Serum Paraoksonaz (PON1) Üzerine Elektromanyetik Alanların Etkisinin Araştırılması

Investigation of The Effects of Electromagnetic Fields on Serum Paraoxonase (PON1)

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ÖZ

GİRİŞ ve AMAÇ: *Toplumda elektrikli cihazların yaygın olarak kullanılması ve bu cihazlarla yakın temas halinde olması hem endişeye hem de halk sağlığını etkilemektedir. Bu çalışmanın amacı, farklı günlerde yüksek gerilim kaynaklı elektromanyetik alan maruziyetinin, sıçanların serum paraoksanaz 1 aktivitesini etkileyip etkilemediğini araştırmaktır.*

YÖNTEM ve GEREÇLER: *Çalışma, ortalama olarak 320 gram ağırlığında 24 erişkin erkek wistar albino sıçanı içermektedir. Rasgele olarak 3 gruba ayrıldı (n: 8); Grup 1: Sham-kontrol, Grup 2: 26 gün Yüksek gerilim (YG) ve Grup 3: 52 gün YG. 26 günlük ve 52 günlük deney gruplarındaki (Grup I, II) farelere her gün 8 saat elektrik ve manyetik alan verildi*

BULGULAR: *Yirmi altı ve elli iki günlük yüksek gerilim maruziyet grubunda paraoksonaz (PON1) aktivitesinde kontrol grubuna göre bir azalma bulduk. Gruplar arasında ise istatistiksel olarak önemli (p<0.05) bir değişimin olduğu bulunmuştur.*

TARTIŞMA ve SONUÇ: *Çalışmamız yüksek gerilim hatlarına maruziyetlerin serum paraoksonaz 1 aktivitesinde bir azalmaya neden olabileceğini belirtmektedir. Kısa dönem maruziyetlerin uzun dönem maruziyetlerle karşılaştırılmasında paraoksonaz 1 aktivitesinde kısa dönemde bir azalmaya yol açabileceğini fark ettik. Bu nedenle çalışmamız bu konuda daha fazla araştırmanın önemine de işaret etmektedir.*

Anahtar Kelimeler: : *Elektromanyetik alan, Oldukça düşük frekans, Yüksek gerilim, Paraoksonaz (PON1)*

ABSTRACT

INTRODUCTION: *The widespread use of electrical devices in the society and being in close contact with these devices cause both anxiety and affect public health. The aim of this study is to investigate whether high voltage induced electromagnetic field exposure on different days affects serum paraoxanase 1 activity of rats.*

METHODS: *The study included 24 adult male wistar albino rats, weighing 320 grams on average. They were randomly grouped into 3 as n: 8. Group 1: Sham-control, Group 2: 26 days High voltage (HV) and Group 3: 52 days HV. The rats in the 26-day and 52-day experimental groups (Groups I, II) received electric and magnetic fields for 8 hours each day.*

RESULTS: *We found a decrease in paraoxonase (PON1) activity in the 26- and 52-day high-voltage exposure group compared to the control group. A statistically significant (p=0.000) change was found between the groups.*

DISCUSSION AND CONCLUSION: *:Our study suggests that the exposure to high voltage line may cause a reduction of paraoxonase 1 activity. We've noticed that short-term exposures, compared to long-term ones, may lead to lower paraoxonase 1 activity. Therefore, our study also points to the importance of further research in this regard.*

Keywords: *Electromagnetic field, Extremely low frequency, High voltage, Paraoxanase (PON1)*

