticos e doença cerebrovascular em crianças com anemia falciforme do Rio do Janeiro, Brasil

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Conflict of interest: There is no conflict of interest to declare.

Received 29 March 2012; Accepted 05 April 2012.

Dear Editors,

We thank Belisário and colleagues¹ for their interest in our study. We are open to further discussions on this relevant subject. We believe that the diversity of clinical manifestations observed in patients with sickle cell anemia (SCA) is a challenging issue that needs to be better understood, and only cohort and multicenter cooperative studies will increase the knowledge about SCA in our population. Here, we clarify the issues raised as follows:

ALPHA THALASSEMIA

As explained in our paper, alpha thalassemia is considered the only genetic polymorphism clearly associated with a specific clinical manifestation in SCA. The majority of reports have stated that co-inheritance with SCA confers a protective effect against cerebrovascular disease (CVD)²⁻⁷. Furthermore, a decrease in the frequency of abnormalities in transcranial Doppler has been observed in patients with alpha thalassemia^{8,9}. Although our results did not show statistical significance, children with alpha thalassemia have had fewer CVD events 15.8% (3/19) than those without alpha thalassemia 84.2% (16/19). Therefore, the results of the two studies are in agreement, and we suppose that the absence of statistical significance was due to the sample size.

β^S GENE CLUSTER HAPLOTYPES

1. Our family studies indicated that no child in our sample was a beta thalassemia carrier. All were homozygous for SCA. All samples classified as Atypical haplotypes were amplified and showed a restriction pattern consistent with this classification according to the method used¹⁰.
2. The correlation between β^S haplotypes and CVD is still controversial probably due to the small number of studies with a restricted number of patients. However, it is clear that different populations present peculiarities that characterize and differentiate them from each other. Bernaudin et al. report that in France, β^S haplotypes were not related to CVD⁹. In Brazil (Salvador), at least one chromosome Bantu was observed in patients with a history of CVD¹¹. In the United States, a higher risk for CVD development was observed in children with four or more alpha genes whose haplotypes were Bantu/Benin, Atypical or Bantu/Bantu than in children with other associations⁶. We believe that a detailed genetic study of β^S haplotypes might contribute to increase the knowledge of their influence on CVD in patients with SCA. Therefore, we are performing gene sequencing of all Bantu/Atypical samples; the obtained sequences will be compared with the samples of other haplotypes of the studied children.
3. In this study, we did not consider the association between hematological features and CVD.

Finally, we agree that differences between the two studies^{1,12} may be related to the study design, as well as to the sample size. With respect to CVD, we would like to emphasize

that our definition has high scientific accuracy, because we followed the current guidelines for the classification of CVD in sickle cell disease.

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