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ALTERATIONS IN CATALASE, SUPEROXIDE DISMUTASE, GLUTATHIONE PEROXIDASE AND MALONDIALDEHYDE LEVELS IN SERUM AND LIVER TISSUE UNDER STRESS CONDITIONS

STRES KOŞULLARINDA SERUM VE KARACİĞER DOKUSUNDAKİ KATALAZ, SÜPEROKSİT DİSMUTAZ, GLUTATYON PEROKSİDAZ VE MALONDİALDEHİT DÜZEYLERİNİN DEĞİŞİMİ

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ABSTRACT

Objective: Chronic stress is a factor that affects organs/tissues and disrupts homeostasis. This condition can lead to increased oxidative stress, which damages cellular components. Antioxidants attempt to prevent this damage by neutralizing free radicals. Our study aimed to investigate the effect of chronic mild stress on the levels of Catalase (CAT), Superoxide Dismutase (SOD), Glutathione Peroxidase (GPx) and Malondialdehyde (MDA) in serum and liver tissue.

Material and Method: In our study, 16 Wistar albino rats were divided into control and experimental groups. The chronic unpredictable mild stress (CUMS) model protocol was employed. The levels of CAT, SOD, GPx, and MDA in serum and liver tissue were measured using the Enzyme-Linked Immunosorbent Assay method.

Result: Upon comparison of serum CAT, SOD, GPx, and MDA levels, no statistically significant difference was observed between the control and stress groups ($p>0.05$). However, when comparing CAT, SOD, GPx, and MDA levels in the liver tissue, a significant increase in the levels of antioxidant enzymes was noted in the stress group ($p<0.05$).

Conclusion: Under chronic stress, liver tissue's antioxidant levels appear to increase. We believe our study may contribute to understanding the connection between stress, free radicals, and antioxidants.

Keywords: Antioxidant, chronic stress, oxidative stress

ÖZET

Amaç: Kronik stres, organ/dokuları etkileyen ve homeostazisi bozan bir faktördür. Bu durum, hücresel bileşenlere zarar veren oksidatif stresin artmasına neden olabilir. Antioksidanlar ise serbest radikalleri notralize ederek bu zararı önlemeye çalışır. Çalışmamızın amacı, kronik hafif stresin serum ve karaciğer dokusundaki Katalaz (CAT), Süperoksit Dismutaz (SOD), Glutatyon Peroksidaz (GPx) ve Malondialdehit (MDA) seviyeleri üzerindeki etkisini araştırmaktır.

Gereç ve Yöntem: Çalışmamızda 16 Wistar albino sıçan kontrol ve deney gruplarına ayrılmıştır. Kronik öngörülemeyen hafif stres model protokolü uygulandı. Serum/karaciğer CAT, SOD, GPx ve MDA düzeyleri Enzyme Linked Immunosorbent Assay metodu ile ölçüldü.

Bulgular: CAT, SOD, GPx ve MDA serum düzeyleri karşılaştırıldığında kontrol ve stres grupları arasında istatistiksel olarak anlamlı fark belirlenmedi ($p>0,05$). Buna karşın, karaciğer dokularındaki CAT, SOD, GPx ve MDA seviyeleri karşılaştırıldığında, stres grubunda antioksidan enzim seviyelerinde anlamlı yükseliş belirlenmiştir ($p<0,05$).

Sonuç: Kronik stres altında, antioksidan enzim seviyelerinin karaciğer dokusunda arttığı görülmektedir. Çalışmamızın stres, serbest radikaller ve antioksidanlar arasındaki bağlantıya yönelik bir katkı sunabileceği kanısındayız.

Anahtar Kelimeler: Antioksidan, kronik stres, oksidatif stres

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INTRODUCTION

Chronic psychological stress has become an inevitable part of modern life, negatively impacting both physical and mental health. It is considered a factor that affects nearly all organs/tissues and disrupts homeostasis (1). Furthermore, it is a subject of current research that chronic stress may elevate oxidative stress at the cellular level, potentially contributing to the development of various diseases (2, 3).