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INTRODUCTION

Electric and magnetic fields interact with human biological systems. For this reason, people exposed to these areas will be at risk because of increased environmental pollution (1). People are constantly interacting with the electromagnetic waves we use in routine life and the waves of electromagnetic fields that surround us. Although these effects are still not fully determined, the interaction between electromagnetic fields depends on the power of the energy source, the transition parameter, and the type of texture (2). Researchers in most countries continue to work on the possible effects of electromagnetic fields. Since these mechanisms of interaction are not fully known, only a few studies have suggested that these areas may cause lipid peroxidation and free radical formation (3). Studies with very low frequency electromagnetic fields (ELF-EMF) have indicated that there is an increase in the level of reactive oxygen species in most people and, in part, a decrease in the level of reactive oxygen species in some studies (4). Antioxidant supplementation to the cell is recommended because of the increase of reactive oxygen species in the cell. It is predicted that in case of excessive increase, it can negatively affect human health (5). Paraoxonase shows a parallel change with total antioxidant level (6). In the human body, chromosome 7, which the localizer in q21-22 paraoxonase multigene family of PON-1, PON-2 and PON-3 is composed of three members of the so-called (7). Paraoxonase is evaluated for different activities (lipid oxidation, enzymatic and antioxidant effects). PON1 protein consists of 354 amino acids with molecular mass 43 kDa (8). In the formation of lipid peroxidation in the cell, paraoxonase plays an important role in the protection of high and low density lipoprotein particles (9). Serum paraoxonase is a test used for analyzes of liver enzyme activities and against oxidative damage and provides an easy, cheap, fast, reliable result (10). ELF- EMFs affect the antioxidant protection system of cells, which counteract oxidative harm; therefore, DNA damage can more readily occur, producing a carcinogenic effect (11,12). When the plasma of individuals exposed to occupational electromagnetic field exposure from high voltage transformer substations for more than 2 years is examined, it is reported that it may cause DNA damage and increased oxidative stress (13).

Increasing electromagnetic fields are causing concern about oxidative stress and antioxidant balance. It was necessary to work because there was a few work on the relationship of the electromagnetic fields to paraoxonase. Paraoxonase (PON1) has been chosen because it act a significant role in assessing both oxidative stress and antioxidant balance. Therefore, in the present study, we aimed to explore serum paraoxonase (PON1) in rats exposed to electromagnetic field originating from high voltage line.

MATERIAL AND METHODS

Experimental protocol

This work was carried out with permission of Medical Faculty Ethics Committee (Dicle University (Diyarbakır, Turkey) animal experiments local ethics committee - DUHADEK:2013/13) and the Research and Applications Centre of Dicle University Prof. Dr Sabahattin Payzın Healthcare Units. This work continued according to ethical standards organized by the Helsinki Declaration. The study included 24 adult male wistar albino rats, weighing 320 grams on average. After a one-week adaptation period, they were randomly grouped into 3 as n:8. Group 1: Sham-control, Group 2: 26 days HV and Group 3: 52 days HV. All animals were kept in suitable environmental conditions (constant temperature of 23±1 ºC and 45-55 % humidity of the air), 12 hours of night and 12 hours of light daylight, respectively, normal food (ad-libitum) and water was always available in the animals' cage. To create electromagnetic fields, two transformers that produced 10 kiloVolt (10,000 V) of high voltage were used. For the first transformer, the input was 220 Volt, and the output was 10 kiloVolt. For the second transformer, the input was 10 kiloVolt, and the output was 220 Volt and 5,000 Volt Amper (in see Figure 1). The rats in the 26-day and 52-day experimental groups (Groups I, II) received electric and magnetic fields for 8 hours each day. Electromagnetic field densities were measured as electric field (80.3 V/m) and magnetic field (2.48 μT), respectively. The arithmetic average of ten measurements taken daily was used to determine the area densities. The electromagnetic field was measured by the aid of a Spectran device NF5035 (AARONIA AG, Strickscheid, Germany), with reference to the method of 6-minute measurement the International Commission on Non-Ionizing Radiation Protection (ICNIRP).

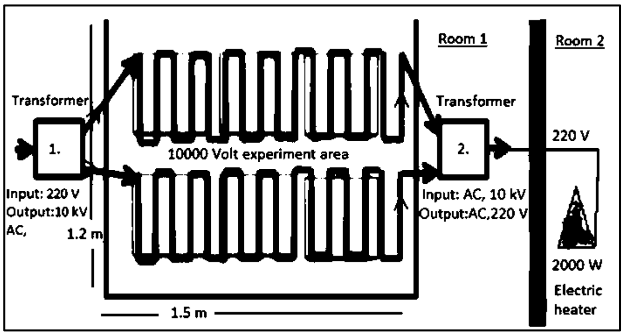

Figure 1. *The experimental design*

Biochemical analyses

Blood collection and storage

At the end of the work, the rats were anesthetized. Then, the blood of the rats from the intracardiac route was collected. Blood samples from control and experimental group of animals were collected (BD Vacutainer 5.0 ml, UK). Serum was separated directly by centrifugation (NF 1200 R Nuve, Turkey) at 5000 rpm for 5 minute and were kept at -20ºC until the analysis.

