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Protective Effects of Ghrelin Following Experimentally Induced Ischemia-Reperfusion in the Rat Ovary

Mahyar Nazari[1], Arash Kheradmand[2]*, Masoud Alirezaei[3], Abbas Raisi[2]

[1] Graduated from the Faculty of Veterinary Medicine, Lorestan University, Khorramabad, Iran.

[2] Department of Clinical Sciences, Faculty of Veterinary Medicine, Lorestan University, Khorramabad, Iran.

[3] Department of Basic Sciences, Faculty of Veterinary Medicine, Lorestan University, Khorramabad, Iran.

Running title: Ghrelin Ovarian Ischemia-Reperfusion

Abstract

Background: Ovarian torsion, a critical gynecological emergency, leads to blockage of the ovarian artery and vein, ultimately causing ischemia in the ovary.

Objective: This study aims to investigate the potential antioxidative effects of ghrelin in the context of ischemia-reperfusion injury in the rat ovary.

Methods: Twenty-one female adult Wistar rats (250-300g) were assigned to three groups (n= 21): 1- Sham operated group (n=7). 2- ischemia-saline group: 100 µl Saline was administered intraperitoneally 30 min prior to the 2-hr of ischemia and simultaneously with the beginning of 2-hr reperfusion (n=7). 3- ischemia-ghrelin group: 10 nmol ghrelin was administered intraperitoneally 30 min prior to the 2-hr of ischemia and simultaneously with the beginning of 2-hr reperfusion (n=7). The right ovaries were excised in each group and underwent biochemical analysis. Malondialdehyde (MDA), superoxide dismutase (SOD), glutathione peroxidase (GPx), total antioxidant score (TAS), and catalase (CAT) were assessed as biochemical parameters.

Result: There were no significant differences among groups in SOD, GPx activities (P>0.05). MDA level was higher in the ischemia-saline group compared to the control group and was lower in the ischemia-ghrelin group compared to the ischemia-saline group, significantly (P≤0.05). CAT and TAS activities were significantly decreased in the saline group compared to the sham-operated group and increased significantly in the ghrelin-treated group compared to the saline group (P≤0.05).

Conclusions: Overall, ghrelin with dosage of 10 nmol preserved rat ovaries from damage caused by ischemia-reperfusion.

Keywords: ghrelin, ischemia-reperfusion, rat ovary, torsion, torsion/detorsion

1. Introduction

Ovarian torsion, a critical gynecological emergency, refers to the rotation of the ovary around its central line ligaments (infundibulopelvic and tubo-ovarian) (Omar and Al-Hendy, 2020, um Tumor and do Ovário, 2022). Reports indicate that the incidence of ovarian torsion is 5.9% per 100,000 women, and the highest incidence is in premenopausal women (Vu and Goh, 2022). Ovarian torsion leads to blockage of the ovarian artery and vein, ultimately causing ischemia in the ovary. Ovarian Ischemia, characterized by reduced energy production in the absence of oxygen, triggers oxidative stress, potentially leading to cell apoptosis. Upon detection of ovarian torsion, detorsion of the twisted ovary, and evaluation of the

tissue reperfusion is recommended to prevent future infertility (He *et al.*, 2022, Omar and Al-Hendy, 2020). It is noteworthy that the process of restoring the ovary to its normal state, such as ovarian torsion, is accompanied by the production of reactive oxygen species (ROS) that results in oxidative damage to the ovary, known as ischemia-reperfusion injury (Celik *et al.*, 2004). ROS, including superoxide anion, hydrogen peroxide, and hydroxyl radical, are byproducts of oxidative metabolism in mitochondria that can interact with biomolecules and harm cellular components such as DNA, RNA, and proteins (Juan *et al.*, 2021, Ghotbitabar *et al*., 2022, Elahinia *et al*., 2023). These mediators also impact cell membrane lipids, contributing to the production of toxic products like MDA. Additionally, ROS diminishes the levels of natural antioxidants such as GPx, SOD, and CAT while increasing oxidant molecules (Tok *et al.*, 2012).

Cells employ several methods to safeguard themselves against damage from reactive oxygen species (ROS). One approach involves scavenging enzyme systems, such as catalase (CAT), which converts hydrogen peroxide into water, and superoxide dismutase (SOD). SOD plays a role in breaking down the superoxide radical (O2-) into either ordinary molecular oxygen (O2-) or hydrogen peroxide (H2O2) (Ighodaro and Akinloye, 2018).

To prevent tissue damage in ovaries resulting from the ischemia-reperfusion process, various antioxidant agents have been employed in previous studies. Numerous studies have provided data to

identify the antioxidant effects of Vardenafil, Propolis, lycopene, Eugenol and dexamethasone (Yurtcu *et al.*, 2015, Koc *et al.*, 2019, Kirmizi *et al.*, 2021, Barghi *et al.*, 2021, Omairi *et al.*, 2022, Parham *et al.*, 2022). Although antioxidants were effective in reducing damages caused by ovarian torsion/detorsion, the most effective drug have not yet been found.

