International Journal of Computational and Experimental Science and ENgineering (IJCESEN)

Vol. 11-No.3 (2025) pp. 6843-6848
http://www.ijcesen.com

ISSN: 2149-9144

Research Article

Effect of Physıcal Therapy on Bıochemıcal Parameters in Female Patıents wıth Gonartrosıs

Aysel Güven[1*], Hacı Ahmet Deveci[2], Mustafa Gülşen[3], Esra Tekinyıldız[4]

[1]Baskent University, Vocational School Department of Pathology Laboratory, Ankara, Turkey.
* **Corresponding Author Email:** ayselguven@hotmail.com, **ORCID:** 0000-0002-3519-8497

[2]Gaziantep University, Faculty of Health Sciences, Department of Nutrition and Dietetics, Gaziantep, Turkey.
Email: h.ahmet_deveci@hotmail.com, **ORCID:** 0000-0002-5613-0520

[3]Baskent University, Vocational School of Health Services, Department of Therapy and Rehabilitation, Ankara, Turkey,
Email: mgulsen81@hotmail.com, **ORCID:** 0000- 0002-8826-8524

[4]Baskent University, Vocational School of Health Services, Program of First and Emergency Aid, Ankara, Turkey.
Email: esratekinyildiz@baskent.edu.tr, **ORCID:** 0000-0003-0195-9718

Article Info:

DOI: 10.22399/ijcesen.1451
Received : 30 March 2025
Accepted : 10 May 2025

Keywords

Gonarthrosis
physical therapy
lipid peroxidation
antioxidant
triglyceride

Abstract:

This study investigated the effects of hotpack, transcutaneous electrical nerve stimulation, ultrasound and home exercise program applied around the knee on blood lipid peroxidation system and antioxidant system in female patients with gonarthrosis.The group (n=32) underwent a hotpack, transcutaneous electrical nerve stimulation, ultrasound and home exercise. Sociodemographic and clinical characteristics of patients were recorded. Kan lipit peroksidasyon seviyeleri and total oxidant levels are measured with blood samples before and after treatment (4th week). A significant, positive, moderate level relationship (p=0.00) was found between reduced glutathione level and oxidative stress index level before physical therapy in female patients with gonarthrosis, and a statistically significant, negative, moderate level relationship was found between reduced glutathione level and paraoxonase activity level before physical therapy (p=0.03).No statistically significant difference was found between the reduced glutathione level and lipid peroxidation, high density lipoprotein, triglyceride and low-density lipoprotein levels of the participants (p>0.05). This will also contribute to the scientific literature by providing a new dimension that various physical therapy methods used in OA treatment can also be determined by monitoring biochemical parameters.

1. Introduction

Free radicals are electron-accepting molecules that can easily exchange electrons with other molecules, thereby damaging their structure. These active oxygen derivatives are called oxidants [1,2].Oxidants are structures that damage cell membranes, deoxyribonucleic acid (DNA), ribonucleic acid (RNA), and genetic material by stealing electrons from target molecules, and affect various enzymatic events [3].These disorders can lead to various clinical manifestations, including anemia, hemolysis, inflammation, and impaired oxygen-carrying capacity [4].In normal metabolism, there are antioxidant systems that reduce or eliminate the effects of these damages, and the ratio of oxidants to antioxidants is in a state of equilibrium. When the balance is disturbed in favor of free radicals, cellular damage occurs [5,6]. As in the pathogenesis of many diseases, free oxygen radicals (FOR) are the main factors in cartilage matrix degradation in knee osteoarthritis (gonarthrosis) [7,8]. Reactive oxygen derivatives (ROD) can break down proteoglycans in extracellular intermediates (ECI) or extracellular fluids and impair the mechanical properties of collagen. This can cause mechanical damage to the cartilage and changes in its water retention capacity [8-10]. Reduced tensile strength can be seen in cartilage with osteoarthritis (OA) associated with collagen fiber damage [11]. This damage in collagen fibers has been shown to originate from the

