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Original Article

The therapeutic effect of naringin on ovarian and lung damages created by adnexal torsion/detorsion: A biochemical study

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Abstract

Aim: In this study, naringin was examined against injuries in lung and ovarian tissues caused by ovarian torsion/detorsion (T/D).
Material and Methods: The animals were grouped as sham, T/D, 50 mg/kg Naringin and 100 mg/kg Naringin. In sham group, the abdomen was incised and then sutured but T/D model wasn't performed. In T/D group, torsion and detorsion (ischemia 3 hours/reperfusion 3 hours) were carried out. In naringin treatment groups, naringin was applied intraperitoneally at the doses of 50 and 100 mg/kg about 30 minutes prior to detorsion. After detorsion period, experimental animals were immolated and the ovarian and lung tissues were excised, homogenized and the biochemical analyzes were done.
Results: The activity of MPO, IL-1β, MDA, TNF-α levels, TOS and OSI parameters raised significantly but SOD activity and TAS values declined in T/D group when it is compared to sham group. On the other side, naringin treatments reversed these parameters.
Conclusion: Thereby, naringin demonstrated therapeutic effect against the injuries of ovarian and lung tissues in rat T/D model.

Keywords: Lung; naringin; ovary; rat; torsion/detorsion

INTRODUCTION

Ovarian torsion (O/T) is generally observed in women with reproductive period (1). There are several health conditions cause O/T which results in irreversible tissue injuries (2). Early diagnosis and treatment play key role in the maintaining of fertility (3-5). Reperfusion is the main reason of free oxygen radicals that cause tissue injury resulting in necrosis and apoptosis (6-8). Reactive oxygen species (ROS) damage lipids, proteins, and DNA (9,10). Antioxidant system has several enzymes including superoxide dismutase (SOD) that prevent tissue injury resulting from ROS (11). Oxidative stress means impairment of free oxygen radical and antioxidant balance (12). Inflammatory mediators, free oxygen radicals and neutrophils are the components of I/R pathophysiology (13). Interleukin-1β (IL-1β) and tumor necrosis factor-alpha (TNF-α) elevate in the start of inflammation and free radicals are released by active neutrophils (14). I/R both damages primary and remote organs through inflammatory respond and oxidative processes (15,16). There has been no ovarian torsion/detorsion (T/D) related remote organ injury study in literature. Upon this reason, this study will make a significant contribution to the literature.

Nar is of flavanone and available in several nutrients like grapefruit, beans, tomato and citrus fruits (17). It acts in bone remodeling. It has anti-osteoporotic, antiapoptotic, antioxidant and anti-inflammatory effects (18,19).

Here, the therapeutic effects of Nar were examined on T/D induced ovarian and lung tissue injuries.

MATERIAL and METHODS

Animals and Ethical Approval

Experimental protocols of the study were admitted by the Experimental Animal Ethics Committee of Ataturk University (protocol no:27.04.2018-105). 32 female rats (Albino Wistar-250–270 g) were received from Atatürk University Experimental Animal Research and Application Center. They were held in experimental standard

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conditions. Rat pellet and tap water were given until 12 hours to experimental step.

Preoperative Phase and Chemicals

The animals were fixed in supine position, abdominal regions were shaved and cleaned. 10 mg/kg xylazine hydrochloride (Rompun®, Bayer, İstanbul) and 60 mg/kg ketamine (Ketalar®, Pfizer, İstanbul) were preferred as anesthetic during surgical processes and administered intraperitoneally (i.p.) to rats. 10% povidone iodine (10% Baticonol, Dermosept, İstanbul, Türkiye) was used for the disinfection of surgical regions. Naringin (Naringin 98%, Sigma Aldrich, ABD) was administered to the rats in treatment group.

