Physiological changes in glucose uptake by GLUT-4 in Gestational Diabetes Mellitus

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Abstract: This study aimed to identify the physiological changes that occur in the GLUT4 in glucose uptake in patients with gestational diabetes mellitus, which changes have resulted due to the increase of counterregulatory hormones insulin at physiological stress imposed by pregnancy and by predetermining factors that can be genetic and / or environmental factors, inflammatory mediators and insulin resistance. Given that all these metabolic changes interfere directly or indirectly in glucose uptake by GLUT-4, there was a literature review with descriptive, explanatory and qualitative approach about the changes suffered by this carrier in gestational diabetes mellitus. It is therefore concluded that metabolic changes suffered in DMG interfere directly in the expression and translocation of the GLUT-4 glucose transporter. Keywords: Metabolism; Gestational diabetes; Receivers; Insulin resistance.

OVERVIEW

Gestational diabetes mellitus (GDM) is characterized by an intolerance to carbohydrates, resulting in hyperglycemia, peripheral insulin resistance, and hyperinsulinemia, originated for the first time during pregnancy. The pathophysiology of GDM results from increased of insulin counterregulatory hormones, due to the physiological stress imposed by pregnancy and by predetermining factors that may be genetic and/or environmental (Nascimento et al., 2017; Ribeiro et al., 2020).

Hyperglycemic hormones such as cortisol, estrogen, progesterone and prolactin are fully involved with insulin resistance (IR) during pregnancy, however the placental lactogen is considered as the main hormone related to this type of resistance. In this aspect, IR is characterized as a reduced capacity of the tissues insulin sensitive, with respect to glucose uptake, respond to normal levels of the hormone (Leitão, 2019).

Muscle and white (adipose) tissues have some protein isoforms glucose transporters, such as GLUT-1, which is responsible for transporting glucose in the basal state (Ryder et al., 2001) and GLUT-4, which is responsible for glucose uptake excited by insulin as well as muscle contraction (Seo, 2017).

GLUT-4 has also been found in the intravillous stroma of the human placenta, which is richly endowed with insulin receptors (Tiago, 2013). Based on these assertions, questions about what changes occur in GLUT-4 in glucose uptake in GDM, because the same is an insulin-sensitive glucose transporter and is present in tissue fat and muscle.

Therefore, it is suggested that physiological changes in hormones hyperglycemic and genetic and environmental predetermining factors interfere with the uptake of glucose by GLUT-4 in pregnant patients with diabetes mellitus (DM).

When compared to other types of diabetes, studies on GDM are scarce. Some populations may have an increased risk of developing GDM due to some gene mutations in the monogenic form of diabetes, Maturity Onset Diabetes of the Young (MODY). A common polymorphism in the promoter region of the GCK gene and HNF1A linked to MODY, was identified in a study carried out in a Scandinavian population. Although some gene mutations determine the monogenic form of diabetes, have also been found in some pregnancies with GDM, it is presumable that it may there is a polygenic risk factor in this pathology, as there are several evidences that correlate GDM and DM2, giving it a polygenic characteristic (Olivia et al., 2018).

Some DM2-associated loci are known to contribute to the development of the DMG, in particular, variants of eleven genes, namely: TCF7L2, KCNJ11, CDKAL1, KCNQ1, CDKN2A/CDKN2B, HHEX/IDE, IGF2BP2, SLC30A8, TCF2, FTO, PPARG and WFS1 which is not surprising given the common origin between these two types of diabetes (Huang, Merriman & Gong, 2019).

HLA-DR3 and DR4 antigens are more frequent in women with GDM than women with normal pregnancy, this being another important aspect in the genetics of the DMG, other histocompatibility alleles such as HLA-DR7/DQ2 pertinent to preeclampsia, are also linked with DMG (Evangelista, 2012). The correlation between the DMG and the DM1 is still uncertain. Polymorphic sites were noted in some pregnant women with GDM of the MICA gene pertinent to DM1, while the HLA haplotypes identified are dissimilar. There is evidence that certain patients may have a form of GDM (Sarrazola et al., 2018).

The development of obesity and insulin resistance, a factor of such importance for DMG, is potentially linked to decreased expression of glucose transporter, GLUT-4. This statement is confirmed in the occurrence of the syndrome of polycystic ovaries, in Diabetes Mellitus, as well as in pregnancy in which there is a considerable reduction in the expression of this transporter (Junior, 2011).

Meira (2013), also states that regardless of whether it is skeletal muscle or adipose tissue, any inference there may be, causing any change in expression of the gene that encodes the GLUT-4 transporter, such alterations can directly infer the increase or even decrease in insulin sensitivity.