Oxidative stress is a biological imbalance from accumulating reactive molecules, known as free radicals, within cells (4). The accumulation of free radicals within cells and resultant oxidative damage from oxidative stress can prompt a spectrum of morphological alterations in tissues. Such changes can affect the structure and functionality of cells, leading to potential harm across various organs. The liver, which has an important function in detoxification processes, is primarily affected by this process (1). Also, chronic psychological stress can increase cortisol levels and cause oxidative stress (5). Chronic stress can also impact the immune system, producing heightened inflammatory responses. In such cases, there is an increase in the secretion of pro-inflammatory cytokines, which may contribute to the formation of free radicals (6).

Moreover, chronic psychological stress can negatively affect mitochondrial function. Under the influence of stress, dysfunctions in mitochondria may arise, potentially contributing to an increase in oxygen radicals (2, 7). Additionally, chronic stress can impact antioxidant defense systems, reducing their effectiveness (4).

The organism responds to the harmful effects of oxidative stress with the antioxidant defense system. This defense system tries to prevent oxidative damage by neutralizing free oxygen radicals in cells (8). The biological system that prevents the progression of oxidation/peroxidation by reacting with oxygen radicals is defined as 'Antioxidant defense' (9). The primary members of the cellular antioxidant defense mechanism are Catalase (CAT), Superoxide Dismutase (SOD), and Glutathione Peroxidase (GPx). These enzymes trigger a series of biological activities that facilitate the removal of oxidative stress factors, which could disrupt the homeostatic balance of the cell (10).

Catalase is an important enzyme that plays a fundamental role in protecting cells from the harmful effects of hydrogen peroxide in almost all aerobic organisms (11). CAT serves as an efficient catalyst, facilitating the breakdown of hydrogen peroxide into water and molecular oxygen. This compound is generated as a byproduct during diverse cellular activities. The fundamental significance of the CAT enzyme lies in its role as a potent antioxidant agent within the biological system. Iron ions in CAT catalyze hydrogen peroxide oxidation (2). Hydrogen peroxide forms a compound that, as a reactive oxygen species, can damage cellular components, lipids, proteins, and genetic material (7). CAT, which also plays a role in detoxification, is found mainly in liver tissue (12).

Superoxide dismutase is a critical enzyme that provides an effective antioxidant defense mechanism against reactive oxygen species (ROS), especially superoxide anion radicals (13). SOD facilitates reactions that convert superoxide radicals into oxygen molecules and transform other superoxide radicals into hydrogen peroxide, which is a less reactive compound. This process enables cells to shield themselves effectively from oxidative harm induced by superoxide anions and ROS (14). SOD is an antioxidant enzyme that plays an important role in maintaining cellular homeostasis and is considered a key component in combating oxidative stress (10).

Glutathione peroxidase is an antioxidant enzyme that has important functions in maintaining the cellular redox balance. It also plays an important role in preventing lipid peroxidation, which can cause cellular damage (8). GPx reduces cellular peroxide compounds and organic hydroperoxide and turns them into harmless ones. This increases the resistance of cells to oxidative damage (9). GPx functionally interacts with GSH 'γ-glutamyl-cysteinyl-glycine,' enabling the formation of the reduced form of GSH and thereby counteracting the effects of oxidative stress (15). GPx plays a crucial role in reducing the oxidation of polyunsaturated fatty acids within cell membranes, thereby preserving cellular integrity through maintaining membrane structure. GPx constitutes a significant component of the cellular antioxidant defense system (16). It works together with other antioxidant enzymes, SOD and CAT, to provide an effective defense of cells against reactive oxygen radicals (17).

Malondialdehyde is generated through the interaction of oxygen molecules and free radicals with polyunsaturated fatty acids in the cell membrane. MDA is a common biomarker for evaluating the levels of oxidative stress in cells and tissues (18). Monitoring MDA levels can provide insights into the extent of oxidative stress and potential cellular damage. Elevated MDA levels indicate increased oxidative damage to cell membranes and lipids (10, 19).

Within this framework, the primary objective of our investigation is to ascertain the concentrations of antioxidant enzymes in the serum and liver tissues subjected to chronic stress. Our goal is to assess the impact of chronic mild stress on cellular oxidative stress by juxtaposing potential alterations in enzyme levels against those of the control group. This research will enhance the comprehension of the mechanisms by which chronic psychological stress may influence oxidative stress and potential cellular injury.