surroundings of chondrocytes. Although chondrocytes are said to be the source of ROD formation, there is limited knowledge about how ROD production is affected at low oxygen pressure levels [10,12].However, there are considerable studies indicating that lipid-derived oxidative stress may play a role in the development of osteoarthritis (OA) [6,10].At the same time, it is stated that FOR causes significant damage to the collagen structure in the knee region by causing deterioration in the structure of collagen hyaluronan and proteoglycan [13].It is thought that chondrocytes and synoviocytes in the joint are affected by oxidative stress and cause degradation of cartilage matrix and decrease in viscosity of synovial fluid [14].In the literature, the effectiveness of treatments in gonarthrosis is generally expressed with clinical studies and physical therapy methods [15,16]. Physical therapy (PT) is a widely used treatment method all over the world. Physical therapy uses electrotherapy agents, surface and deep heaters together. PT uses many treatment methods such as hotpack (HP), ultrasound (US), transcutaneous electrical nerve stimulation (TENS), short wave diathermy, and laser. Although the combination of these methods increases the effectiveness of treatment, the effectiveness of these methods is still [17,18]. For this reason, we aimed to contribute to the discussions by comparing the effect of PT on the pathogenesis of gonarthrosis with oxidative stress and lipid peroxidation and some biochemical parameters before and after treatment [19-21]. Thus, this study investigated both the disease mechanisms, lipid peroxidation, and antioxidant defense system in female cases with OA in the knee joint, as well as the effects of physical therapy on lipid peroxidation and the antioxidant system.The study's main finding is that physical therapy can reduce oxidative stress and lipid peroxidation in patients with gonarthrosis. This is an important finding, as oxidative stress and lipid peroxidation are thought to play a role in the development and progression of gonarthrosis.The study's limitations include its small sample size and the fact that it was conducted in a single center. Further research is needed to confirm the findings of this study and to determine the optimal dose and duration of physical therapy for the treatment of gonarthrosis.

2. Material and Methods

This study consisted of 32 female cases over 40 years of age who were diagnosed with knee OA by a specialist doctor and applied to Başkent University Ankara Hospital. After the cases participating in the study were medically examined by the specialist physician, the cases that were not an obstacle to be included in the study were graded according to the "Kellegren-Lawrence Staging Scale". Cases with Stage II and III were included in the study. Before the 10-session physical therapy program, the sociodemographic characteristics of the patients were recorded. The treatment program consisted of 20 minutes HP, 20 minutes TENS with a frequency range of 60-100 Hz, pulse duration of 60 and in a way that the patient will receive comfortable sensation, and 10 minutes continuous US (Enraf-Nonius-B Delftechpark 39; 1-MHz; 1.5 watt/cm2) around the knee along with a home exercise program to strengthen the muscles around the knee. Those who had acute inflammation in the knee joint, those who had undergone surgical operation in the knee joint for any reason or had a history of trauma in any lower extremity, those who had a history of uncontrolled hypertension, those who had any neurological or vestibular problem, those who had steroid injection use in the last two months, and those who had any systemic disease that would affect the study for any reason were excluded from the study.The Kellegren-Lawrence Staging Scale is a scale used to radiologically assess knee osteoarthritis (OA). The scale classifies the progression of knee OA into five stages, taking into account the formation of osteophytes on the joint surface, narrowing of the joint space, and loss of cartilage.

Stage 0: Normal knee joint.

Stage 1: Possibility of osteophytes. There is a possibility for the formation of osteophytes on the joint surface, but it is not certain.

Stage 2: Definite osteophytes, possible narrowing of the joint space. The formation of osteophytes on the joint surface is certain and there is a possibility of narrowing of the joint space.

Stage 3: Moderate osteophytes, definite narrowing. There is moderate osteophytes formation on the joint surface and the joint space is definitely narrowed.

Stage 4: Wide osteophytes, significant narrowing, sclerosis. There are wide osteophytes on the joint surface and the joint space is significantly narrowed. Cartilage loss is also present.

