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The Effect of *Momordica charantia* on Ovarian Ischemia-Reperfusion

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Abstract

Ovarian torsion is one of the gynecological emergencies that affect ovarian tissue integrity and fertility. In this study, we aim to investigate the effects of *Momordica charantia* (MC) on ovarian tissue injury induced by ovarian ischemia-reperfusion. Twenty-four rats were assigned to three groups: control group, ischemia-reperfusion (I/R) group and IR + MC group. 600 mg/kg MC extract were given rats via orogastric route. 3-hour ischemia and 3-hour reperfusion were performed for IR protocol. At the end of experiment, ovarian tissues were excised, fixed in zinc-formalin and processed for routine paraffin wax tissue embedding. Sections were stained with hematoxylin and eosin. Ovarian sections of control group showed regular histological appearance. In ovarian sections of I/R group, hemorrhage, fibrin accumulation, mononuclear cell infiltration and degenerated follicles were observed. I/R + MC group showed improved histopathology caused by I/R injury. We think that MC extract may protect ovarian tissue integrity and its histological structures.

Keywords

Follicles, Histology, Ischemia, *Momordica charantia*, Ovary, Reperfusion

1. Introduction

Ovarian torsion is the rotation of the peduncle with arteries and veins of the ovary on its axis by partially or full turn, preventing blood flow. As a result of torsion, ischemia develops in tissues and tissue damage occurs. Ovarian torsion is seen in 2.7% of gynecological emergencies. Although it affects all age groups from female fetuses to menopause, it is more common in women of reproductive age [1] [2]. The etiology of ovarian torsion is not known exactly, but most cases have functional cysts or neoplasms of the ovary. Delay or mistake in the

diagnosis may cause decrease the follicle reserve or disfunction of the ovary in the patient [3]. When clinical signs of acute abdomen (peritoneal irritation) are present, most cases go to diagnostic laparotomy or laparoscopy [4]. However, in most cases of torsion, the clinical findings are indistinct. As a result, both diagnosis and treatment delay [5].

Plant extracts are still popular as a treatment method that has continued for centuries in the treatment of various diseases. Scientists have been focused on the use of those plants used in different diseases and have included in their studies. Many plants with anti-inflammatory, immunomodulatory and antioxidant activities have been used to cure ovarian ischemia/reperfusion injury in tissues [6] [7] [8]. *Momordica charantia* (MC, bitter melon) is a tropical plant belonging to the Cucurbitaceae family. It contains plenty of vitamins and is the most bitter of all fruits and vegetables [9]. It is a popular herb used in the treatment of many diseases such as diabetes mellitus, inflammation, constipation, ulcers, malaria and cancers [10].

Once the ovaries rotate (torsion), the blood flow to the ovary decreases and ischemia develops. Reflow of blood to ovary is called detorsion (reperfusion). Even though, the ovaries are re-blooded, complete recovery cannot be achieved in the tissues. The treatment options are pharmacochemical (pain relievers) or surgical operations (laparotomy) which may have some complications and side effects. Ovarian torsion causes hemorrhage, tissue necrosis, and edema. In this study, we aimed to investigate the effects of MC extract on rat ovary tissues in the experimental ischemia-reperfusion injury model.

2. Materials and Methods

The ethical approval was obtained by the Dicle University Animal Experiments Local Ethics Committee with the protocol number 2020/08. This study was financed by Dicle University Scientific Research Platform (DUBAP) with the project number TIP.20.009. The MC plant was purchased from a local seller and its ethanolic extract was obtained in the Pharmacognosy laboratory of Dicle University. Twenty-four female Sprague Dawley rats (12 weeks old, average 250 - 300 g) were divided into three groups with eight rats in each group.

Control group: Under general anesthesia, the abdomen of the rats was opened with a surgical protocol and the abdominal layers were closed without any further intervention. At the end of the experiment, the animals were sacrificed and their ovaries were excised.

Ischemia/reperfusion (I/R) group: The abdomen was opened under general anesthesia and the ovarian adnexa was clamped with bulldog clamp. Ischemia procedure was applied for 3 hours. Then, the ovaries were returned to their normal positions, placed in their anatomical location and reperfused for 3 hours. At the end of the experiment, the animals were sacrificed and their ovaries were excised.

I/R + MC group: The abdomen was opened under general anesthesia and the

ovarian adnexa was clamped with bulldog clamp. Ischemia procedure was applied for 3 hours. After the ischemia procedure, the animals were given 600 mg/kg MC extract by orogastric route. Then, the ovaries were returned to their normal positions, placed in their anatomical location and reperfused for 3 hours. At the end of the experiment, the animals were sacrificed and their ovaries were excised.

