Genotype analysis of single nucleotide variant in *NCF4* and *CBR3* genes associated with reduced systolic fractional shortening in pediatric patients with acute lymphoblastic leukemia treated with doxorubicin.

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Abstract

Cardiotoxicity (CT) is a frequent complication due to the use of anthracyclines (AC) in chemotherapy in various types of cancer. The reduction in the systolic shortening fraction (SF) is an echocardiographic parameter that, together with other biochemical values, is used to assess the presence of CT. Studies suggest that some genetic variants may be involved in the risk of cardiotoxicity due to the use of anthracyclines. Although it has been reported that SF alone cannot be taken as a measurement to definitely assess CT due to the use of AC, reports documenting the impact of single nucleotide variant (SNV) on CT risk considering SF as a marker in pediatric patients from Latin American countries with cancer, are scarce. This study aimed to evaluate the association between the genotypic status of *NCF4* rs1883112 and *CBR3* rs1056892 SNV with the SF indicative of CT by AC in a group of Mexican children with acute lymphoblastic leukemia (ALL). Sixty-nine children (6 to 17

years of age) with ALL were treated at the Centro Estatal de Cancerología (CECAN) in Durango-Mexico. The *NCF4* and *CBR3* genotypes were examined by real-time PCR. Fractional shortening was evaluated as a marker of systolic CT due to the use of AC. The homozygous AA genotype of the *NCF4* rs1883112 SNV was significantly associated with reduced SF by the use of AC (OR = 8.87, 95% CI = 1.8066 to 147.6678, p = 0.01). There was a significant association between the dominant homozygous GG genotype of the CBR3 rs1056892 SNV and the reduced SF by the use of AC (OR = 5.33, 95% CI = 1.4008 to 20.3060, p = 0.01). This pilot study suggests that selected SNV may affect the risk of CT by AC, SF may be a value that, together with other parameters such as left ventricular ejection fraction (LVEF) and diastolic filling volume may give a broader picture of CT risk in Mexican pediatric patients treated with AC.

Keywords: Fractional shortening, Cardiotoxicity, Anthracyclines, Leukemia.