Biochemical analyses

The spectrophotometric method described by Placer et al. [22] was used to determine lipid peroxidation (MDA). Incubation of the upper organic layer with thiobarbituric acid (TBA) in an aerobic environment with a pH of 3.4 forms malondialdehyde (MDA), a secondary product of lipid peroxidation. The

resulting MDA forms a pink complex with TBA. Lipid peroxidation is detected by spectrophotometric measurement of the pink color at 532 nm. 10µl of 1, 1, 3, 3 tetraethoxypropane was taken for standard curve drawing. Then it was dissolved in 10 ml absolute ethanol and stored in a dark bottle at +4ºC. The spectrophotometric method described by Sedlak and Lindsay was used to determine GSH levels. The dissolution of the sulfhydryl group of GSH in acid and the measurement of the thiol group by enzymatic or chemical processes form the basis of the quantification of this compound. The determined absorbance values were calculated as µmol/ML from the GSH standard curve [23,24].Paraoxonase (PON1) activity measurement: PON1 activity measurement was performed according to the methods of Eckerson and colleagues and Gülcü and Gürsu. PON1 activity was determined by measuring the absorbance of the colored product formed by the enzymatic hydrolysis of paraoxon (Sigma Co, London, UK), which was used as a substrate, at 25°C and 412 nanometers in a spectrophotometer. For paraoxonase activity, the enzyme activity in 1 ml serum that converts 1 nmol paraoxon to 4-nitrophenol in 1 minute was defined as unit and the results were given as U/L. [25]. Oxidative Stress Index was calculated according to the following formula: OSI (Arbitrary Unit): TOS (µmol H_2O_2 equiv./L) / TAS (mmol Trolox eqiv./L[26]. Triglyceride, LDL (Low density lipoprotein) and HDL (High density lipoprotein) cholesterol levels were measured by Biotrol brand kit in autoanalyzer, LDL-cholesterol level was calculated according to Friedwold formula [27].

Statistical Analysis

Data were evaluated with SPSS (Statistical Package for the Social Sciences) for Windows version 25.0 (IBM Corp., Armonk, NY, USA). Frequency, percentage, mean and standard deviation (SD) were used to present categorical and continuous variables. In the intra-group comparison, the Shapiro Wilk test was applied by taking the difference between the measurements within the experimental and control groups. Paired sample t test was applied for those with normal distribution and Wilcoxon test for those without normal distribution. For comparison between groups, Shapiro Wilk test was applied to continuous data, independent sample t test was applied for those with normal distribution, and Mann Whitney U test was applied for those with non-normal distribution. The significance level was accepted as $p<0.05$.

Ethics statement

It was approved by Baskent University Institutional Review Board and Ethics Committee (Project no: KA23/328) and supported by Baskent University Research Fund. The study was conducted in accordance with the Helsinki Declaration of 1975. For the research, permission was obtained from the dialysis center where the study would be conducted. Written informed consent was obtained from the participants after a detailed explanation was given to the participants about the study.

3. Results

The average of sociodemographic characteristics and oxidative values of the patients included in the study are given in Table 1. It was determined that 50% of the patients were Grade 2, 59.38% had a history of the disease, and 59.38% also had a family history of the disease. It was determined that 56.25% of the patients included in the study did not work in any job and 59.37% did not do physical activity. It was determined that the weekly physical activity duration of the patients was 30.00±5.00 minutes, body mass index (BMI) was 30.25±4.60, age average was 59.71±11.90, height was 159.43±5.98 centimeters, and weight was 76.20±9.33 kilograms (Table 1). The comparison of some parameters before and after physical therapy in patients with gonarthrosis is given in Table 2.

Table 1. *Sociodemographic characteristics of the individual*s

Specifications		**n**	**%**
Grade	**2**	16	50.00
	3	16	50.00
Background	**illness**	19	59.38
	no illness	13	40.62
Family history	**illness**	19	59.38
	no illness	13	40.62
Working	**yes works**	14	43.75
	not working	18	56.25
Physical activity level	**yes**	13	40.63
	no	19	59.37

	X̄±SD	**Median (Min-Max)**
Physical activity duration in a week (minutes)	30.00±5.00	32.00(21.00-41.00)
BMI	30,25±4,60	31,83(21.20-40.72)
Age	59,71±11,90	59.00(40.00-90.00)
Height	159.43±5.98	160.00(148,00-174,00)
Weight	76.20±9.33	78.00(59.00-93.00)

n: number, X̄: mean, SD: standard deviation, min: minimum, max: maximum

Table 2. *Comparison of some parameters before and after physical therapy in patients with gonarthrosis*