Ovaries were fixed in 10% formaldehyde for 48 hours, then subjected to routine paraffin wax tissue processing. 5-micron sections were cut from paraffin blocks with a microtome and stained with Hematoxylin-Eosin to examine the tissue histopathology.

3. Results

Ovarian tissues of each group were stained with hematoxylin and eosin staining. Normal ovarian and follicular histology was observed in the ovarian sections of the control group. Primary and graafian follicles were observed together with the oocyte and the surrounding zona pellucida. Corpus luteum was observed to develop. The internal and external theca layers around the follicle were also evident. Formation of cumulus oophorous was observed (Figure 1). Pathology was observed in histological tissue in the ovarian section of the ischemia/reperfusion (I/R) group. Hemorrhage, fibrin accumulation and mononuclear cell infiltration were observed in the interstitial stroma. Follicle development was inhibited, and degenerated follicles were formed. Vascular dilatation was common. Cell degeneration was observed in the germinal epithelium (Figure 2). In the I/R + MC ovarian section, pathological appearances mostly improved. Follicle development continued (primary, secondary, graafian, degenerated follicles) with primary oocyte and zona pellucida. Hemorrhage and fibrin accumulation decreased, but dilatation partially continued (Figure 3).

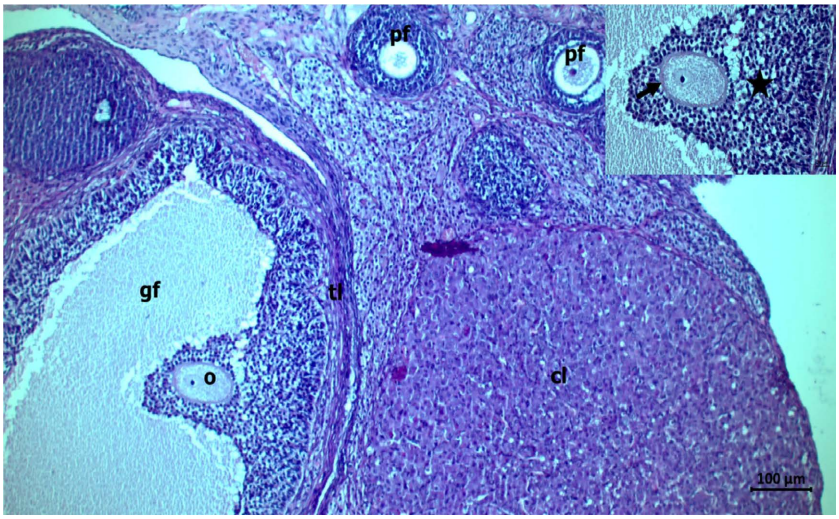

Figure 1. Ovarian section of control group. pf: primary follicle, gf: graafian follicle, cl: corpus luteum, tl: theca layers, o: primary oocyte, star: cumulus oophorous, arrow: zona pellucida. İnset shows high magnification of graafian follicle.

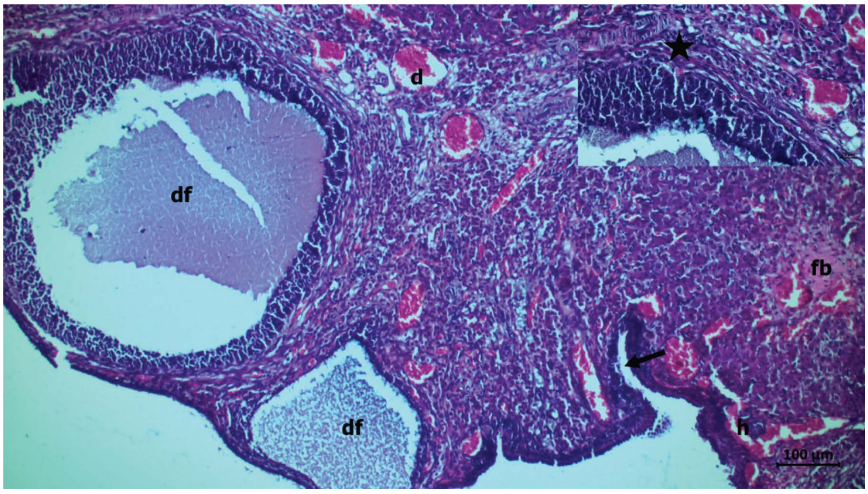

Figure 2. Ovarian section of IR group. df: degenerated follicle, d: vascular dilatation, fb: fibrin accumulation, h: hemorrhage, star: mononuclear cell infiltration, arrow: germinal epithelium. İnset shows high magnification of the large, degenerated follicle.

