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Serum sialic acid changes in non-insulin-dependant diabetes mellitus (NIDDM) patients following bitter melon (*Momordica charantia*) and rosiglitazone (Avandia) treatment

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Abstract

Diabetes mellitus is associated with an increase in sialic acid concentration along with other complications. Sialic acid changes in NIDDM patients were investigated following bitter melon (55 ml/24 h) and rosiglitazone (4 mg/24 h) treatment. A total of 25 patients of both sexes were used in each experimental group. Patients following bitter melon treatment showed no significant difference of serum sialic acid (57.95 ± 4.90 vs. 57.6 ± 5.56 mg/dl, $p = 0.17$) and serum glucose concentration (93.7 ± 9.63 vs. 88.35 ± 6.31 mg/dl, $p = 0.78$) as compared to control subjects. However, the concentration of total cholesterol was significantly high in these patients as compared to control subjects (192 ± 14.23 vs. 170.6 ± 15.1 mg/dl, $p < 0.03$) but within normal range (160–200 mg/dl), suggesting the significant hypoglycemic and lipid-lowering properties of bitter melon. The patients following rosiglitazone treatment showed a significant increase of serum sialic acid concentration (60.2 ± 5.80 vs. 57.6 ± 5.56 mg/dl, $p = 0.01$) along with glucose (112 ± 6.2 vs. 88.35 ± 6.31 mg/dl, $p < 0.04$) and total cholesterol concentration (216.45 ± 20.2 vs. 170.6 ± 15.1 mg/dl, $p < 0.01$) as compared to control subjects. In addition six of the patients had retinopathy, two of whom were suffering also from myocardial infarction and they still had a higher serum sialic acid (61.05 ± 1.20 mg/dl), glucose (187 ± 2.11 mg/dl), total cholesterol (239.10 ± 5.04 mg/dl) and triglyceride (183 ± 4.14 mg/dl) concentration, indicating a poor response of these patients to rosiglitazone. Comparison of serum sialic acid concentration of patients, following bitter melon and rosiglitazone treatment revealed no significant difference but the study showed that bitter melon could be more effective in the management of diabetes and its related complications as compared to rosiglitazone.

Keywords: Sialic acid; Diabetes (NIDDM); Bitter melon; *Momordica charantia* Rosiglitazone; Cardiovascular complications

Introduction

Since antiquity diabetes has been treated with plant medicines. Bitter melon (*Momordica charantia*) is traditionally used for diabetes in developing world particularly India and Pakistan, which have a long history of the use of herbal remedies in diabetes

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(McNeill and John 1999). Bitter melon is a traditional plant used by ayurvedic doctors of medicines to benefit various conditions including diabetes (Basch et al. 2003). It may be of benefit to lower plasma lipids and blood sugar in animal studies. It has been shown to ameliorate diet-induced obesity and insulin resistance (Grover and Yadav 2004; Chaturvedi 2005; Krawinkel and Keding 2006). It is composed of several compounds with confirmed antidiabetic properties. Charantin, extracted by alcohol, is a hypoglycemic agent composed of mixed steroids that is more potent than the drug tolbutamide, which is often used in the treatment of diabetes. It also contains insulin-like polypeptide, polypeptide-p, which lowers blood sugar level when injected subcutaneously into Type1 diabetic patients. The oral administration of 50–60 ml of the juice has shown good results in clinical trails. It has also got lipid-lowering effect that is associated with increased lipid oxidative enzyme activities and uncoupling protein expression (Nerurkar et al. 2006; Bouham 2006; Raman and Lau 1996). Rosiglitazone (Avandia) belongs to a group of oral antidiabetic agents called thiazolidinediones, also known as glitazones, and it binds to PPARs, a type of nuclear regulatory proteins involved in transcription of genes regulating glucose and fat metabolism. These PPARs act on peroxysomes proliferators responsive elements (PPRE) (Eurich et al. 2007). The PPRE influence insulin-sensitive genes, which enhance production of mRNAs of insulin-dependent enzymes. The final result is the better use of glucose by cells (Erdman et al. 2007). Although glitazones have beneficial effects on diabetes, there is concern about the safety of rosiglitazone (Rendell 2004; Barnett et al. 2003; Khanderi et al. 2008) and a Food and Drug Administration Panel voted with some controversy, 20:3 that available studies "supported a signal of harm" but voted 20:1 to keep the drug on the market (Nissen and Steven 2007; Wood and Shelly 2007) and is widely used in Pakistan. Sialic acids are derived from neuraminic acid whose main derivative is N-acetylneuraminic acid, which is generally used as a synonym for sialic acid (Ledeen and Yu 1976). Sialic acids are widely distributed in nature as non-reducing termini of glycoproteins and glycolipids. About 70% of the total sialic acid of eukaryotic cells has been found on the cell surface and the remainder is distributed among endoplasmic reticulum, mitochondria, lysozymes, etc. Because of their acidic nature they impart negative charge to the cell surface and are important in cell-to-cell or cell-to-matrix interaction. Sialic acid may also be involved in the masking of cell-surface antigens and may act as receptor for lectins, virus particles, some hormones and antibodies (Jeanloz and Codington 1976). There is a large body of evidence suggesting that the serum concentration of sialic acid is increased in diabetes mellitus and that the serum concentration of sialic acid is a strong predictor of cardiovascular mortality (Crook et al. 1994; Lindberg et al. 1991, 1992, 1993; Pickup et al. 1995; Yokohama et al. 1995). Wakabayashi et al. (1992) have also reported raised serum sialic acid concentration in patients who had high concentration of cholesterol and triglyceride. The evidence of raised level of sialic acid as a risk factor for cardiovascular diseases signifies the importance of its status in diabetes mellitus.

Therefore the present study was undertaken to elucidate quantitative changes in serum sialic acid concentration in NIDDM patients following bitter melon (*Momordica charantia*) and rosiglitazone (Avandia) treatment to illustrate the comparative effect of these drugs on sialic acid content of the patients. An attempt has also been made to evaluate the effect of these drugs on other complications related to diabetes.

Subjects and methods

Source and preparation of bitter melon juice and rosiglitazone

Momordica charantia (family Cucurbitaceae, commonly known as ku gua, bitter melon, karela or bitter gourd) was purchased from a local market in N.W.F province, Pakistan, and authenticated by a pharmacognosy expert before juice preparation. The juice was prepared by the method proposed by Chen et al. (2003). Unripe bitter melon fresh fruit was washed thoroughly with water, cut open and the seeds removed. The juice was extracted by crushing the fruit in a mortar and straining through a muslin cloth. The yield was 370 ml/kg.

Rosiglitazone is an oral antidiabetic drug, manufactured by Sigma Chemical Company and marketed by Glaxo SmithKline.

Research design and clinical studies

The Kohat Institute of Medical Sciences medical ethics committee passed the research project. The volunteer patients of NIDDM were explained about the research protocol and their written consents were obtained for the study. NIDDM patients ($n = 50$) between age 30 and 60 years were investigated during the course of the present study, divided into two groups: group B comprises patients following rosiglitazone (Avandia) and group C following bitter melon (*Momordica charantia*) treatment, whereas group A served as control. The patients were randomly selected from Kohat Institute of Medical Sciences Hospital, Kohat and Afghan Dawakhana, Lakki Marwat, NWFP, Pakistan. The patients of both the groups were on controlled diet and were not taking any other antidiabetic or cholesterol-lowering drug that might alter sialic acid, glucose or cholesterol level.