Experimental Design

4 groups were created as follows (n=8): Sham group; abdominal regions of the rats were incised and closed with 3-0 silk suture. T/D group; incision same procedure with sham group was applied to the rats. Before suturation, bilateral ovaries, fallopian tubes and other structures were rotated in clockwise 360 degrees and clamped (torsion phase). Following 3 hours, blood flow restarted through releasing clamps (detorsion phase) and the incision area was sutured. Ovarian T/D model was referenced through the previous researches (20; 21). T/D+Nar 50 mg/kg group (Nar 50 mg/kg group); 50 mg/kg Nar was administered to the rats i.p. 30 minutes before detorsion. T/D+Nar 100 mg/kg group (Nar 100 mg/kg group); 100 mg/kg Nar was administered to the rats i.p. 30 minutes before detorsion. Naringin dose was referenced through the previous research (22). The ovarian and lung tissues were excised after the experiment. They were washed and kept as frozen for analysis.

Biochemical Measurements

Malondialdehyde (MDA) measurement (23), SOD activity (24) and Myeloperoxidase (MPO) measurement (25) were based on previous studies. Total antioxidant status (TAS) and total oxidant status (TOS) were gauged with appropriate kits (Rel Assay Diagnostics). TOS to TAS rate was accepted as the oxidative stress index (OSI). TNF-α and IL-1β values were measured by available kits (Elabscience, Wuhan, China).

Statistical Analysis

One-way ANOVA and Duncan tests were used for the evaluation of the date through SPSS programme. Descriptive statistic was demonstrated as the Mean±SD. The results were considered statistically significant at the level of $p<0.05$.

RESULTS

All biochemical data of ovarian and lung tissues were shown in Table 1, 2, Figure 1 and 2. Here, TOS, OSI values, MPO activity, MDA, TNF-α and IL-1β levels elevated in T/D group compared to sham group. On the contrary, these parameters diminished in groups treated with 50 and 100 mg/kg Nar. Moreover, 100 mg/kg Nar group was more effective than Nar 50 mg/kg group. SOD activity and TAS levels, as an indicator of antioxidant levels, declined significantly in T/D group, while they increased in 50 and 100 mg/kg Nar groups. 100 mg/kg Nar group was more successful in supporting the antioxidant defense than 50 mg/kg Nar group.

Table 1. Ovarian tissue TAS, TOS, OSI values, SOD, MPO activities and MDA level in all groups

Groups (n=8)	Sham (1)	T/D (2)	Nar 50 mg/kg (3)	Nar 100 mg/kg (4)
TAS (mmol/L)	0.68 ± 0.11	0.34 ± 0.05*	0.56 ± 0.07#	0.61 ± 0.05#
TOS (μmol/L)	5.36 ± 0.37	8.51 ± 0.78*	6.06 ± 0.58#	5.57 ± 0.57#
OSI (arbitrary unit)	0.80 ± 0.16	2.51 ± 0.59*	1.09 ± 0.17#	0.90 ± 0.10#
SOD (U/mg protein)	359.18 ± 53.34	165.53 ± 26.00*	318.61 ± 39.39#	348.98 ± 42.08#
MPO (U/g protein)	265348.02 ± 38650.09	526490.80 ± 133973.72*	269332.16 ± 39617.34#	247755.86 ± 22698.90#
MDA (μmol/g protein)	62.55 ± 8.65	104.66 ± 19.51*	70.02 ± 6.78#	64.26 ± 2.85#

*p < 0.001 compared to sham group. #p< 0.001 compared to T/D group

Table 2. Lung tissue TAS, TOS, OSI values, SOD, MPO activities and MDA level in all groups

Groups (n=8)	Sham	T/D	Nar 50 mg/kg (3)	Nar 100 mg/kg (4)
TAS (mmol/L)	0.96±0.07	0.58±0.04*	0.88±0.05#	0.96±0.14#
TOS (μmol/L)	6.65±0.63	8.91±0.95*	7.15±0.80#	7.06±0.79#
OSI (arbitrary unit)	0.69±0.09	1.52±0.18*	0.81±0.12#	0.75±0.15#
SOD (U/mg protein)	262.58±37.33	133.89±14.39*	227.90±29.14#	258.54±25.62#
MPO (U/g protein)	141852.20±19523.65	295947.58±34966.95*	169759.20±18838.44#	152316.36±15114.71#
MDA (μmol/g protein)	59.21±4.93	97.05±15.02*	67.94±6.12#	62.31±7.12#

