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Original article

Therapeutic effect of quercetin on renal function and tissue damage in the obesity induced rats

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1. Introduction

Obesity has been defined as excess fat existing in the body locally or generally. Among the basic reasons of the obesity, there are genetics, occasions increasing the energy intake to the body and decreasing the energy consumption [1]. The two most direct causes of death in obese patients are cancer and cardiovascular disease. Obesity is also the risk factor for many illnesses such as the cardiovascular disease, diabetes mellitus, hypertension, dislipidemi and renal dysfunction [2–4]. In different researches, it has been determined that the fat mass increases in the renal sinus as a result of the fat accumulation in the abdominal area [5–9]. This situation causes structural and functional changes in the renal tissue. It has been reported that the pressure to the renal vein by the accumulated fat around the kidney and in the renal sinus causes the increase in the kidney volume as well as the pressure in the interstitial area and consequently the decrease in the sodium (Na+) excretion [10–13]. Obesity causes the pathological lesions in the renal tissue, increases the uriner albumin extraction (UAE), dicreases the glomerular filtration rate and the chronic renal disease, too. QE (3, 5, 7, 3′,4′-pentahydroxyflavone) is a natural flavanoid and can be found in many vegetables and fruits. Lots of epidemiological and experimental researches have been reported that this molecule has antioxidant, anti-inflammatory, anti-angiogenic, anti-proliferative, anti-mutagenic, anti-cancer, anti-viral, anti-thrombotic, anti-ischemic and pro-apopotic effect [14–18]. Also in another renal glomerular research, it has been determined that the quercetin has an antiapoptotic effect [19]. In another study, it has been determined that it decreased the oxidative tissue damage formed by methotrexate (MTX) and apoptosis [20]. Our aim in this study is to determine the therapeutic effect of the QE, which has anti-apoptotic and antioxidant effect, on the renal tissue damage and the renal function on the experimentally obesity created rats.

2. Materials and methods

2.1. Animal housing and procedure

In this study, 24 healthy adult male Sprague–Dawley rats weighting between 150 and 180 g were used. The animals were housed under standard laboratory conditions (12 h light and 12 h dark) in a room with controlled temperature (22 ± 3C) during the experimental period. Rats were divided control, obesity and quercetin + obesity into three groups.

2.2. Obesity induction

Twenty-four, weighting 150–180 g and ten weeks old Sprague Dawley rats were fed a moderately high fat diet (35 kcal% as fat) for experimental model of obesity 120 days according to previous

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Table 1
Biochemical analysis of uric acid, creatinine, K^+, Na^+, Cl^- and urea levels in the serum samples of all groups. $p < 0.05$ (n = 8).

Groups	Creatine ± SD	Uric acid ± SD	Urea ± SD	K^+ ± SD	Na^+ ± SD	Cl^- ± SD
Control	$0,35 \pm 0,03^a$	$1,22 \pm 0.14^a$	$34,83 \pm 8.38^a$	$5,65 \pm 1.20^a$	$136,50 \pm 21.65^a$	$102,83 \pm 38,21^a$
Obesity	$0,47 \pm 0.05^c$	$1,65 \pm 0.36^c$	$49,29 \pm 11.54^c$	$6,50 \pm 0.96^b$	$143,67 \pm 37.36^a$	$105,17 \pm 44.55^a$
Quercetin + Obesity	$0,39 \pm 0.06^b$	$1,40 \pm 0.46^b$	$35,83 \pm 9.24^b$	$6,44 \pm 1.67^b$	$140,29 \pm 34,83^a$	$102,57 \pm 41.72^a$

The letters were indicate the statistical differences among groups, p value was considered as 0.05 (n = 8).

studies [21,22]. Control group rats were fed with normal ad libitum diet (10 kcal% as fat). Body weight gains were measured initial of study and weekly together with food consumption. The body weight gain ratio for obesity and control groups were indexed for obesity evaluation. For the obesity, the index values of obese rats were defined as those with weight gains equal to or more than the heaviest control rats.

2.3. Quercetin treatment

After the occurring of obesity (30% gaining of weight more than control), quercetin dissolved in 1 ml corn oil was orally given to the quercetin-obesity group in the doze of 50 mg/kg for 15 days. As for the obese group, corn oil was orally given 1 ml a day for 15 days. Following the study, all the animals were anesthetized with xylazine hydro- chloride (10 mg/kg^{-1}) (Rompun, Bayer, Turkey) and ketamine hydrochloride (40 mg/kg^{-1}) (Ketalar, Pfizer, Turkey). After collection of the blood samples, the rats were sacrificed and their kidney tissues were removed for biochemical and histologic examination.