Ghrelin, the natural ligand for the growth hormone secretagogue receptor (GHS-R), is a recently discovered 28-amino acid peptide mainly produced in the stomach and hypothalamus (Dar *et al.*, 2020, Ketaby and Mohammad-Sadegh, 2023, Emadi *et al*., 2022). Moreover, the ghrelin gene is expressed in different tissues, including the small intestine, brain, adrenal glands, ovaries, and testes, with the highest expression found in the stomach (Motta *et al.*, 2016). The functional ghrelin receptor (GHS-R1a) has been identified in oocytes, follicular cells, and luteal cells in the rat ovary, which indicates a potential direct influence of ghrelin on ovarian function (Pan *et al.*, 2020). Recent evidence suggests that ghrelin may act as an antioxidant. Numerous studies have shown that ghrelin can prevent lipid peroxidation and the reduction of antioxidant enzyme activities and glutathione levels, particularly in response to oxidative stress induced by pentylenetetrazole in rat erythrocytes (Bademci *et al.*, 2021). Another research conducted by Alirezaei et al. has confirmed that ghrelin significantly increases the activity of antioxidant enzymes like GPx, SOD, and CAT in renal cells in the Lipopolysaccharide-Mediated Renal Failure in Rats (Alirezaei *et al.*, 2015).

As mentioned earlier, numerous studies have explored the role of ghrelin in ischemia-reperfusion injury. While most studies favor the daily administration of ghrelin before the surgical procedure, our objective was to investigate the potential protective effect of ghrelin on oxidative stress parameters including SOD, GPx, CAT, and TAC following ovarian ischemia/reperfusion, leading us to administer ghrelin prior to the procedure (Kheradmand *et al.*, 2010). Several pharmacological agents exist for preventing reperfusion injury, but unfortunately, many of them are impractical for clinical use in cases of ovarian torsion. However, ghrelin stands out in this regard. Notably, the parenteral administration of ghrelin is advantageous, especially in emergency situations.

2. Materials and Methods

2.1. Drugs and chemicals

Rat lyophilized acylated ghrelin (n-octanoylated research grade) was obtained from Tocris Cookson Ltd. (Bristol, UK). Ghrelin was dissolved in a sterile physiologic saline solution before injection. The kits used in the measurement of antioxidant enzyme activities were provided by Kiazist commercial assay kit. (Kiazist, Hamedan, Iran). All other chemicals were procured from the Sigma-Aldrich Company in St. Louis, MO, USA, unless specified otherwise.

2.2. Animals

The experiment was carried out on twenty-one adult female Wistar rats at 10 weeks of age (250-300g). The animals were obtained from the Razi Research Institute in Kermanshah, Iran. The rats -were housed (seven rats per cage) in the animal room under controlled lighting (14 h light: 10 h darkness, lights from 06:00 h) and temperature (21–24 °C) conditions. The rats were fed with standard rodent chow and had access to water ad libitum. All of the experimental procedures were carried out between 1.00 and 5.00 pm. All investigations were conducted in accordance with the Guiding Principles for the Care and Use of Research Animals. All animals were treated humanely and in compliance with the recommendations of the Animal Care Committee for the vet college of Lorestan University (Khorram Abad, Iran). This study was carried out in compliance with ARRIVE's guidelines.

2.3. Experimental design

Animals were randomly separated into three groups (n=21): the control (sham operation, n=7), the IR (torsion-detorsion, n=7), and the IR-G (torsion/detorsion plus ghrelin, n=7). The rats were anesthetized with 75 mg/kg ketamine hydrochloride (Ketalar, Eczacıbası, Turkey), and injection of xylazine hydrochloride (10 mg/kg, Rompun, Bayer, Leverkusen, Germany) intraperitoneally (Taheri *et al.*, 2021, Raisi *et al.*, 2020). In the control group or Sham, after anesthesia, the abdominal area was shaved and

