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Ameliorative effect of royal jelly against nephrotoxicity induced by gentamicin

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Abstract

Introduction: Royal jelly is a natural product that has antioxidant properties and has protective effects against gentamicin-induced renal toxicity.
Objectives: In this study, antioxidant effect of royal jelly were investigated against gentamicin-induced nephrotoxicity.
Materials and Methods: Fifty adult male Wistar rats were randomly divided into five group 1) Animals received gentamicin (GM) (80 mg/kg, i.p.) for 7 days and saline for 10 days, group 2) Received 100 mg/kg body weight/d royal jelly for 10 days, group 3) Received 100 mg/kg body weight/d royal jelly for 3 days and then royal jelly plus GM (80 mg/kg; ip) for 7 more days, group 4) Received GM for 7 days and then royal jelly for 10 days, group 5) Received saline for 10 days. Histological changes were evaluated for severity of renal injury (epithelial cell degeneration, vacuolization, tubular dilatation, tubular cell flattening, and hyaline cast and also debris materials in tubular lumen on a semi-quantitative score from 1 to 5, while the score of zero was designated to the normal tissue without damage.
Results: Gentamicin significantly increased mean of delitation, degeneration, vacuolization and score level ($P<0.05$). Royal jelly has a protective effect against gentamicin-induced kidney injury by ($P<0.05$).
Conclusion: In vivo result showed that royal jelly is a potential protector against gentamicin- induced oxidative stress and histological.

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Introduction

Renal failure is a common disease that treatment and prevention of this disease has significant clinical importance. Many factors are involved in causing renal failure and acute renal failure such as using some drugs (1). Natural or semi-synthetic aminoglycoside antibiotics are a heterocyclic structure. Gentamicin group is one of the aminoglycoside antibiotics which can be used as an animal model for proximal tubular cell injury (2). The main problem of gentamicin is renal nephrotoxicity in treatment of infections caused by gram-negative bacteria (3,4). The administration of gentamicin in different clinical condition is limited due to renal nephrotoxicity effects and the increased risk of renal toxicity during treatment. If period of treatment take longer than 14 days complication will reach 50% (5). An average 20% to 30% of patients who have been treated with gentamicin for more than 7 days had kidney failure (6). Therefore, finding a way to prevent or treat kidney damage is very useful for these patients. The administration of antioxidant types such as royal jelly recommended to prevent free oxygen radicals injury and reducing the renal toxicity of gentamicin

Core tip

Renal failure is a common disease that treatment and prevention of this disease has significant clinical importance. Patients with chronic renal failure have many dietary and medications constraints. Occasionally, prescription may be inevitable, and prevention of its complications is very important. One of the medications that have nephrotoxicity is gentamicin. The prevention of gentamicin side effects is important, especially in patients who are prone to renal failure. Royal Jelly is one of the ingredients that can be useful in this regard.

(7,8). Royal jelly is secreted from cephalic glands of honeybees. An anti-oxidative activity of royal jelly has protected tissue DNA against the oxidative damage (9). Additionally, it protects tissue DNA against the oxidative damage. The effect of the royal jelly diet on mice show that after feeding royal jelly, the levels of an oxidative stress marker were significantly reduced in kidney DNA and serum (10). Royal jelly collected 24 hours after the larval transfer has the strongest anti-oxidative activity (11). The anti-oxidative activity of royal jelly has been proven in various in vitro experimental on laboratory animals (12-14). Royal jelly has phenolic compounds such as flavonoids (9). It has been reported that royal jelly is useful for intoxication events such as hypotension and respiratory depression. Phenolic compounds present in it are antioxidant capacity and ability of them to the prevention of enzymatic browning (9) whilst natural products such as phenolic compounds and flavonoids have properties to scavenge free radicals (15).

Objectives

Considering the antioxidant activity of royal jelly, the aim of this study is to evaluate the antioxidant effect of royal jelly gentamicin-induced nephrotoxicity (16).

Materials and Methods

Drugs and chemicals

Royal jelly was purchased from a local provider in Shahrekord, Central part of Iran. In this study rats received 80 mg/kg body weight/day of gentamicin, based on a previously reported protocol.

Animals

In this experimental study, 50 male Wistar rats weighing 200-250 g were purchased from Shahid Beheshti University of Medical Sciences, Tehran, Iran. All animals were similarly handled in the animal house of Medical Plants Research Center of Shahrekord University of Medical Sciences, Shahrekord, Iran. The animals were housed in a controlled environment with 50%-60% humidity and temperature of 25 ± 3°C. Furthermore, the rats were kept with a 12 hours dark-light cycle (lights on at 7.00 AM) and allowed free access to pelleted diet and tap water. During the experiment, the animal's general health state and activity was monitored closely.

Experimental Design

In this study experimental study 50 male Wistar rats were designated into five equal groups and treated as follows;
Group I; animals in this group received GM (80 mg/kg; intraperitoneally, i.p.) for 7 days and saline for ten days.
Group II; received 100 mg/kg body weight/d royal jelly for 10 days.
Group III; received 100 mg/kg body weight/d royal jelly for three days and then royal jelly plus GM (80 mg/kg; i.p.) for 7 more days.
Group IV; received GM for 7 days and then royal jelly for 10 days.
Group V; received saline for 10 days.