MATERIALS and METHODS

Animals and standard procedures

In the study, 4-month-old 190-200 gr female Wistar albinos (n=16) were used. We divided the rats into two groups in standard cages two weeks before the study process started and provided the standard room conditions. The menstrual cycles of rats were considered and analyzed. Rats in the same menstrual phase were included in the study. During anesthesia, a combination of ketamine hydrochloride (90 mg/kg; Ketalar, Parke-Davis) and xylazine hydrochloride (12 mg/kg, 2%; Rompun, Bayer) was administered intraperitoneally to rats. The anesthesia process of the rats was started approximately 15 minutes before. Muscle movements and reactions to pain were tested and processed. Euthanasia was performed by cervical dislocation after intracardiac blood collection. The principles of "Guidelines for the Care and Use of Laboratory Animals" were applied. Ethical approval of the study was obtained from the Kocaeli University Animal Experiments Local Ethics Committee (Date: 26.07.2023, No: 6/4-2023).

Stress model and groups

In our study, the chronic unpredictable mild stress (CUMS) protocol which was previously defined in the literature, was used as a stress model (20). Using the CUMS model, rats are prevented from learning stressors, which consequently inhibits their ability to develop resilience to the stress model. A total of 8 different stressors were identified, and the order of the stressors was previously determined (Box 1). At the end of the experiment, anhedonia behaviors, considered an indicator of the depression status of the animals, were closely monitored and measured.

Box 1: Stressors applied in Chronic Unpredictable Mild Stress (CUMS) model

1. Cage inclination, 45 °C/24 hours
2. Hanging from the tail, 1 minute
3. Buoyancy in cold water 4 °C/5 minutes
4. Buoyancy in hot water 45 °C/5 minutes
5. Changing day-night cycle
6. Cage shaking, 10 minutes
7. Cage wetting 200 mL/24 hours
8. Exchanging sawdust between cages

In our study, two groups were formed: experimental and control groups. Then, we applied the stressors to the experimental group for 28 days. Before the start of the experiment, the order in the application protocol was determined randomly.

Tissue lysis procedures

To prevent possible blood contamination, tissues were washed with a saline solution containing 0.09% NaCl. Subsequently, the tissues were weighed and homogenized in a 1/10 ratio of phosphate-buffered saline with a pH of 7.4. The homogenization was carried out at 24,000 revolutions per minute using a T25 Basic Ultra Turrax homogenizer (IKA Werke Deutschland/Germany). Following homogenization, the samples were centrifuged at 10,000 times the force of gravity for 15 minutes at a temperature of 4°C. The resulting homogenate was then divided into smaller tubes and preserved for further analysis based on tissue-specific measurements. The modified Lowry method determined the protein content (21). The total protein concentration of the liver tissue was equalized before the ELISA process.

Enzyme-linked immunosorbent Assay (ELISA) method and biochemical procedures

Blood samples (3 mL) were taken from the left ventricle. Blood specimens were allowed to clot for two hours at room conditions and centrifuged for 15 minutes at 1000g force at 4-8 °C. Serum samples were stored at -40°C. The supernatants were collected and diluted 1/10 before the assay. Serum and tissue GPx, CAT, and SOD levels were determined with ELISA (ELISA; BT Lab, Zhejiang, China) kits and measured with ‹Alisei Quality System Seac Radim Company analyzer› (Italy/Rome)-ELISA reader based on the manufacturer›s instructions (GPx-1, Code E1172Ra; CAT, Code E0869Ra; SOD-1, Code E1444Ra). Serum and tissue MDA levels were determined using a colorimetric MDA assay (BT Lab, Zhejiang, China) and measured with UV-1280 UV-VIS Spectrophotometer (Shimadzu, Kyoto, Japan) based on the manufacturer›s instructions (MDA, Code SH 0020). The dilution coefficient was multiplied by the results, and their concentrations were calculated according to the kit›s standards.

Data analysis and statistics

The Kolmogorov-Smirnov analysis was performed for the normal distribution suitability test in the statistical evaluation of our results. An Independent T-test was applied for the values that correspond to normal distribution. 'The Mann Whitney U' statistic method was used for the values that do not comply with the normal distribution. P values of 0.05 or less were considered statistically significant. The Statistical analysis SPSS 22.0 (IBM, SPSS Corp., Armonk, NY, USA) was used. The GraphPad Prism 8 package program was used for graphics design.

