Research in athletes with sickle cell trait: just do it

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THE SICKLE CELL TRAIT (SCT) genotype, a condition found in an estimated 300 million people worldwide and 8–9% of African Americans is characterized by the heterozygous inheritance of a single defective beta globin gene. Inherited in the homozygous form, the beta globin gene mutation leads to sickle cell disease (SCD). Patients with SCD have profound clinical manifestations that can be associated with significant morbidity and mortality. On the contrary, individuals with SCT do not have a disease.

The SCT phenotype is almost always benign. Rarely, under ill-defined conditions of environmental and physical extremes, individuals with SCT can have clinical symptoms. Despite their exceedingly uncommon occurrence, several complications can occur, the most newsworthy of which is a presumptive association between SCT and sudden death during intense physical activity. The causative pathophysiological mechanisms and risk factors that lead to the development of symptoms in individuals with SCT remain unknown.

In 2010, the National Collegiate Athletic Association (NCAA) implemented a mandate requiring all incoming Division I student athletes to undergo testing for SCT (3). Should they choose not to be tested, an athlete has the option of either showing proof of a prior test or signing a release of liability waiver absolving their academic institution and the NCAA from liability. Since its inception, this policy has been mired in controversy. The polemic nature of the subject stems from the fact that the mandate, a policy issued in response to litigation rather than one driven by evidence-based science, has impasioned implications pertaining to genetic privacy, genetic discrimination, social stigmatization, and racial profiling. The mandate, in our opinion, comes precariously close to violating the fundamental ethical principles of beneficence and nonmaleficence. Numerous leading organizations including the American Society of Hematology, the Department of Health and Human Service’s Secretary’s Advisory Committee on Heritable Disorders in Newborns and Children, and the Sickle Cell Disease Association of America, have issued policy statements in opposition to the NCAA’s mandated screening (1, 4). Moreover, these organizations strongly support and advocate for organized biomedical and epidemiologic research investigating the rare but potential pathophysiologic implications of SCT.

In their study in the Journal of Applied Physiology, “Exercise Training Blunts Oxidative Stress in Sickle Cell Trait Carriers,” Chirico et al. (2) investigated the impact of regular physical activity on plasma markers of oxidative stress, nitric oxide metabolism, and endothelial adhesion in individuals with SCT compared with controls. In this paper, the authors present data to show that exercise has a potential modulatory effect on oxidative stress and nitric oxide metabolism in individuals with SCT. The authors compared exercise-trained SCT carriers to their untrained counterparts and found that physical activity could be a conceivably viable method of controlling oxidative stress. Although there are large clinical differences between SCT and SCD, the authors suggest that exercise training could also have potentially beneficial effects on patients with SCD.

This paper clearly shows that carefully conducted studies need to be performed to fully define and characterize modifiable risk factors in carriers of the sickle beta globin gene mutation.

Unfortunately, very few well-controlled studies have been performed correlating exercise physiology to the genetic, biologic, and clinical aspects of individuals with SCT. The controversy over the NCAA mandate has generated a national discussion, the theme of which underscores and substantiates the need for focused research that better defines risk factors for these individuals. Such studies are in our view essential. Promising young high school athletes who pursue their education and passion for sport would be far better served by well-conducted studies that define and characterize risk factors, thereby enabling us to provide evidence-based anticipatory guidance, than by the uncertainty and possible stigma generated by the currently mandated genetic test. Chirico et al. (2) show that such studies can be done. We charge others to simply just do it as well.

DISCLOSURES

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