Parameters		X̄±SD	t/Z	p
MDA	MDA-before	1.53±0.16	10.86*	**0.00**
	MDA-after	1.33±0.14		
GSH	GSH-before	8.05±0.86	-56.84*	**0.00**
	GSH-after	22.58±1.19		
OSİ	OSİ-before	0.53±0.08	-39.58*	**0.00**
	OSİ-after	1.71±0.21		
PON	PON-before	116.79±22.49	-19.90*	**0.00**
	PON-after	145.04±24.25		
HDL	HDL-before	43.84±1.20	0.45*	0.65
	HDL-after	43.77±0.87		
Trigliserit	Trigliserit-before	112.09±7.73	1.28*	0.20
	Triglisерit-after	110.59±3.62		
LDL	LDL-before	109.78±2.66	-2.11**	**0.03**
	LDL-after	110.80±1.50		

*X̄: mean, SD: standard deviation *Paired sample t test was performed; **Wilcoxon test was performed; p<0.05 is statistically significant; Z: Wilcoxon signed ranks test; t: Paired sample t test coefficient.*

GSH: µmol/L, MDA: µmol/L, PON: U/L, *OSİ* (*Arbitrary Birim*): TOS (µmol H_2O_2 equiv./L) / TAS (mmol Trolox eqiv./L), *HDL: mg/dl, LDL: mg/dl,* Trigliserit*: mg/dl*

A significant, positive, moderate relationship was found between the GSH level and OSI level of female patients with gonarthrosis before physical therapy (p = 0.00). A statistically significant, negative, moderate relationship was detected between the patients' GSH level and PON level before physical therapy (p = 0.03). No statistically significant difference was found between the participants' GSH level and MDA, HDL, Triglyceride and LDL levels (p>0.05)

4. Conclusion

Free radicals are generated in our body by several systems. A balance among free radicals and antioxidants is an important matter for appropriate physiological function [28]. Gonarthrosis, which is one of the most common joint arthroses affected by free radicals, is at the forefront of the structures affected by free radicals. In the literature, there are conflicting results about antioxidant levels in OA patients. Yılmaz et al. found nitric oxide (NO) and malondialdehyde levels significantly higher in the joint synovial fluid of the OA patient group. It has been stated that inflammatory agents affect NO and oxygen radical formation. Similarly, in another study, the role of ROD in knee OA pathogenesis was emphasized by stating that excessive production disrupts protein, lipid, nucleic acid and matrix structures [29]. It has been suggested that antioxidant treatments that prevent ROD formation or reduce oxidative stress may be effective in OA treatment [30]. In this study, lipid peroxidation and antioxidant defense system in the blood taken before and after treatment in patients with gonarthrosis were measured and compared by analyzing the role of the disease mechanism. In community health screenings, for the first time, physical therapy that can be used primarily to relieve pain, improve functional status and minimize possible deformities in patients with gonarthrosis who complain of pain, stiffness, instability and function loss was compared with biochemical oxidative stress and antioxidant levels [31]. In our study, a significant, positive, moderate level relationship was found between GSH level and OSI level before physical therapy in patients with gonarthrosis, and a statistically significant, negative, moderate level relationship was found between GSH level and PON level. No statistically significant difference was found between lipid peroxidation product malondialdehyde (MDA) and reduced glutathione (GSH) levels of free radicals. In addition, a positive relationship was found between GSH and OSI levels and GSH and triglyceride levels after treatment. This result suggests that it may be related to the applied treatment models.When the results of this study conducted with patients with gonarthrosis are reviewed collectively; It was observed that significant changes were obtained in almost all of the lipid peroxidation and antioxidant criteria with the treatment modalities applied after the treatment. This

will add a new dimension to the fact that various physical therapy methods used in the treatment of OA can be determined by monitoring biochemical parameters, and will also contribute to the scientific literature. Thus, further studies can be conducted on routine biochemical measurements of biochemical parameters as well as clinical criteria in order to evaluate the effectiveness of gonarthrosis treatment.