after scraping as usual, the abdomen was opened through the midline, and the ovaries were slightly manipulated and then closed with 3/0 silk sutures. In the ischemia-reperfusion group, a 2.5-3 cm incision was made from the midline, then the ovaries were twisted around the axis of the tubo-vavarin ligaments and the vascular pedicle of the ovary was taken one centimeter above and below the ovary with a hemostatic forceps. A tampon was placed on it and it remained in this state for 2 hours ischemic conditions were created for the animal, and then the forceps were removed from the vascular pedicle for 2 hours and then it remained in reperfusion mode for 2 hours, and then the right ovaries were removed to measure the biochemical parameters. Thirty min prior to ischemia and at the same time as the ovaries were restored to normal, 100 microliters of saline was injected into the rats of the ischemia-saline group. In the group treated with ghrelin, the same procedure was performed, with the difference that 100 microliters of ghrelin (10 nmol) was injected 30 minutes prior to ischemia and at the same time as reperfusion (Demir *et al.*, 2021, Kalyoncu *et al.*, 2020). The choice of a 10 nmol of ghrelin, and the ovarian ischemia and reperfusion periods were chosen following a review of previously published studies, but we noted that there was a lack of data in the literature about the dose-related effects of ghrelin in animal studies (İşeri *et al.*, 2005). At the end of the experiment and after removing the right ovaries, rats were euthanized under deep anesthesia with intracardiac injection of magnesium sulfate

(Magnesiject 40%, Maki Dam, Tehran, Iran) (Underwood and Anthony, 2020), and the ovaries were frozen at -70° C for antioxidant enzymes assays.

2.4. Sampling and tissue preparation for enzyme assay

Immediately after sacrificing the rats, the right ovaries were taken and carefully separated from fat and surrounding tissue and processed immediately. In order to perform enzymatic and lipid peroxidation assays, frozen ovaries were quickly homogenized manually in cold phosphate buffer (pH 7.2) and the residues were removed by centrifugation at 4500 g for 15 min. The clear supernatants were recovered and stored at -70°C for subsequent enzyme and protein assays (Davoodi *et al.*, 2020).

2.4.1. Protein measurement

The total protein concentration in the tissue samples was determined according to Bradford's method using bovine serum albumin as a standard and measures were provided as mg protein (Bradford, 1976).

2.4.2. Measurement of tissue lipid peroxidation

Lipid peroxidation in each tissue sample was evaluated by measuring the level of MDA as a thiobarbituric acid-reactive substance. Briefly, Cayman's TBARS (TCA Method) Assay Kit provides a simple, reproducible, and standardized tool for assaying lipid peroxidation in the ovary. The MDA-TBA

adduct formed by the reaction of MDA and TBA under high temperature (90-100°C) and acidic conditions is measured calorimetrically at 530-540 nm MDA levels were calculated from a standard calibration curve using tetra ethoxypropane and expressed as nmol/mg protein.

2.4.3. SOD assay

SOD catalyzes superoxide anion to molecular oxygen and Hydrogen peroxide because it supplies the essential part of the antioxidant defense mechanism. In brief, a test volume sample and a volume of chloroform and ethanol mixture (3.5 V/V) were mixed in a centrifuge tube. The precipitate was removed by Centrifuge at 3000 rpm for 40 minutes. The assay solution contains Sodium carbonate buffer (400 mM), xanthine 0.3 mM, 150 mmol/L Nitro blue tetrazolium (NBT), 0.6 mmol/L Na2EDTA, 1 g/L cattle Serum albumin, xanthine oxidase 167 U/L and the sample were mixed in a cuvette. The activity was measured using xanthine and xanthine oxidase to produce superoxide radicals, which react with NBT. One unit of SOD was defined as the amount of protein that inhibited the rate of NBT reduction by 50%. As described by Sun et al, SOD activity was (U/mg protein) (Sun *et al.*, 1988).

2.4.4. CAT assay

Cayman's Catalase Assay Kit utilizes the peroxidic function of CAT for the determination of enzyme activity. The method is based on the reaction of the enzyme with methanol in the presence of an

optimal concentration of H2O2. The formaldehyde produced is measured calorimetrically with 4-amino-3-hydrazino- 5-mercapto-1,2,4-triazole (Purpald) as the chromogen.1,2 Purpald specifically forms a bicyclic heterocycle with aldehydes, which upon oxidation changes from colorless to a purple color.1,2. The CAT activity was expressed as the unit that is defined as µmol of H2O2 consumed per min per gram of wet tissue (Johansson and Borg, 1988).

2.4.5. GPx assay

Cayman's GPX Assay measures GPX activity indirectly by a coupled reaction with glutathione reductase (GR). Oxidized glutathione (GSSG), produced upon reduction of hydroperoxide by GPX, is recycled to its reduced state by GR and NADPH (Paglia and Valentine, 1967):

$$\text{R-O-O-H} + 2\text{GSH} \xrightarrow{\text{GPX}} \text{R-O-H} + \text{GSSG} + H_2O$$

$$\text{GSSG} + \text{NADPH} + H^+ \xrightarrow{\text{GR}} 2\text{GSH} + \text{NADP}^+$$

The oxidation of NADPH to NADP+ is accompanied by a decrease in absorbance at 340 nm. Under conditions in which the GPX activity is rate limiting, the rate of decrease in the A340 is directly proportional to the GPX activity in the sample.