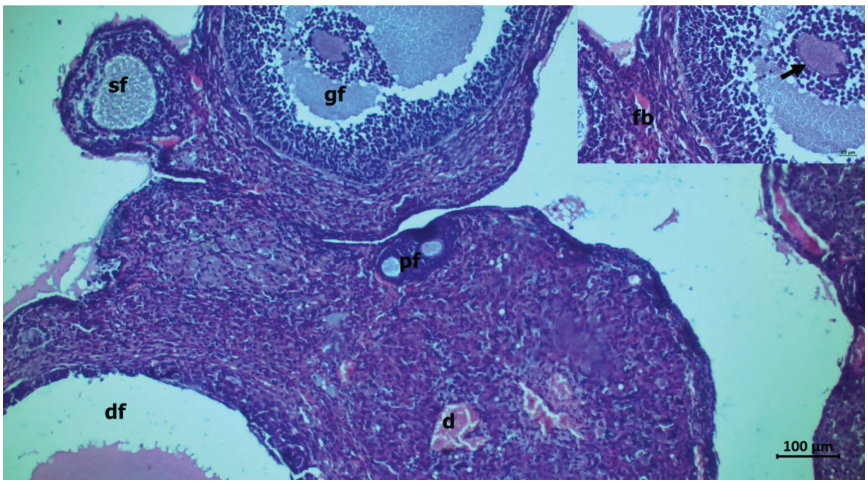

Figure 3. Ovarian section of IR + MC group. pf: primary follicle, sf: secondary follicle, gf: graafian follicle, df: degenerated follicle, d: vascular dilatation, o: primary oocyte, fb: fibrin accumulation, arrow: primary oocyte.

4. Discussion

The ovary, an element of the female reproductive system, is responsible for gamete cell production and secretion of steroid hormones. Ovarian torsion is the name given to the obstruction of blood flow (ischemia) as a result of the rotation of the peduncle around itself, where the arteries and veins are located. Detorsion (reperfusion) is re-blooded of ischemic tissue [11]. Ovarian torsion is a rare phenomenon, but urgent intervention is required [12]. Gangrene, tissue damage, peritonitis and even infertility may occur in case of late treatment or long-term torsion. The degree of ischemic injury varies according to the exposure time, tissue or organ type, and metabolic requirements in the organ. Ischemic tissue becomes hypoxic due to oxygen deficiency and the production of reactive oxygen species increases (ROS). ROS deteriorates antioxidant system, leading to

tissue damage [13]. Reperfusion of ischemic tissue may increase the damage. The resulting I/R injury causes the formation of excess oxygen radicals (hydroxyl radical, hydrogen peroxide, superoxide anion) and a decrease in nitric acid production.

Momordica charantia (MC) is an herb widely used in traditional Chinese medicine. The active ingredients and mechanism of action of MC are not fully known. It has been used for years in the treatment of many diseases, including cardiac, cancer and diabetes [14]. The protective effects of MC on different tissues were studied. In the cerebral I/R experiment of Nerurkar *et al.*, they stated that MC administration slowed down oxidative stress and inflammation in mutant mice fed a high-fat diet and normalized the levels of inflammatory markers such as NF-kB1, IL-16, IL-22 in the cerebral tissue [15]. In another global cerebral I/R study on diabetic mice, it was noted that different doses of MC fruits reduced oxidative stress and damage, corrected neurological defects and showed antidiabetic effects [16]. Parikh et al. reported that after liver I/R, 200 mg/kg MC fruit extract returned normal levels of liver damage markers SGOT, SGPT, ALP; tissue damage marker LDH and inflammatory marker CRP [17]. In our study, normal histological appearance and folliculogenesis were observed in ovarian sections of the control group (**Figure 1**). Interstitial hemorrhage, follicular degeneration, vascular dilatation, mononuclear cell infiltration and fibrin were observed in the I/R group (**Figure 2**). In the I/R + MC group, most of the pathology in the ovaries were restored and follicle formation was re-initiated however, hemorrhage, dilatation and fibrin accumulation continued (**Figure 3**). MC supplementation before ischemia promoted the re-formation of follicles in the ovary, partly preserved the ovarian histological structure, but was not very effective in vascular structures.

5. Conclusion

MC is a plant that has many biological and medical activities and has been used in traditional medicine for centuries. In our study, acute treatment of MC cured the pathologies in ovaries caused by ischemia-reperfusion injury.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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