Topiramate induces weight loss and improves insulin sensitivity in dietary obese rats: comparison to sibutramine

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Abstract

Background and Objectives: Topiramate is newly approved as anticonvulsant that seems to promote body weight loss in humans. The present study was designed to evaluate the weight-controlling properties of topiramate in dietary obese female rats in comparison with sibutramine.

Materials and Methods: Fifty rats were assigned as normal, high fat diet (HFD), HFD + sibutramine (7.5 mg/kg, p.o.), HFD + topiramate (25 mg/kg, p.o.) and HFD + topiramate (50 mg/kg, p.o.). Body weight was registered, anxiety was tested in Vogel’s test and blood pressure (BP) was measured. In addition, liver index, adipose tissue index, fasting blood glucose and serum lipid profile were measured in all groups. Further, serum insulin, leptin and adiponectin were determined.

Results: Feeding with HFD induced significant increase in body weight of rats as well as insulin resistance and serum lipids as compared to normal group (p<0.05). These measurements were suppressed by sibutramine treatment. However, a significant elevation in BP and anxiety behavior were detected as compared with HFD group (p<0.05). Topiramate group showed weight loss, improved insulin resistance, lessened anxiety behavior without influence on BP.

Discussion: Our data ensures the findings that topiramate has a weight controlling properties with no anxiogenic or hypertensive effects. Further investigations are needed to determine the utility of topiramate in the clinical management of obesity.
Pentoxifylline and melatonin in combination with pioglitazone ameliorate experimental non-alcoholic fatty liver disease

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Abstract

Insulin resistance, oxidative stress and cytokine imbalance are key pathophysiological mechanisms in non-alcoholic fatty liver disease (NAFLD). This study aimed at evaluating the effect of treatment with the insulin sensitizer, pioglitazone, the tumor necrosis factor-α inhibitor, pentoxifylline, and the antioxidant, melatonin and their combinations in rats with NAFLD. Rats were fed a high-fat diet (HFD) for eight weeks to induce NAFLD. For an additional eight weeks, rats were fed the HFD along with pioglitazone pentoxifylline, melatonin alone or in combination. Liver index and insulin resistance index were calculated. Serum liver enzyme activities, total cholesterol, triglycerides and tumor necrosis factor-α (TNF-α) were determined. Tissue triglycerides, malondialdehyde and reduced glutathione were measured and liver injury was evaluated by histopathological examination.

HFD induced severe hepatic steatosis, inflammation and fibrosis. In addition, liver index, insulin resistance index, activities of liver enzymes and serum level of total cholesterol, triglycerides and TNF-α were elevated. This was coupled with an increase in tissue triglycerides, malondialdehyde and depletion of reduced glutathione. Pioglitazone, pentoxifylline and melatonin, alone or in combination; reduced the insulin resistance index, activities of liver enzymes, hepatic malondialdehyde and increased hepatic reduced glutathione level. Pentoxifylline led to a decrease in serum TNF-α level, however, pioglitazone and melatonin reduced serum total cholesterol and triglycerides.

In conclusion, data in this study indicate that pentoxifylline and melatonin can be used as promising adjuvant therapies to pioglitazone in the clinical management of NAFLD.
Effect of Evening Primrose Oil and Omega-3 PUFAs on the Cardiovascular Risk of Celecoxib in Rats

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Abstract

Experimental data raised the specter of increased cardiovascular risk with selective cyclooxygenase-2 inhibitors. The study aimed to investigate the celecoxib cardiovascular risk through studying its effect on blood pressure (BP) and thrombogenesis in rats. We tested the possible protective effects of evening primrose oil (EPO) or omega-3 polyunsaturated fatty acids (n-3 PUFAs). Male Wistar rats were assigned as vehicle, celecoxib, celecoxib/n-3 PUFAs, celecoxib/EPO, n-3 PUFAs and EPO. Rats were treated with celecoxib (20 mg/kg/day) by gastric gavage for six weeks. Mean BP was recorded, blood samples were collected for testing prothrombin time and activated partial thromboplastin time. Platelet aggregation assay and collagen-induced platelet consumption were utilized as models of thrombogenesis. Celecoxib increased BP without affecting coagulation parameters and accelerated thrombogenesis by increasing platelet aggregation and collagen-induced thrombocytopenia. EPO and n-3 PUFAs decreased the celecoxib-induced BP elevation. While EPO significantly decreased platelet aggregation and collagen-induced thrombocytopenia, n-3 PUFAs did not. Celecoxib elevated BP and increased risk of thrombogenesis in rats. Combination of celecoxib with the selected natural supplements is suggested as a novel approach to minimize celecoxib cardiovascular risk.