2.4.6. TAC assay

TAC levels were measured using commercially available kits (Relassay, Turkey). Erel previously described TAS values against free radicals with a fully automatic method (Erel, 2005). This assay kit has a very low error rate that is lower than 3%. The results were presented as nmol/mg.

2.5. Statistical analysis

Data analyses were performed using SPSS version 16.0 for Windows. All quantitative data were tested for normality and thereafter by the *Levene static test* for homogeneity of variance. When the variance was homogenous, the results were separately analyzed using one-way ANOVA and Tukey test as post hoc, in order to determine differences among groups. The results are presented as means ± standard error of the mean (SEM); p-values < 0.05 were considered to be statistically significant.

3. Results

The mean values of antioxidant (SOD, CAT, GPx, and TAC) and oxidant (MDA) parameters in the rat ovaries among different groups are presented in five figures.

There were no significant differences among the groups for GPx and SOD levels (P>0.05). The amount of GPx changes among different groups is shown in Figure 1. The average activity of this enzyme (Mean ±

SD) in the sham, ischemia-saline, and ischemia-ghrelin groups was 3.03±0.7, 3.63±0.8 and 3.07±0.83 u/mg protein, respectively.

The amount of SOD changes among different groups is shown in Figure 1. The average activity of this enzyme (Mean ± SD) in the sham, ischemia-saline, and ischemia-ghrelin groups was 5.6±2.95, 12.66±6.27 and 5.73±2.25 u/mg protein, respectively.

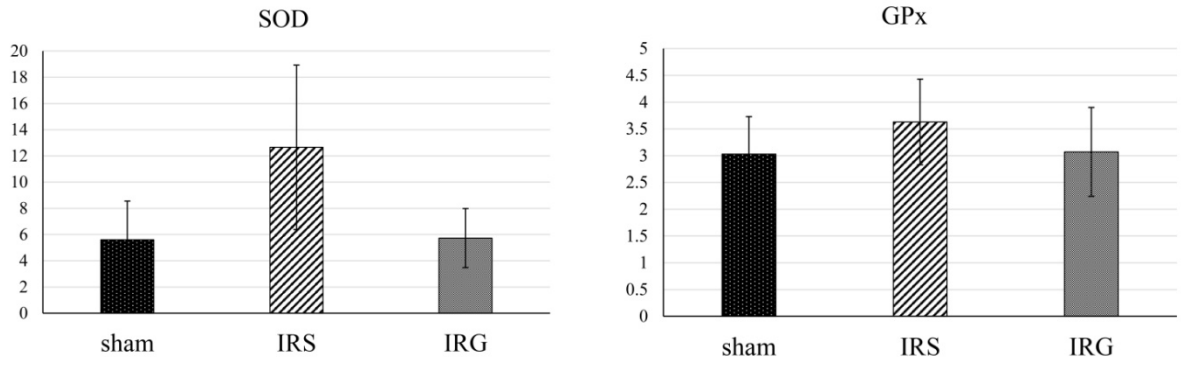

Figure 1. No significant differences were observed among groups for SOD (u/mg protein) and GPx (u/mg protein).

The level of CAT was decreased significantly in I/R groups. However, intraperitoneal administration of ghrelin inverted the process and increased the activity of CAT in the ovarian tissue in ghrelin treated group. The value of CAT activity in the I/R/ghrelin group was significantly higher than those of the other

experimental groups ($P \leq 0.05$). The average activity of this enzyme (Mean ± SD) in the sham, ischemia-saline, and ischemia-ghrelin groups was 2.01±0.8, 1.46±0.13 and 2.08±0.13 u/mg protein, respectively and they are shown in Figure 2.