RESULTS

The mean serum CAT level and standard error were recorded as 0.4354±0.00002 pg/mL for the control group and 0.4357±0.00008 pg/mL for the stress group. Upon comparison of serum CAT levels, no statistically significant difference was observed between the control and stress

groups (p>0.05). The liver tissue CAT mean level and standard error were 75.1530±2.6575 pg/mg for the control group and 97.2244±4.3709 pg/mg for the stress group. Upon comparison of the CAT levels in liver tissue, a significant difference was noted between the stress and control groups (p=0.001). CAT levels were increased in the liver tissues of the rats belonging to the stress group (Figure 1).

When the SOD serum levels were compared, no statistically significant difference was determined between the control and stress groups (p>0.05). The serum SOD mean level and standard error mean; 0.3153±0.0004 ng/mL for the control group, 0.3155±0.0005 ng/mL for the stress group. However, when the liver tissue SOD levels were compared, a significant difference was observed between the stress and control groups (p=0.002). The mean SOD level in liver tissue and the associated standard error were 53.4895±1.9065 ng/mg for the control group and 69.7734±3.4213 ng/mg for the stress group. Elevated SOD levels were observed in the liver tissues of rats subjected to stress (Figure 2).

The Glutathione peroxidase serum mean level and standard error were 0.1464±0.0001 ng/mL for the control group and 0.1465±0.0001 ng/mL for the stress group. When GPx serum levels were compared, no statistically significant difference was determined between the control and stress groups (p>0.05). The liver tissue GPx mean level and standard error mean were 24.9962±0.8778 ng/mg for the control group and 32.3813±1.4753 ng/mg for the stress group. Upon comparing GPx levels in liver tissue, a significant difference was found between the stress and control groups (p=0.001). There was a significant increase in GPx levels in the liver tissues of the rats in the stress group (Figure 3).

When MDA serum levels were compared, no statistically significant difference was determined between the control and stress groups (p>0.05). Serum MDA mean level and mean standard error: 2.4091±0.0612 ng/mL for the control group and 2.5675±0.0798 ng/mL for the stress group. Upon comparison of MDA levels in liver tissue, a significant difference was found between the stress and control groups (p=0.001). The mean MDA level in liver tissue and the mean standard error were 721.6182±26.6123 ng/mg for the control group and 924.2219±40.3367 ng/mg for the stress group. MDA levels were elevated in the liver tissues of the rats in the stress group (Figure 4).

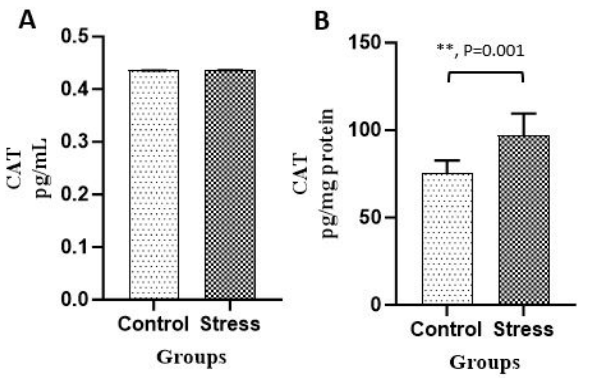

Figure 1: Mean Catalase (CAT) levels between groups: A) Serum CAT (pg/mL) level, B) Liver tissue CAT (pg/mg) level

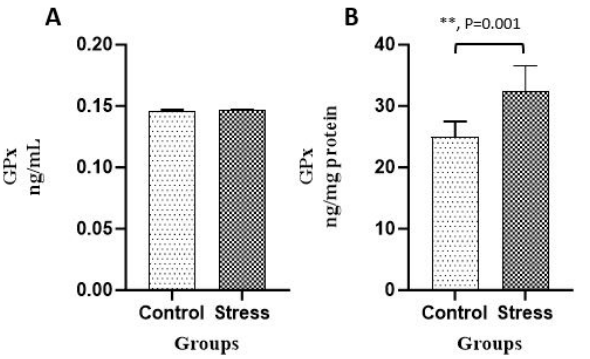

Figure 3: Mean Glutathione Peroxidase (GPx) levels between groups: A) Serum GPx (ng/mL) level, B) Liver tissue GPx (ng/mg) level

