Genetic modifiers and phenotype of Duchenne muscular dystrophy: A systematic review and meta-analysis

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Abstract

The transforming growth factor beta (TGFβ) pathway could modulate the Duchenne muscular dystrophy (DMD) phenotype. This meta-analysis aims to estimate the association of genetic variants involved in the TGFβ pathway, including the latent transforming growth factor beta binding protein 4 (LTBP4) and secreted phosphoprotein 1 (SPP1) genes, among others, with age of loss of ambulation (LoA) and cardiac function in patients with DMD. Meta-analyses were conducted for the hazard ratio (HR) of LoA for each genetic variant. A subgroup analysis was performed in patients treated exclusively with glucocorticoids. Eight studies were included in the systematic review and four in the meta-analyses. The systematic review suggests a protective effect of LTBP4 haplotype IAAM (recessive model) for LoA. It is also suggested that the SPP1 rs28357094 genotype G (dominant model) is associated with early LoA in glucocorticoids-treated patients. The meta-analysis of the LTBP4 haplotype IAAM showed a protective association with LoA, with an HR = 0.78 (95% CI: 0.67–0.90). No association with LoA was observed for the SPP1 rs28357094. The LTBP4 haplotype IAAM is associated with a later LoA, especially in the Caucasian population, while the SPP1 rs28357094 genotype G could be associated with a poor response to glucocorticoids. Future research is suggested for SPP1 rs11730582, LTBP4 rs710160, and THBS1 rs2725797.

Author keywords

Duchenne muscular dystrophy; LTBP4; Meta-analysis; Polymorphism; SPP1; Systematic review; TGFβ