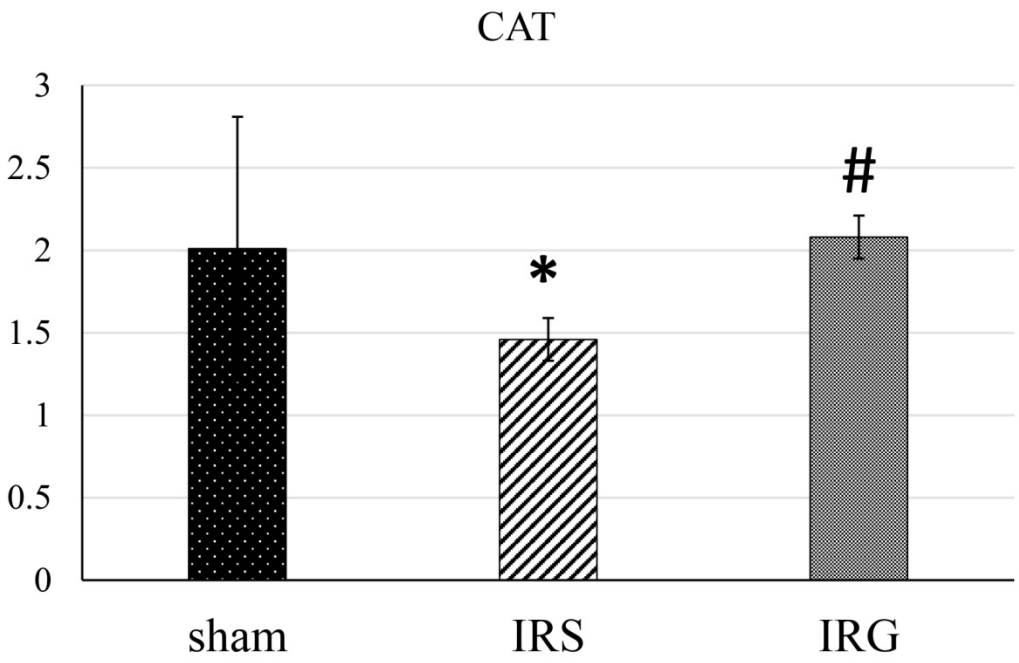

Figure 2. Ovarian CAT activities (u/mg protein) in three groups. Values represent the mean± SEM of CAT activities in each group. * means significant changes compared to the sham group. # means significant changes compared to the saline group.

The value of TAC content was lower significantly in the ischemia-saline group compared to the sham and ischemia-ghrelin groups ($P \leq 0.05$). Administration of ghrelin could enhance TAC level up to 1414.42±129.12 nmol/mg. The average activities of this enzyme (Mean ± SD) in the sham and ischemia-saline groups were 1381.86±118.6 and 928.01±79.53 nmol/mg protein, respectively and they are shown in Figure 3.

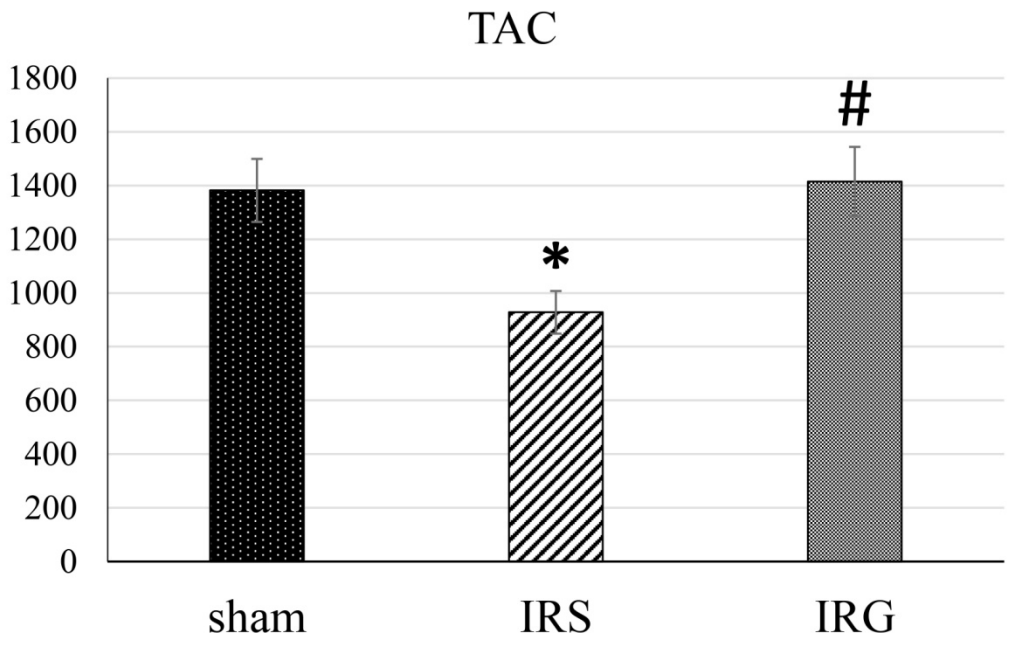

Figure 3. TAC level (nmol/mg protein) was significantly lower in the I/R group than in the ghrelin + I/R group and sham group ($P \leq 0.05$).

Figure point:

IRS: ischemia-reperfusion-saline

IRG: ischemia-reperfusion-ghrelin

*: significant changes compared to sham group.

#: significant changes compared to the saline group.

MDA levels were significantly higher in the I/R group than in the sham + ischemia-ghrelin sham groups ($P \leq 0.05$). The average activity of this enzyme (Mean ± SD) in the sham, ischemia-saline, and ischemia-ghrelin groups was 972.81±98.42, 1388.46±125.99 and 811.36±103.68 nmol/mg protein, respectively and they are shown in figure 4.

