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Abstract

Sex hormone-binding globulin (SHBG) enhances mitochondrial dynamics and biogenesis while attenuating inflammation in adipose-derived mesenchymal stem cells (ASCs) derived from equine metabolic syndrome (EMS)-affected horses †

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Abstract: Equine metabolic syndrome (EMS), in related to the onset of chronic low-grade inflammation, as well as dysregulations in the mitochondrial dynamics and metabolism, and predisposition to laminitis. In fact, EMS is a critical endocrine disorder among the most prevalent conditions affecting horses from different breeds. According to the most recent research, low human sex hormone-binding globulin (SHBG) serum levels correlate with an increased risk of obesity, insulin resistance and diabetes, and may contribute to overall metabolic dysregulations. This study aimed to test whether exogenous SHBG could protect EMS affected adipose-derived stromal stem cells (EqASCEMS) from the mitochondria dysfunction and inflammation. EqASCEMS wells were treated with 50 nM of exogenous SHBG, whose biocompatibility was tested after 24 of incubation. Several parameters including cell viability, mitochondria dynamics, metabolism and biogenesis were assayed; as well as inflammatory and anti-inflammatory markers expression were analyzed. Obtained data demonstrated that exogenous SHBG treatment significantly enhanced the mitochondrial biogenesis by improving the expression of MFN, PARKIN, PINK and Cytochrome C at both genes and proteins levels; furthermore, the SHBG exogenous treatment displayed same effect regarding the expression of the genes related to mitoribosomes and the mitochondrial oxidative phosphorylation (OXPHOS) system (NDUFA9, COX4L1, COX4L2, MTERF4 and OX1AL). Furthermore, SHBG alleviated the inflammation caused by EMS; thus, via the reduction of the gene expression of cytokines such as IL-1β, IL-6 and TNF-α and by enhancing the gene expression of anti-inflammatory markers (IL-4, IL-10 and IL-13). Our study suggests that the SHBG is endowed with crucial beneficial effects on ASC metabolic activities and could serve as a valuable therapeutic target for the development of efficient EMS treatment protocols.

Keywords: EMS; SHBG; mitochondria; OXPHOS; Inflammation

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