

ABSTRACT

The Effect of Metformin on Plasma Total Homocysteine, Plasma Basal Insulin and Plasma Creatinine in a Rat Model of Type 2 Diabetes Mellitus

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Metformin is commonly prescribed for type 2 diabetes mellitus (type 2 DM), but may elevate homocysteine levels. Elevated homocysteine in type 2 DM compounds the risk of cardiovascular disease. Insulin and creatinine levels also influence plasma homocysteine level. The nicotinamide and streptozotocin (NA-STZ)-treated rat produced a model of type 2 DM. This study investigated the effect of metformin on plasma homocysteine, basal insulin and creatinine levels in the NA-STZ-treated rat.

The experiment consisted of two stages. First, type 2 DM was induced in adult male Sprague-Dawley rats using a combination of nicotinamide (50 mg/kg Body Weight [BW], IP) and streptozotocin (40 mg/kg BW, IP); while controls received saline. Type 2 DM was identified by an oral glucose tolerance test and a glibenclamide challenge. In the second stage, type 2 diabetic rats were treated

with metformin (25 mg/kg BW) for 4 weeks; while controls received distilled water. Glucose tolerance was assessed after treatment. Plasma homocysteine, basal insulin and creatinine levels were assessed at both stages of the experiment.

NA-STZ-treated rats displayed significantly elevated post-prandial blood glucose (BG) concentrations at 30, 60, 90 and 120 min ($p < 0.01$); and also significantly lowered [BG] at 60, 90 and 120 min after being given glibenclamide ($p < 0.01$). NA-STZ treatment caused lowered plasma homocysteine ($p < 0.05$), but did not significantly affect basal insulin and creatinine levels ($p = 0.53$, & $p = 0.79$, respectively). Metformin did not significantly affect plasma homocysteine ($p = 0.38$) or plasma basal insulin ($p = 0.40$); but significantly decreased plasma creatinine levels ($p = 0.005$).

NA-STZ treatment produced form of type 2 DM, characterised by deteriorated glucose tolerance, and the ability to respond to glibenclamide. The results suggest that metformin does not increase the risk of cardiovascular disease in type 2 diabetics by elevating plasma homocysteine.

Keywords: Basal insulin, glibenclamide challenge, metformin, oral glucose tolerance test, rat model, streptozotocin, total homocysteine, type 2 diabetes.