ABSTRACT

The Impact of G6PDH Deficiency and Antioxidant Status in a Diabetic Trinidadian Population

Fariyal Hosein Hardit-Singh

Glucose-6-phosphate dehydrogenase (G6PDH) is the primary source of NADPH which many enzymes require as the principal intracellular reductant. These include enzymes of the antioxidant pathways, the polyol pathway, the production of GSH and activation of the hexosamine pathway**.** The production of free radicals in healthy individuals is offset by antioxidant activity. NADPH plays a pivotal role in regularizing the antioxidant status. However in conditions where hyperglycaemia prevails it is thought that the equilibrium between reactive oxygen species and antioxidant activity is shifted toward free radical production, initiating oxidative stress.

The aim of this study was to assess the impact of G6PDH deficiency on antioxidant status in diabetic and non-diabetic individuals**.** Antioxidant status was determined by measuring Glutathione Peroxidase ($GSHP_x$), G6PDH, Total Antioxidant Status (TAS) and Nitric Oxide of diabetic individuals and non-diabetic individuals with and without deficiencies in G6PDH activity, normotensives and hypertensives and chronic and non-chronic complicated individuals. It was observed that GSHPx activity was significantly lower for individuals with diabetes as compared to non-diabetic individuals. Hypertensive individuals also had significantly lower $GSHP_x$ activity. Chronically complicated individuals had significantly lower GSHPx activity as compared to either healthy individuals or to diabetic individuals who lacked chronic complications.

GSHPx activity has been shown to be decreased in conditions of oxidative stress. This includes conditions of diabetes mellitus, hypertension and chronic complicated patients in our study. NADPH which is a major reductant, seems to be compromised resulting in decreased GSHPx activity and this exacerbates oxidative stress levels**.** Nitric oxide levels showed no correlation with blood pressure, G6PDH activity, diabetic status or the presence of diabetic complications. Hypertensive individuals had significantly lower TAS levels than healthy individuals. Decreases in TAS levels seen in hypertensives may be attributed to a failure of upregulation of one or more antioxidants in response to stabilize the increase in oxidative stress independent of NO production.

Diabetes mellitus is linked to G6PDH deficiency because of the hyperglycaemic condition which initiates cellular damage making them vulnerable to oxidative stress which is exacerbated as a result of reduced NADPH production associated with G6PDH deficiency. There are other metabolic pathways which generate NADPH, however G6PDH is the predominant contributor in the defense mechanism utilised by the cells against oxidative stress. Subjects with chronic complications had lower G6PDH activity resulting in decreased levels of NADPH. Where no significant differences occurred as in the levels of nitric oxide between hypertensives and healthy individuals, diabetics and healthy individuals, and G6PDH deficients and healthy individuals the current study's results seem to suggest that an upregulation in other antioxidants was produced in response to increased oxidative stress. An effective strategy for reducing diabetic complications may lie in treatment through antioxidants, which can possibly abate oxidative stress.

Keywords: antioxidants; antioxidant status; chronic complications; diabetes mellitus; G6PDH deficiency; glutathione peroxidase; nitric oxide; total antioxidant status.