Histopathological evaluations

At the end of the experiment the animals' kidneys were dissected out and fixed in buffered formalin for 12 hours and processed for histopathological examination. Three µm-thick paraffin sections were stained with hematoxylin and eosin (H&E) for microscopic examinations using conventional protocol (17).
Histopathological studies were performed under a light microscope. Slides were coded and examined by a nephropathologist who was blinded to the treatment groups. All specimens were examined for morphologic parameters including epithelial cell degeneration, vacuolization, tubular dilatation, tubular cell flattening, hyaline cast and debris materials in tubular lumen on a semi-quantitative score from 1 to 5, while the score of zero was designated to the normal tissue without damage (17).

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The project was confirmed by the Ethical Committee of Shahrekord University of Medical Sciences. All animal experimentations were conducted in accordance with the National Institute of Health guide for the careful use of laboratory animals (#91-01-75-978).

Statistical analysis

Data were expressed as mean ± SEM. To compare the pathology damage score between the groups, Kruskal-Wallis and Mann-Whitney U tests were applied. Values of $P<0.05$ were considered statistically significant.

Results

Table 1. Effects of royal jelly on histopathology variables of kidney injury induced by gentamicin

Variables	Dilatation	Degeneration	Vacuolization	Score
	Mean± SD			
Gentamicin	51.5±16	49.3±12	55±11	42.7±6
Royal jelly	0.4±0.8	2.9±1	3.2±1	1.5±0.7
Royal jelly+ GM	6.2±3	14.6±8	18.5±13	8.5±5
GM+ Royal jelly	3.5±2	7.3±2	6±4	4.7±2
Control	0.4±1	2.2±2	0.9±1	0.5±0.5

*$P<0.05$ compared with other groups.

The histopathology damage scores for all groups of experiments are demonstrated in Table 1. The results indicate that the nephrotoxicity in the group 1 which received 80 mg/kg/d GM is higher than the control group. Gentamicin dramatically increased dilatation, degeneration and vacuolization in comparison to control group ($P<0.05$). In this study royal jelly had no effects on the kidney of normal rats. However, administration of royal jelly before or following GM injection reduced the indicators of renal injury. Although there are differences between the groups 3 or 4 which received royal jelly along or following GM, in comparison with control group. However, the injury indicator scores in these two groups are significantly less than the ones in group one which just received GM ($P<0.05$).

Discussion

In this study 80 mg/kg/d gentamicin-induced nephrotoxicity in rats and lead to dilation and vacuolization kidney compared to control group. Royal jelly had no effects on the kidney of normal rats. Consuming 100 mg/kg royal jelly for 10 days after gentamicin-induced could reduce injure of kidney tissue also consuming 100 mg/kg royal jelly for three days and then royal jelly plus gentamicin for seven days was prevented damage kidney caused by gentamicin. Gentamicin is a bacterial antibiotic which is using in clinical but nephrotoxicity and ototoxicity are the most common adverse. Concentration above 2 µg/mL gentamicin caused to nephrotoxicity due to free radical generation, pyridoxal phosphate deficiency and ascorbic acid depletion (18). It is effective in protecting against on cisplatin-induced nephrotoxicity (19) whilst its treatment leads to increased lipid peroxidation level in liver and kidney. Bioactive compounds are amino acids such as lysine, leucine, aspartic acid, cysteine and valine which are the antioxidant activity (17). The next property would be protective effects against radiation-induced oxidative stress, biochemical and histological in Wistar male rats. On the other hand its effect on the antioxidant system conducted by increasing major scavenger enzymes and prevents liver toxicity, genotoxicity and nephrotoxicity (20). This natural product is a viscous substance that contains bioactive substances such as 10-hydroxy-trans-2-decenoic acid, antibacterial protein, and 350-kDa protein. It has been reported beneficial physiological and pharmacological effects in mammals (21,22).

Our findings are similar to above results. The experimental data showed that treated with royal jelly whole nephrotoxicity induced gentamicin significantly reduced structural changes tissue kidney. The gentamicin-induced changes in histopathological findings of kidneys were partially reversed by treatment with royal jelly.

The present study suggests that daily waster of royal jelly have a beneficial effect in treatment nephrotoxicity induced gentamicin. Also it could improvement oxidative stress parameters.

Conclusion

Royal jelly is a natural product and has plenty therapeutic properties. In vivo result showed that royal jelly is a potential protector against gentamicin-induced oxidative stress and histological changes. Some of its therapeutic activities have been confirmed, but many health benefits are unknown yet. More experimentation would be needed to prove useful benefit and action mechanism of royal jelly.

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Authors' contribution

MRK and SA conducted the research. They searched and gathered the related articles as well as writing the paper. MK and MRT edited the draft. BY edited the final manuscript several times. MRK finalized the final paper and conducted the final revisions. All authors read and signed the final paper.

Conflicts of interest

The authors declare no conflicts of interest.

Ethical consideration

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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