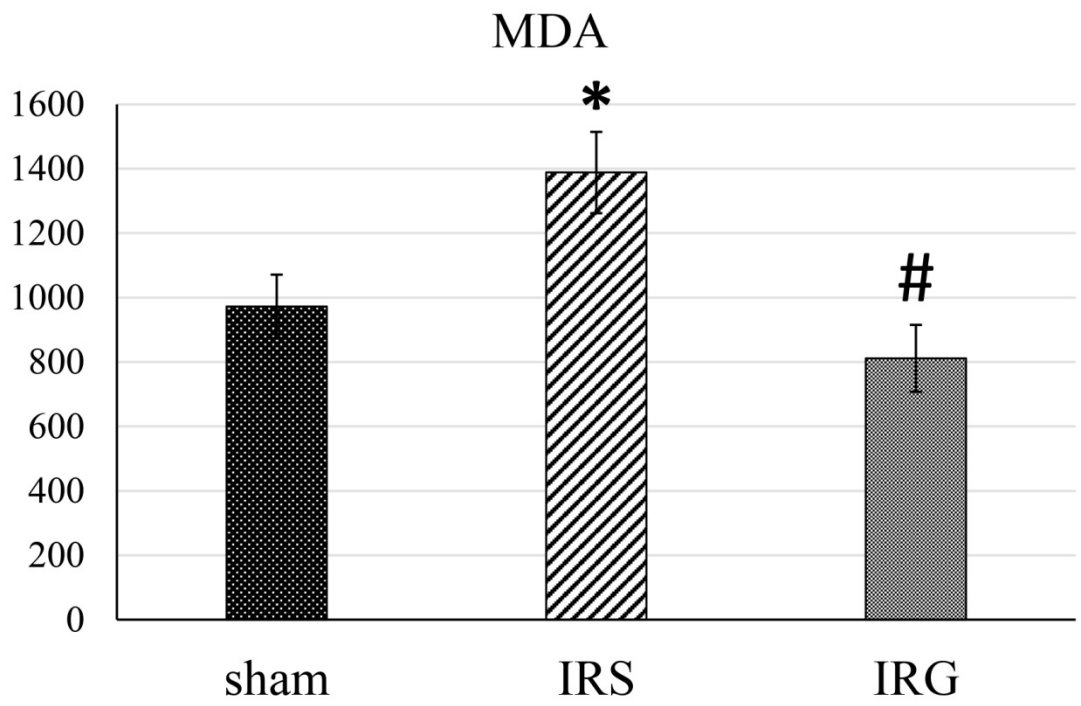

Figure 4. MDA levels (nmol/mg protein) were significantly higher in the I/R group than in the ghrelin + I/R group and sham group ($P \leq 0.05$).

4. Discussion

In this research, we investigated the protective capabilities of ghrelin against oxidative damage caused by ovarian ischemia-reperfusion injury in a rat model. The findings of our study demonstrated that the administered dose of ghrelin effectively mitigated biochemical damage associated with oxidative stress in ovarian ischemia-reperfusion injury.

Adnexal torsion occurs when the ovarian vascular pedicle twists, disrupting blood flow and causing ovarian ischemia (Ghosh and Mukharjee, 2022). This condition leads to elevated levels of lactic acid, hypoxanthine, and lipid peroxides in the blood. While detorsion is a common treatment, it can trigger oxidative stress, characterized by an imbalance between free oxygen radicals and antioxidants (Değer and Çavuş, 2020, Sengul *et al.*, 2013, Park *et al.*, 2013, Engwa *et al.*, 2022).

After ovarian detorsion, increased oxygen levels interact with hypoxanthine and xanthine, generating reactive oxygen species (ROS). These ROS, including superoxide, cause tissue damage by promoting cell membrane peroxidation and affecting mitochondrial lipids. This process, known as ischemia-reperfusion injury, exacerbates damage caused by ischemia (Sengul *et al.*, 2013, Park *et al.*, 2013, Soares *et al.*, 2019). Malondialdehyde (MDA), an indicator of oxidative damage, increases, leading to cell membrane disruption, disturbance in the ion transport system, reduced enzyme activity, and dysfunction in cell organelles (Liu *et al.*, 2016, Akdemir *et al.*, 2014).

Several studies demonstrate the impact of antioxidant molecules on the ischemia-reperfusion injury of the rat ovary. These studies motivated us to explore the influence of ghrelin on rat ovarian ischemia-reperfusion. Our findings indicate that administering ghrelin before ischemia-reperfusion has a positive effect on oxidative damage in the ovaries. In our study, the level of MDA significantly decreased in the ghrelin group compared to the ischemia-saline rats, suggesting that ghrelin can reduce lipid peroxidation. Similarly, in a report, it was observed that Agomelatine significantly decreased the ischemia/reperfusion-associated rise in MDA in ovarian tissue compared to the IR group (Gutteridge, 1995). Additionally, oxytocin administration was found to decrease MDA levels significantly in rats treated with ovarian torsion (Lee *et al.*, 2002).

