ABSTRACT:

Background: Diabetic neuropathy is one of the most frequent and severe complications of diabetes. Hyperglycemia, oxidative stress and apoptosis have key roles in pathogenesis of diabetic neuropathy. There are local and even cellular renin-angiotensin systems (RAS) in different tissues such as neural tissue. Local RAS are involved in physiological and pathophysiological processes such as inflammation, proliferation and apoptosis. This study aimed to investigate the role of local renin-angiotensin system on high glucose-induced cell toxicity, apoptosis and reactive oxygen species (ROS) production in PC12 cells, as a cell model of diabetic neuropathy.

Method: PC12 cells exposed to a high glucose (27 mg/ ml) concentration, and captopril (as an ACE inhibitor), telmisartan and losartan (as AT_1 antagonists), and also PD123319 (as an AT_2 antagonist) were administered before and after induction of high glucose toxicity. Then cell viability was assessed by MTT assay and apoptotic cells and intracellular ROS production detected by annexin V-propidium iodide and DCFDA, respectively, using flow cytometry.

Results: High glucose concentration decreased cell viability, while increased apoptotic cells and intracellular ROS production in PC12 cells. In PC12 cells pretreatment and treatment by the drugs showed a significant improvement in cell viability and reduced apoptosis in captopril, telmisartan and PD123319 treated groups but only captopril and telmisartan were able to reduce ROS production. Losrtan significantly lowered ROS but didn't show any improvements in cell viability and apoptotic cells.

Conclusion: The results of the present study showed that RAS inhibitors reduce cell toxicity, apoptosis and ROS production induced by high glucose concentration. It may be suggested that local RAS has a role in high glucose toxicity. The ability of captopril and telmisartan but not PD123319 in reducing high glucose-induced ROS production in PC12 cells suggests that the protective effects of captopril and telmisartan partly performed by their antioxidant properties but the protection of PD123319 mediates by other mechanism(s). The effectiveness of telmisartan but not losartan along with some evidences which report the absence of AT_1 receptors on PC12 cells suggest the involvement of other receptors like PPAR-γ.

Keywords: High glucose toxicity, Oxidative stress, Apoptosis, Renin-angiotensin system, PC12

Abstract

The incidence of urinary stones is very high in population. Treatment of patients with kidney stones in primary stages can reduce the side effects and also may prevent the surgical operations and postoperative complications.

Several effects have been reported for Nigella Sativa (N.S) seeds; they include anti analgesic, anti inflammatory, lowering serum lipids, increasing glutathione in kidney and repairement of kidney tissues after nephrotoxicity. The aim of this study is to investigate the effects of the ethanolic extract of N.S seeds on kidney stones in rat. Thirty two Wistar rats with 200±10g body weight were randomly divided into 4 groups. Group A as intact control was received tap drinking water for thirty days. Group B (ethylene glycol control), groups C and D as exprimental animals all were received 1% ethylen glycol in drinking water for 30 days. Furtheremore Group C was also treated with 250 mg/kg B.W N.S ethanolic extract for 30 days, while group D was also treated with 250mg/kg. B.W N.S extract from 14^{th} day through the end of the expriment. One day before the start of study and on 7^{th} , 14^{th} and 30^{th} days of the study each animal was placed in a metabolic cage for collection of 24 hr urine samples for determination of urinary calcium oxalate levels. After 30 days all rats were killed by guillotine and kidneys were removed and sections were prepared with routine histological techniques, slides were examined under light microscope to count calcium oxalate deposits.

The results showed that the number of calcium oxalate deposits were significantly increased in group B vs A ($P<0.001$). The number of deposits in group C and D were significantly less than group B ($P< 0.05$), while the number of calcium oxalate deposits in group C and D in comparison with group A were statistically insignificant. The calcium oxalate concentration in urine at the end

ABSTRACT:

Background:

Diabetes mellitus is a chronic metabolic disorder and is one of the most common endocrine diseases. Diabetes mellitus prevalence is increasing throughout the world. It affects numerous organ systems in the body. Gastrointestinal complaints are common among diabetic patients. Several studies indicate that about 70–75% of diabetic patients have at least one gastrointestinal symptom. The gastrointestinal tract of vertebrate species contains melatonin, which participates in several physiological functions. Melatonin, is a neurohormone that mainly synthesized and secreted in pineal gland and is also produced in GIT. It has a potent antioxidant effect, reduces lipid peroxidation, scavenges oxyradicals and stimulate endogenous antioxidant systems in liver and blood such as superoxide dismutase, glutathione oxidase, glutathione S- transferase and total thiol. Higher doses of melatonin provide protective effects, especially in relation to inflammatory injuries of the GI tissues. The aim of this study was to investigate the effects of melatonin in diabetic rats.

Method:

Male Wistar rats (250±20g) were randomly divided into 5 groups, including: control, diabetic and diabetics treated with melatonin dissolved in ethanol 4%+ salin, at doses of 5, 10, 20 mg/kg BW for 2 weeks. Diabetes was induced by a single dose i.p. injection of 60 mg/kg STZ. At the end of treatment period MDA, total thiol, GSH, SOD and CAT activity, HDL-c, LDL-C, triglyceride, cholesterol, serum glucose, body weight, gastric motility, acid and mucus concentration were measured.

Results:

Diabetic rats showed a significant increase in MDA, LDL-C, triglyceride, total cholesterol and serum glucose and a significant decreased in total thiol, GSH, SOD and CAT activity, HDL-C, body weight, gastric motility, acid and mucus concentration *vs.* control rats. Under our experimental conditions melatonin treatment (5, 10, 20 mg/kg BW) significantly decreased LDL-C, triglyceride and cholesterol and significantly increased total thiol, SOD activity and gastric mucus concentration and melatonin at 10 and 20 mg/kg doses significantly decreased MDA and serum glucose and significantly increased GSH and gastric motility *vs.* diabetic group. CAT activity significantly increased at 20 mg/kg melatonin treatment group *vs.* diabetic group.

Melatonin had no significant effect on body weight, HDL and gastric acid concentration.

Conclusion:

Our findings demonstrate that melatonin has an improvement effects on gastrointestinal complications due to diabetes in diabetic rats. Therefore, it may be suggested that it can be used in the treatment of gastrointestinal complications in diabetic patients.

Keywords:

Melatonin, STZ, diabetes mellitus, gastrointestinal complications.