Effects of 7 days melatonin introduction on the hydrogen sulfide and glutathione level in the blood of diabetic rats with nephropathy

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Diabetes mellitus and its complications represent a major sociomedical problem today. Hyperglycemia is a driving force for the development of diabetic nephropathy [5]. Changes in the concentration and production of hydrogen sulfide play an important role in the pathogenesis of pancreas β-cell dysfunction and in the pathogenesis of endothelial injury, which develop on the basis of elevated circulating glucose levels in diabetes mellitus [4]. The experiment was carried out on male albino rats with the body weight of 0.16 – 0.18 kg. Experimental diabetes was induced by 5% alloxan monohydrate solution in the dose of 150 mg/kg. Nephropathy was induced in diabetic rats by injection of glycerol (10 mg/kg) after fasting overnight. After diabetes and nephropathy were confirmed, rats were divided into five groups: 1) control rats; 2) alloxan diabetic rats; 3) animals with overt diabetes, which introduced to melatonin intragastrically in the dose of 10 mg/kg at 8 a.m. during 7 days; 4) animals with diabetic nephropathy; 5) animals with diabetic nephropathy, introduced to melatonin intragastrically in the dose of 10 mg/kg at 8 a.m. during 7 days. We determined concentration of H_2S and glutathione in the blood, activity of glutathione-S-transferase (G-S-T) and glutathione peroxidase (GPx) in the blood, activity of cystathionine-β-synthase (CBS), cystathionine-γ-lyase (CSE) in the liver. Fasting blood glucose level was increased in diabetic rats in 2.3 times, but the introduction of melatonin promoted normalization of the level of basal glycaemia in diabetic animals, indicating hypoglycemic action of melatonin. In rats with diabetic nephropathy the level of glucose increased in 1.9 times as compared with the level of glucose in control rats. Melatonin does not show hypoglycemic action in combined pathology. Our study shows the plasma H_2S level is

significantly reduced in the alloxan induced diabetic rats in 1.3 times and in rats with nephropathy in 1.8 times as compared with plasma level of H_2S in control rats. In the blood of alloxan diabetic rats receiving melatonin the content of H_2S increases as compared with the groups of diabetic rats and rats with nephropathy in 1.2 and 1.6 times accordingly. Our examination demonstrates a reduction of CSE activity in the liver of alloxan-diabetic rats in 1.5 times and in 2.6 times there was reduction in rats with diabetic nephropathy. Similar changes have been observed in activity of CBS in the liver of alloxan-diabetic rats and rats with combination pathology. The introduction of melatonin contributes to the increasing CSE activity in the groups of diabetic rats and activity of CBS in rats with combined pathology. Hyperglycemia leads to depletion of the antioxidant defense mechanism, thus promotes the generation of free radicals resulting in an endothelial dysfunction [3]. Metabolism of glutathione is known to be associated with the metabolism of sulfur-containing aminoacids and hydrogen sulfide. The glutathione system is one of the most powerful antioxidant cell systems, interaction of free radicals, and protects against lipid peroxidation [1, 2]. Our results indicate the level of glutathione in red blood is reduced as compared with the level in control rats (in 1.3 times in the alloxan induced diabetic rats and in 1.2 times in diabetic rats with nephropathy). The activity of G-S-T and GPx increased in red blood cells in 1.25 times in the alloxan induced diabetic rats, and in 1.2 times in diabetic rats with nephropathy. The introduction of melatonin contributes to the normalization an activity of G-S-T in the alloxan induced diabetic rats and in rats with nephropathy, and the activity of GPx normalizes only in group of animals with diabetes mellitus. It may indicate the protective functions against oxidative stress. Study of H_2S concentration and its producing enzymes may prove to be an effective strategy for modulating diabetes treatment. The disorders of metabolism of hydrogen sulfide in alloxan diabetic rats can lead to the imbalance between oxidative and reductive species. Our results suggest that melatonin is effective for the normalization of metabolism of hydrogen sulfide and glutathione system in diabetic rats. The introduction of melatonin in the group of diabetic rats with nephropathy didn't show reliable changes, and therefore needs further studies using melatonin for a longer period of

time.

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