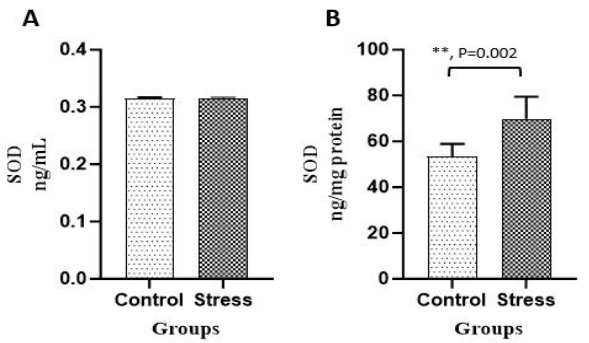

Figure 2: Mean Superoxide Dismutase (SOD) levels between groups: A) Serum SOD (ng/mL) level, B) Liver tissue SOD (ng/mg) level

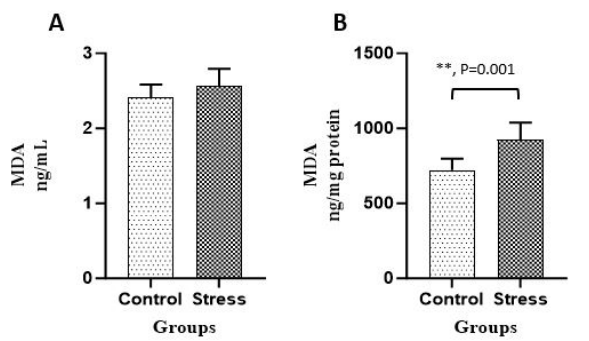

Figure 4: Mean Malondialdehyde (MDA) levels between groups: A) Serum MDA (ng/mL) level, B) Liver tissue MDA (ng/mg) level

DISCUSSION

Chronic psychological stress is increasingly recognized as a significant health issue in contemporary society, adversely impacting both the physical and mental well-being of individuals (22). At the core of this interaction lies the potential for stress to enhance oxidative stress at the cellular level (2). Homeostasis is the organism's ability to regulate and maintain its cellular balance against environmental factors. Stress is considered a factor that disrupts homeostasis (23). Oxidative stress factors cause changes in various intercellular reflex communication pathways in the organisms (24). Free radicals interact with proteins within the cell, changing their structure and disrupting their functions. In particular, the activities of enzymes can be affected in this way, leading to abnormalities in cellular processes (2). Moreover, it can cause cellular balance disorders by interacting with cell membranes, lipids, and genetic material (7). Depending on this biological change, cardiovascular pathologies, metabolic diseases, neurodegenerative changes, and related functional disorders may occur (3, 6).

Chronic psychological stress is recognized for its association with increased cortisol levels in the body. This elevation in cortisol has been identified as a factor that can intensify oxidative stress at the cellular level. Elevated cortisol can enhance the generation of free radicals and simultaneously impair the cellular antioxidant defense systems (5, 24). Cortisol binds to intracellular glucocorticoid receptors (GR), triggering a conformational change that facilitates the translocation of the resulting bio-complex into the nucleus. Within the nucleus, the GR-cortisol complex interacts with specific glucocorticoid response elements, modulating the transcriptional activity of certain genes (25). This modulation affects protein synthesis and cellular functions, producing the cortisol's anti-inflammatory, immunosuppressive, metabolic, and neurological effects.

Additionally, cortisol regulates its secretion through negative feedback by affecting the hypothalamus and pituitary gland (1). The study investigating the effects of acute, subacute, and chronic stress on oxidative radicals showed that chronic stress causes both oxidative stress and increased antioxidant biomolecules in the brain (22). In addition, the effects of various stressors on oxidation and antioxidant levels have been investigated. As a result, significant increases in plasma corticosterone levels and lipid and protein oxidations were observed. Nevertheless, increases in antioxidant enzyme levels have also been reported (26). Our study determined an increase in antioxidant biomolecules in the liver tissues of rats exposed to chronic mild stress. Increased oxidative stress at the cellular level can damage cell components, proteins, and genetic material, disrupting the normal functions of cells and causing various pathological conditions. In this process, excessive accumulation of free radicals and weakening of antioxidant defense mechanisms play a critical role (10).

Catalase enzyme constitutes one of the critical antioxidant mechanisms that combat oxidative stress at the cellular level. Its primary function is to convert hydrogen peroxide molecules accumulated in cells into water and molecular oxygen compounds (11). This reaction prevents oxidative damage by reducing reactive oxygen species within the cell and contributes to maintaining cellular homeostasis (4). Cells under stress accelerate detoxification processes through the CAT enzyme to cope with oxidative stress (2). CAT is found in high concentrations, especially in the liver tissue, where detoxification processes are intense in cases where oxidative stress increases and free radicals and reactive oxygen species can cause damage by changing (12, 24).