2.4. Biochemical analysis

The collected blood samples were centrifuged at 1500g for 10 min within 1 h after collection to obtain sera samples. The sera were stored in the freezer at −80 °C before they were analyzed. In the obtained serum samples, the levels of creatinine, uric acid, urea, K^+, Na^+ and Cl^- were measured by the auto-analyzer device (Beckman Coulter; DXI 800 USA). The kidney tissues were homogenized by a tissue homogenizer. The homogenates were centrifuged at 10,000g for 20 min at 4 °C, and the supernatants were obtained; superoxide dismutase (SOD) activity and malondialdehyde (MDA) and glutathione (GSH) levels were determined as previously described (Table 1).

2.5. Histologic analysis

At the end of the study, obtained kidney tissues were fixed in 10% neutral formaldehyde for 72 h. The fixed tissues were dehydrated with ascendent alcohol series and cleaned with xylene, and then embedded in paraffin blocks. The paraffin blocks were cut thickness of 5-μm and stained with Crossman modified Mallory's Triple staining. The sections were assessed under convectional light microscope (Nikon eclipse 50i, Japan). The kidney tissues were also stained with Bax (1/50 dilution, Abcam) and Bcl-2 (1/50 dilution, Abcam) antibodies by immuno-histochemical method. The intensity of staining was scored as no staining (−), low (+), slight (++), and moderate (+++), severely (++++).

2.6. Statistical analysis

Data are expressed as mean ± Standard deviation (SD). Statistical significance of differences among groups was assessed by one-way ANOVA followed by Duncan *post hoc* test. The results were considered statistically significant when $p < 0.05$.

3. Results

3.1. Biochemical findings

In the biochemical serum analysis uric acid levels were higher levels in the obesity group than quercetin-obesity group and control group ($P < 0.05$). Also, serum urea and Creatine levels were higher in the obese group than other groups ($p < 0.05$). Additionally, there were higher levels of potassium (K^+), sodium (Na^+) and clor (Cl^-) in obese group than obese treated with quercetin group, but not statically significant ($P > 0.05$). But serum potassium level of control group was found lower than other groups ($P < 0.05$).

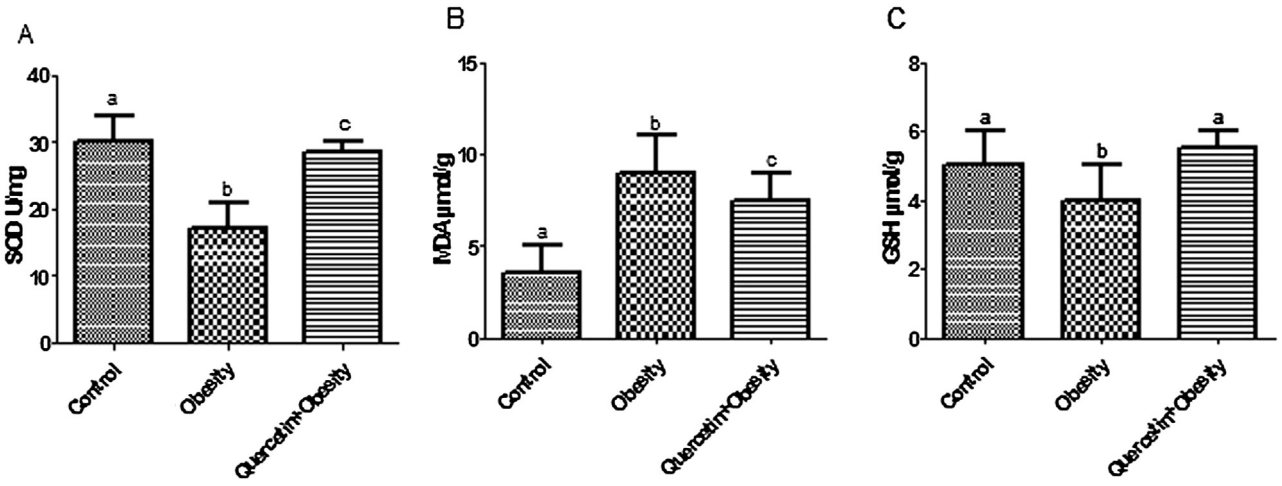

Fig. 1. Analysis of SOD activity (A), MDA (B) and GSH (C) levels kidney tissues of all groups. $p < 0.05$, (n = 8).