The body maintains a balance between antioxidant and oxidant systems. Antioxidant systems, comprising enzymatic and non-enzymatic antioxidants, actively scavenge reactive oxygen species (ROS) to protect tissues from oxidative damage. However, if, for any reason, the oxidant mechanisms overpower this balance, it results in lipid peroxidation and tissue damage (Lee *et al.*, 2002). One crucial antioxidant enzyme is SOD. SOD plays a significant role in rapidly converting superoxide into a less harmful component, namely hydrogen peroxide. Additionally, GPx and CAT further convert this hydrogen peroxide into water (Anjum *et al.*, 2016).

In our study, superoxide dismutase showed an increase in the ischemia-reperfusion group compared to the sham group and a decrease compared to the treated group, although these changes were not statistically significant. In contrast, Yakan et al. observed statistically significant differences among SOD groups in rat ovaries (Ozlem *et al.*, 2018). This discrepancy could be attributed to variations in the interval between the tests, the duration of ischemia-reperfusion, and other factors. Changes in SOD activity might be linked to fluctuations in the levels of its substrate, the superoxide radical (Cigsar *et al.*, 2015). An increase in enzyme activity is often associated with a rise in the production of its substrate during metabolic processes. On the other hand, the decrease in antioxidant enzyme activity in the treatment group could be explained by a reduction in the levels of reactive oxygen species (ROS) or their substrates (Cigsar *et al.*, 2015). Consistent with our findings, a recent study investigating the antioxidant effects of Osajin on ischemia-reperfusion injury in rat ovaries reported a decrease in SOD activity in the treatment group, along with a decrease in the level of MDA compared to the ischemia-saline group. This suggests that similar to Osajin, ghrelin has the capability to reduce lipid peroxidation of the cell membrane and the specific substrate of the SOD enzyme (superoxide) through pathways independent of antioxidant enzyme activity (Cigsar *et al.*, 2015).

In our study, GPx increased in the ischemia-reperfusion-saline group compared to sham and decreased in the ischemia-reperfusion-ghrelin group compared to the ischemia-saline rats and none of these

changes were significant. Probably, one of the reasons for this finding may be due to the presence of non-enzymatic antioxidants in the follicular fluid or it may be due to the lack of changes in hydrogen peroxide concentration. In contrast to our study, in which the antioxidant effect of vardenafil on ischemia-reperfusion ovary had been investigated, a significant increase in GPx was observed in the treated group (Ugurel *et al.*, 2017).

Another biochemical parameter in our study was catalase (CAT). Catalase is a vital component of the cellular antioxidant system, responsible for converting hydrogen peroxide into water and molecular oxygen. This enzymatic process serves to protect the cell from oxidative damage (Nandi *et al.*, 2019). We observed a significant decrease in the saline group compared to the sham group, and a notable increase in catalase enzyme activity was observed in the ghrelin group compared to the saline group. This significant variation in catalase enzyme activity between the ischemia-saline and ischemia-ghrelin groups indicates a respective increase and decrease in the substrate of this enzyme (H2O2). Similar to our findings, in an investigation of erdosteine on ischemic-reperfusion ovary, catalase was significantly decreased in the saline group compared to the sham group and significantly increased in the ghrelin group compared to the saline group (Yao *et al.*, 2007).

In the normal state, cells possess a biochemical defense system that includes low-weight molecules and reactive free radicals, such as vitamin C, along with enzyme components like GPx, SOD, and CAT,

collectively contributing to the total antioxidant capacity (Yurtcu *et al.*, 2015). In our study, we observed a significant decrease in the saline group compared to the sham group, and a noteworthy increase in total antioxidant capacity (TAC) was observed in the ghrelin group compared to the saline group. Similarly, Yurtcu et al. observed a significant change in total antioxidant capacity. Additionally, the antioxidative effects of the Nigella sativa plant on ischemic-reperfusion ovaries was investigated and a significant increase in total antioxidant capacity in the treatment group was found (Yurtcu *et al.*, 2015, Atasever and Bakacak, 2017). Consistent with our results, Demir et al. also reported a significant difference in TAC levels between groups (Demir *et al.*, 2021). Although in our study, SOD and GPx parameters did not show a significant increase in the group treated with ghrelin, the substantial increase in catalase enzyme activity in the treatment group alone resulted in a significant enhancement of total antioxidant capacity. This finding underscores the crucial role of the catalase enzyme in managing oxidant parameters.