The CAT enzyme helps preserve the structure and functionality of cells by neutralizing these harmful compounds. This biochemical reaction is catalyzed through changes in the oxidation state of iron ions in the prosthetic groups of the enzyme (11). Under stress conditions, binding the cortisol hormone to cell surface receptors triggers cellular signaling pathways and subsequent modifications. This mechanism is particularly critical in prolonged oxidative stress resulting from chronic psychological stress (5, 25). Chronic stress can induce oxidative stress through elevated cortisol levels. In this case, the enzyme CAT plays a crucial role in the cellular defense mechanism by mitigating oxidative damage (9). Thus, the CAT enzyme has a central role in combating cellular oxidative stress, and the activity of this enzyme is critically important in protecting cells against oxidative damage caused by chronic psychological stress (15). The increased CAT level may be an adaptive response that helps cope with oxidative stress by contributing to cellular detoxification. Although our research did not show a significant difference in serum CAT levels between groups, it revealed a remarkable distinction in liver tissue. A significant increase was observed, especially CAT levels, in the liver tissue of rats under stress conditions. This finding highlights the vital role of CAT in cellular protection and reveals the importance of cellular defense mechanisms against oxidative damage caused by chronic psychological stress.

Superoxide dismutase enzyme is critical in detoxifying reactive oxygen species produced within cells (10). This metalloprotein contains copper, zinc, or manganese and forms a critical part of the cellular defense mechanism against oxidative damage (13). Neutralization of the superoxide radical leads to hydrogen peroxide and oxygen molecules forming. Hydrogen peroxide is converted into water and oxygen by CAT or GPx enzymes and is

rendered harmless (26). SOD, which exists in three different isoforms in the cell, is localized in the mitochondrial matrix, cytosol, and extracellular matrix and regulates intracellular and extracellular ROS accumulation (7). Liver and serum levels of SOD can fluctuate based on metabolic activity, inflammation, and the presence of oxidative stress.

Given that the liver is abundant in antioxidant enzymes, the activity of SOD is vital for safeguarding this organ from oxidative harm (12, 13). Serum SOD levels are commonly indicative of the body's antioxidant defense status and are utilized as markers for various disease states and stress. Under conditions of stress, the level of cellular SOD generally increases (27). This situation aims to increase the cells' capacity to cope with oxidative stress, thereby preserving cellular integrity and functionality (28). While this increase is observed as a rapid adaptive response in acute stress situations, a continuous rise in SOD activity during chronic stress can lead to the depletion of intracellular antioxidant defense systems and potentially to an increase in oxidative damage (29).

Superoxide dismutase enzyme prevents cellular oxidative damage by biochemically detoxifying superoxide radicals. This enzyme is found in various localizations inside and outside the cell, and its cellular levels increase in cases of oxidative stress (14). The levels of SOD in the liver and serum reflect the antioxidant status in the body, providing information about various biological and pathological conditions (12). In a study investigating the effects of stressors such as cold application and immobilization on oxidative stress, it has been shown that there is a significant increase in SOD levels parallel to the increase in lipid/protein oxidation (26). In the study carried out on patients with traumatic stress due to spinal fractures, researchers detected a significant elevation in serum SOD and MDA levels when compared to the control group. However, there was no observed change in GPx levels within the same group of patients (30). Under stress conditions, changes in the levels of cellular SOD signify the cells' adjustment and defensive response to oxidative stress (29). In our study, while there is no significant difference between serum SOD values in the stress group, there is an increase in liver tissue levels in the stress group.

Glutathione peroxidase is a family of enzymes that contain selenocysteine and protect cellular membranes and other cellular components from oxidative damage by reducing hydrogen peroxide or organic hydroperoxides (17). This enzyme contributes to the antioxidant defense mechanism, especially through GSH-dependent reactions (15). GPx uses hydrogen peroxide as a substrate and converts it into water and oxygen molecules while producing the oxidized form of glutathione. This reaction occurs to maintain intracellular redox balance and provide defense against oxidative stress (4).