*p < 0.001 compared to sham group. #p< 0.001 compared to T/D group

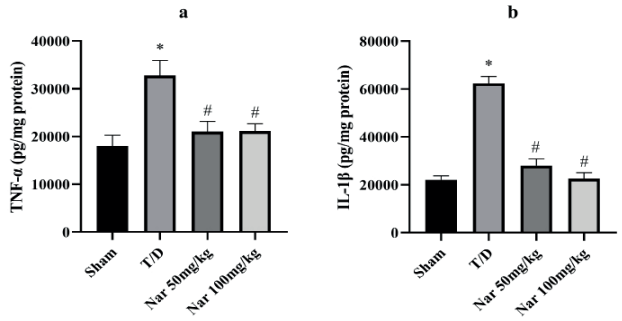

Figure 1. Ovarian tissue TNF-α and IL-1β levels in all groups. *p<0.001 compared to sham group. #p<0.001 compared to T/D group

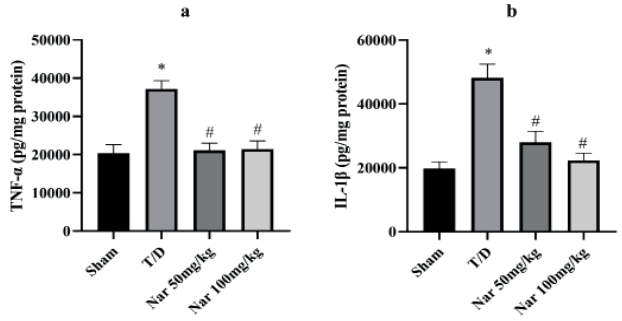

Figure 2. Lung tissue TNF-α and IL-1β levels in all groups. *p<0.001 compared to sham group. #p<0.001 compared to T/D group

DISCUSSION

Torsion is the rotation of adnexa and the severity is related with the grade and duration. O/T leads to I/R and even necrosis in untreated cases (2). I/R causes ROS and MDA production. O/T takes role in neutrophil activation and ROS is produced by the neutrophils (11,26). ROS cause lipid peroxidation that is detrimental to cells (27). Lipid peroxidation leads to MDA production which alters enzyme activity and ion permeability negatively (28). ROS production and leukocyte infiltration enhance during ROS generation (29). ROS is eliminated by antioxidant enzymes (30) such as SOD which fights against free radicals (31). TOS and TAS are indicators for I/R injury (32). TAS is inversely proportional with TOS (33). In the current study, Nar, which has proven antioxidant properties, was used in ovarian T/D model.

There are various Nar-related studies in the literature supporting the results of current study. Here, Nar administration caused a decrease in T/D-induced oxidant and inflammatory parameters in lung and ovarian injuries. Nar prevented renal I/R injury by increasing SOD level in rats (22). Nar decreased proinflammatory cytokines such as TNF-α, IL-6 and ROS levels besides, increasing antioxidant levels and thus, it performed a protective effect against UVB-induced inflammation (34). Nar elevated SOD activity and diminished IL-6 and TNF-α levels in liver injury (35). Nar elevated SOD activity and decreased MDA levels and prevented cardiotoxicity in rats (36). It also increased SOD activity and diminished TNF-α, IL-6 and some proinflammatory cytokines in an acid-induced neurotoxicity rat model (37). Nar mitigated alcohol-induced liver injury through diminishing oxidative stress (38). In another study, Nar was effective against lung injuries by decreasing IL-1β, IL-6 and TNF-α levels in mice (39). Nar enhanced SOD activity and decreased IL-1β, IL-6, TNF-α levels in 5-fluorouracil-induced hepatotoxicity and nephrotoxicity in rats (40). In T/D group of this study, SOD and TAS levels declined while OSI, MDA, TOS, MPO, IL-1β and TNF-α values elevated and Nar treatment reversed these parameters.

CONCLUSION

Nar performed therapeutic effect against T/D-induced ovarian injury. Nar treatment diminished ovarian and lung damages in experimental animals exposed to T/D model.

Competing interests: The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports.

Ethical approval: Experimental protocols of the study were admitted by the Experimental Animal Ethics Committee of Ataturk University (protocol date and no:27.04.2018-105).

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