Ghrelin expression has been identified in interstitial and luteal hilus cells within the ovary, with its receptors present in the oocyte and ovarian follicle. These observations suggest a potential role for ghrelin in directly regulating the function of follicular and luteal cells. Furthermore, studies have demonstrated the consistent expression of the ghrelin gene in the rat ovary throughout the estrus cycle, with the lowest expression in proestrus and the highest in diestrus. The presence of both the ghrelin

ligand and receptor within the ovary indicates a regulatory pathway for this novel molecule in the physiological functions of the ovary (Caminos *et al.*, 2003, Gaytan *et al.*, 2003). One limitation of the present study was that only the single dose of ghrelin was evaluated. Further research is also needed to determine the different dosage effects

of ghrelin on ovarian torsion/detorsion.

In our earlier study investigating the antioxidant effect of ghrelin on healthy rat ovaries, we noted a significant increase in the antioxidant enzymes CAT, SOD, and GPx, along with a significant decrease in the MDA index in the ghrelin group (Kheradmand *et al.*, 2010). However, in contrast to our findings, a study by Iseri et al., which explored the antioxidative effects of ghrelin on the stomach, reported a significant increase in GPx in the treated group (İşeri *et al.*, 2005). The probable reason for this may be the difference in tissues in which evaluations were performed.

5. Conclusion

In this investigation the aim was to assess the protective effects of ghrelin in ischemia/reperfusion damage caused by ovarian torsion/detorsion. The findings of current study suggest that ghrelin is potent

antioxidant that can reduce oxidative stress. This result aligns with recent reports highlighting the antioxidative properties of ghrelin in various other tissues. One limitation of this study was that the precise timing of the administration of the ghrelin and the appropriate dose to achieve the best effect of the ghrelin were not exactly known, and the dose and time of injection in our study were based on previous documentations. Further research is required to completely understand the suitable dose and administration time to achieve the best treatment efficiency.

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اثرات محافظتی هورمون گرلین متعاقب ایسکمی-رپرفیوژن تجربی در تخمدان موش صحرایی

مهیار نظری[1]، آرش خردمند*[2]، مسعود علیرضائی[3]، عباس رئیسی[2]

1- دانش آموخته دکترای عمومی دامپزشکی، دانشکده دامپزشکی، دانشگاه لرستان، خرم آباد، ایران

2- گروه علوم درمانگاهی، دانشکده دامپزشکی، دانشگاه لرستان، خرم آباد، ایران

3- گروه علوم پایه، دانشکده دامپزشکی، دانشگاه لرستان، خرم آباد، ایران

چکیده:

زمینه مطالعه: تورشن تخمدان، یک اورژانس حیاتی زنان، سبب انسداد شریان و ورید تخمدان و در نهایت باعث ایسکمی در تخمدان می‌شود.

هدف: این مطالعه با هدف بررسی اثرات آنتی‌اکسیدانی بالقوه گرلین در آسیب ایسکمی-رپرفیوژن تخمدان موش صحرایی انجام شد.

روش کار: 21 موش صحرایی ماده بالغ نژاد ویستار (گرم 300-250) به سه گروه (7 تایی) تقسیم شدند: 1- گروه شم. 2- گروه ایسکمی-سالین: 100 میکرولیتر سالین 30 دقیقه قبل از 2 ساعت ایسکمی و همزمان با شروع رپرفیوژن 2 ساعته به صورت داخل صفاقی تجویز شد. 3- گروه ایسکمی-گرلین: 10 نانومول گرلین 30 دقیقه قبل از 2 ساعت ایسکمی و همزمان با شروع رپرفیوژن 2 ساعته به صورت داخل صفاقی تجویز شد. تخمدان های سمت راست در هر گروه برداشته و تحت آنالیز بیوشیمیایی قرار گرفتند. مالون دی آلدهید (MDA)، سوپراکسید دیسموتاز (SOD)، گلوتاتیون پراکسیداز (GPx)، ظرفیت آنتی اکسیدان تام (TAS)، و کاتالاز (CAT) به عنوان پارامترهای بیوشیمیایی مورد بررسی قرار گرفتند.

نتایج: فعالیت SOD و GPx بین گروه‌های مختلف تفاوت معنی‌داری نداشت (P>0/05). سطح MDA در گروه ایسکمی-سالین نسبت به گروه کنترل بالاتر و در گروه ایسکمی-گرلین نسبت به گروه ایسکمی-سالین به طور معنی داری کمتر بود (P<0/05). فعالیت های CAT و TAC در گروه سالین در مقایسه با گروه شم به طور معنی‌داری کاهش یافت و در گروه تحت درمان با گرلین نسبت به گروه سالین به طور معنی داری افزایش یافت (P<0/05).

نتیجه گیری نهایی: به طور کلی، گرلین با دوز 10 نانومول، تخمدان‌های موش را از آسیب ناشی از ایسکمی-رپرفیوژن محافظت کرد.

واژگان کلیدی: گرلین، ایسکمی-رپرفیوژن، تخمدان موش صحرایی، تورشن، تورشن/دتورشن