The glutathione peroxidase enzyme complex is especially abundant in tissues with intense oxygen metabolism, such as the liver, kidneys, and lungs (17, 31). Because these tissues constantly produce free radicals and reactive oxygen species, high levels of GPx and other antioxidant enzymes are critical for maintaining cellular integrity. GPx levels increase in situations of increased oxidative stress. This indicates the cell is strengthening its antioxidant defenses to deal with ROS and free radicals (29). GPx mainly interacts with GSH, selenium, and other cofactors. While GSH is a substrate for the GPx enzyme, selenium is a critical component at the enzyme's active site (17). The association between psychological stress and GPx activity can be attributed to elevated cellular oxidative stress levels by cortisol and other stress hormones, which modulate GPx enzyme activity. Chronic psychological stress may result in prolonged cortisol secretion and heightened oxidative stress (5,25). This condition enhances the production and activity of antioxidant enzymes such as GPx, protecting the cell against oxidative damage. However, under consistently high levels of oxidative stress, GPx and other antioxidant defense mechanisms can be depleted, potentially leading to cellular damage and various diseases (16). A study has shown that while mild stress does not change GPx levels, there is a dramatic increase in severe stress levels (28). In our study, it was found that while the CUMS model did not change serum GPx levels, there was a significant increase in liver tissue levels.

Malondialdehyde is generated through lipid peroxidation, representing a form of reactive aldehyde. Lipid peroxidation occurs due to free radicals oxidizing polyunsaturated fatty acids in the cell membrane. MDA is an end product of this process and can indicate oxidative stress in the cell (18). MDA is a marker of oxidative stress, and because it arises from the peroxidation of lipids in cell membranes, it tends to be higher in tissues rich in lipids, such as the liver, brain, heart, and kidneys. Elevated MDA levels indicate increased oxidative stress and lipid peroxidation within these tissues (32). MDA is a by-product of the lipid peroxidation of polyunsaturated fatty acids and serves as a reliable indicator of oxidative stress. Its accumulation can occur as a result of an increase in free radicals and ROS within cells. To form adducts, MDA can react with proteins, genetic material, glycoproteins, and other cellular components. These interactions can lead to cellular structure and function disruptions, contribute to cellular aging, and are implicated in the pathogenesis of various diseases due to the damage they cause to essential biomolecules (3, 19). It has been stated that various acute and chronic stress models, such as Restraint, immobilization, cold, and psychological stressors, cause an

increase in MDA levels (31, 32). There are studies where no change was observed depending on the stress model. For instance, in rats subjected to acute footshock stress, no change in MDA/Thiobarbituric acid reactivity was noted (28). The link between oxidative stress and idiopathic chronic fatigue has been investigated. While ROS and MDA increased significantly, antioxidant parameters, including total antioxidant activity and CAT, increased significantly (29). It was also found that levels in patients with inflammatory diseases and cancer were higher than in healthy controls (18, 19). In our study, although there was no change in the serum of the rats in the group in which the CUMS model was applied, a significant increase was detected in liver tissue levels. Chronic psychological stress can trigger the continuous release of stress hormones, raising cellular levels of ROS. This elevation stimulates lipid peroxidation and, consequently, MDA production. High levels of MDA indicate oxidative damage within cells and can reflect the damage caused by stress at the cellular level (29).

CONCLUSION

Chronic stress has the potential to modulate oxidative stress in the liver and activate antioxidant enzymes. This suggests that the antioxidant response may function as a potential adaptive mechanism to reduce the adverse effects of stress at the cellular level.

When comparing the levels of serum CAT, SOD, GPx, and MDA, no statistically significant difference was found between the control and stress groups ($P>0.05$). However, when comparing the liver tissue levels of CAT, SOD, GPx, and MDA, a significant difference was observed between the stress and control groups. CAT, SOD, GPx, and MDA levels were found to be increased in the liver tissues of rats belonging to the stress group.

Considering the widespread and profound effects of chronic psychological stress on the body, it is clear that this condition reduces the quality of life. Particularly, the increase in oxidative stress at the cellular level that it causes can pave the way for the development of various diseases. The study results could assist in better understanding the complex interactions between stress, free radicals, and antioxidants.

Ethics Committee Approval: The study has ethical approval from the Kocaeli University Animal Experiments Local Ethics Committee (Date: 26.07.2023, No: 6/4-2023)

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