Author Statements:

- **Ethical approval:** The conducted research is not related to either human or animal use.
- **Conflict of interest:** The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper
- **Acknowledgement:** The authors declare that they have nobody or no-company to acknowledge.
- **Author contributions:** The authors declare that they have equal right on this paper.
- **Funding information:** The authors declare that there is no funding to be acknowledged.
- **Data availability statement:** The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

References

[1] Güven A, Nur G.Deveci H.A. Liver Injury Due to Chemıcal Poisoning and Antioxidant Defense System, Oxsidative Stres and Defanse System. Editör: Aysel Güven. Paris: Livre de Lyon; 2021

[2] Güven A, Güven A, Gülmez M. (2003). The Effect of Kefir on the Activities of GSH-Px, GST, CAT, GSH and LPO Levels in Carbon tetrachloride-Induced Mice Tissues. J. Vet. Med. B 50; 50(1):412-416.

[3] Özcan O, Erdal H, Çakırca G, Yönden Z. (2015). Oxidative stress and its effects on intracellular lipid, protein and DNA structures. Journal of Clinical and Experimental Investigations, 6(3), 331-336.

[4] Jakubczyk K, Dec K, Kałduńska J, Kawczuga D, Kochman J, Janda K. (2020). Reactive oxygen species - sources, functions, oxidative damage. Pol Merkur Lekarski. 22;48(284):124-127. PMID: 32352946.

[5] Güven A, Nur G, Deveci HA. (2019). The Effects of Green tea (Camellia sinensis L.) and Parsley (Petroselinum crispum) Diets on the Activities of GSH-Px, GST, CAT, GSH and LPO Levels in Mice Tissues. Parlar Scientiific publications, 28(9):6521-6527. https://www.researchgate.net/publication/337166886

[6] Fitowska A, Ostałowska A, Dobrakowski M, et al. (2012). Protein metabolism in the synovial membrane in the hip osteoarthritis.Pol Orthop Traumatol 11:77:21-6.

[7] Tudorachi, N. B., Totu, E. E., Fifere, A., Ardeleanu, V., Mocanu, V., Mircea, C., ... & Cărăuşu, E. M. (2021). The implication of reactive oxygen species and antioxidants in knee osteoarthritis. *Antioxidants*, *10*(6), 985.

[8] Hapeta B, Koczy B, Fitowska A, et al. (2012). Metabolism and protein transformations in synovial membrane of a knee joint in the course of rheumatoid arthritis and degenerative arthritis. Pol Orthop Traumatol 77:1-6. 17.

[9] Islam, M. T., Sarkar, C., Hossain, R., Bhuia, M. S., Mardare, I., Kulbayeva, M., ... & Cho, W. C. (2023). Therapeutic strategies for rheumatic diseases and disorders: targeting redox imbalance and oxidative stress. *Biomedicine & Pharmacotherapy*, *164*, 114900.

[10] Amirkhizi, F., Hamedi-Shahraki, S., & Rahimlou, M. (2023). Dietary total antioxidant capacity is associated with lower disease severity and inflammatory and oxidative stress biomarkers in patients with knee osteoarthritis. *Journal of Health, Population and Nutrition*, *42*(1), 104.

[11] Kural A, Kural C, Çetinus ME, Erçin E, Seval H, Koldaş M. (2014). Oxidative Stress in Osteoarthritis Cartilage; Comparative Study. Eur J Basic Med Sci. 4(3), 83-88.

[12] Hollander AP, Pidoux I, Reiner A, Rorabeck C, Bourne R, Poole AR. (1995). Damage to type II collagen in aging and osteoarthritis starts at the articular surface, originates around chondrocytes, and extends into the cartilage with progressive degeneration. J Clin Invest 96:2859–69.

[13] Atay T, Aslan A, Baydar M.L, Ceylan B, Baykal B, Kırdemir V. (2008). Comparison of viscosupplementation applications after arthroscopic debridement in patients with gonarthrosis. Acta Orthop et Traumatol Turc 42(4):228-33.

a. ? Aksoy, N. H., Caliskan, Z., & Ozdemirler, G. (2022). Plasma lipids, lipid peroxides and antioxidant system in osteoarthritic patients underwent spa therapy. *Medical Science and Discovery*, *9*(9), 495-500.

[14] Aslan A, Aydoğan NH, İlhan M, Özerdemoğlu RA, Altuntaş İ, & Yorgancıgil H. (2012). Effect of different intra-articular drug applications on

antioxidant system and lipid peroxidation in gonarthrosis. Gaziantep Medical Journal, 18(1), 1-6.

[15] Belcher C, Yaqub FNM, Fawthrop F et al. (1997). Synovial fluid chondroidin and keratan sulphate epitopes, glycosaminoglycans, and hyaluronan in arthritic and normal knees. Ann Rheum Dis. 56: 299–307.

[16] Nnoaham KE, Kumbang J. (2008). Transcutaneous electrical nerve stimulation (TENS) for chronic pain. Cochrane Database Syst Rev. 16(3), CD003222 doi: 10.1002/14651858.CD003222.pub2.

[17] Sarıfakıoğlu B, Yıldırım Güzelant A, Özduran E. (2014). Comparison of Short-Wave Diathermy and Ultrasound Treatment Efficacy in the Treatment of Gonarthrosis. Turk J Osteoporos. 20:16-20.

[18] Candeniz, Ş., Çitaker, S., Maraş, G., Yavuzer, H. E., Yildirim, H., & Günendi, Z. (2023). Comparison of the effectiveness of instrument-assisted soft tissue mobilization and extracorporeal shock wave therapy in myofascial pain syndrome. *Turkish Journal of Medical Sciences*, *53*(6), 1825-1839.

[19] Wu, T., Li, S., Ren, J., Wang, D., & Ai, Y. (2022). Efficacy of extracorporeal shock waves in the treatment of myofascial pain syndrome: a systematic review and meta-analysis of controlled clinical studies. *Annals of translational medicine*, *10*(4), 165.

[20] Toopchizadeh, V., Izadseresht, B., Eftekharsadat, B., Salehi-Pourmehr, H., & Dolati, S. (2024). Effectiveness of transcutaneous electrical nerve stimulation (TENS) modality for treating myofascial pain syndrome: A systematic review and meta-analysis. *Journal of Research in Clinical Medicine*, *12*(1), 14-14

[21] Filiz MB, Firat SC. (2018). Effects of Physical Therapy on Pain, Functional Status, Sagittal Spinal Alignment, and Spinal Mobility in Chronic Non-specific Low Back Pain. Eurasian J Med. 51(1):22–26. doi:10.5152/eurasianjmed.2018.18126.

[22] Placer ZA, Cushman LL, Johnson BC 1966 Anal Biochem. 16, 359-364

[23] Sedlak J, Lindsay RH. (1968). Anal Biochem. 25;192-205.

[24] Eckerson HW, Romson J, Wyte CM, La Du BN. (1983). The human serum paraoxonase polymorphism: Identification of phenotypes by their response to salts. Am. J. Hum. Genet 35, 214-227.

[25] Kösecik M, Erel O, Sevinc E, Selek S. (2005). Increased oxidative stress in children exposed to passive smoking. Int J Cardiol. 100, 61-64.

[26] Friedewald WT, Levy RI, Fredrickson DS (1972). Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the prepartive ultracentrifuge, Clin Chem, 18: 499- 505.

[27] Alkadi H. (2020). A review on free radicals and antioxidants. Infectious Disorders-Drug Targets (Formerly Current Drug Targets-Infectious Disorders), *20*(1), 16-26.

[28] Sutipornpalangkul W, Morales PN, Harnroongroj T. (2009). Free radicals in primary knee osteoarthritis.J Med Assoc Thai 92:268-71.

[29] Yılmaz E, Yılmaz S, Karakurt L, Serin E. (2004). Nitric oxide and malondialdehyde levels in osteoarthritis. Arthroplasty Arthroscopic Surgery Journal. 15(1):7-11.

[30] Sutipornpalangkul W, Morales PN, Harnroongroj T. (2009). Free radicals in primary knee osteoarthritis.J Med Assoc Thai 92:268-71.

[31] Aksoy, N. H., Caliskan, Z., & Ozdemirler, G. (2022). Plasma lipids, lipid peroxides and antioxidant system in osteoarthritic patients underwent spa therapy. *Medical Science and Discovery*, *9*(9), 495-500.