Paraoxonase measurement

Paraoxonase 1 blood serum values of the rats (U/L) were measured spectrophotometrically (PON1; Product Code: RL0031, Rel Assay® Kits, Turkey). An automated analyzer method was applied for the analysis of the data (Abbott Architect® c16000). Two different reagents were used by the autoanalyzer and the result was analyzed at 412 nm absorbance (14,15)

Statistical analyses

According to Levene homogeneity test, group variances were homogeneous (Levene statistics value is 0.621; p=0.547). The Shapiro-Wilk Normality Test was used to determine whether our data fit the normal distribution. Our data were analyzed by one way ANOVA because normal distribution was appropriate. A statistically significant difference was found between the groups as a result of one way ANOVA. The Bonferroni test, which is a binary comparison test, was used to determine which group this difference originated from. The results were evaluated as mean and standard deviation. p<0.05 was considered statistically significant. A statistical analysis was performed with Windows SPSS 21.0. (IBM SPSS Statistics for Windows, Version 21.0, Armonk, NY: IBM Corp., USA).

RESULTS

In the final phase of the study the average paraoxonase 1 serum values of the experiment and the control groups were compared. A primary finding of our study, which involved exposure to high voltage, shows that the paraoxonase 1 values of the 26-day and 52-day application groups decreased compared to the control groups, which resulted in a significant change between the groups (p<0.05). (in see Table 1, Table 2 and Figure 2) As a result of the analysis of our study, the average of the control group was found to be significantly higher than the average of the other groups.

Table 1. *Biochemical analysis results from serum PON1 from control group male rat and experimental group male rats. Data are presented as mean ± SD, median, minimum and maximum values.*

Groups	Mean ± SD	Median	Min	Max	P
Group 1 (Control)	108,36±16,22	108,33	84,25	141,49	P=0.000
Group 2 (26 day HV)	79,95±07,41	76,96	72,80	90,23	<0.05
Group 3 (52 day HV)	89,48±10,29	85,95	83,43	114,37	

One-way analysis of variance revealed that p <0.05 was considered statistically significant among the groups.

Table 2. *Pairwise comparison, Bonferroni test results *(p<0.05, **p>0.05)*

Groups	Group 1-Group 2	Group 1-Group 3	Group 2- Group 3
P-value	0.000*	0.014*	0.372**

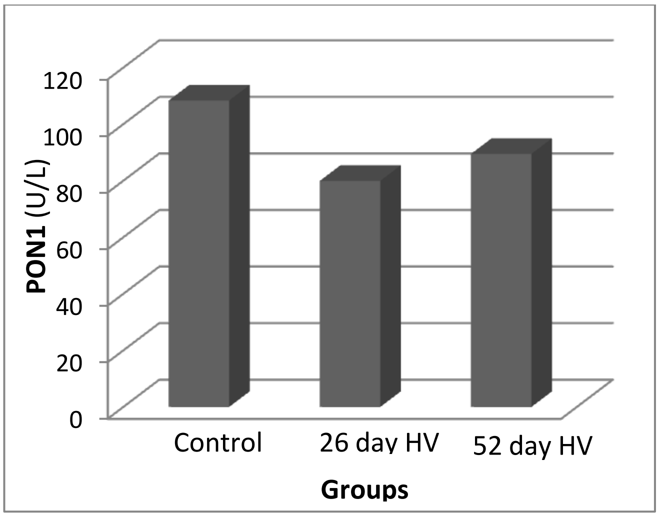

Figure 2. *The concentrations of some serum PON1 in rats exposed to the experimental groups and the control group.*

The Bonferroni test was used to determine which group resulted in a significant difference between the groups. For this reason, a statistically significant difference was found between Group 1 and Group 2 (P=0.00). A statistically significant difference was found between Group 1 and Group 3 (P=0.01). There was no statistically significant difference between Group 2 and Group 3 (P=0.37).

DISCUSSION

ELF-MF exposure may disrupt the antioxidant and oxidant balance and this disruptive effect depends on the duration and dose of administration. Static and electromagnetic fields in vitro have been reported to affect paraoxonase 1 activity (16). When ELF-EMF was administered, the researchers stated that the level of paraoxonase was lower in the experimental group than in the control group (17). Findings in our study are parellel to previous studies. Similar findings were found.

Extremely low frequency (ELF) magnetic field exposures produce oxidative stress which is harmful to the cell by changing the antioxidant and oxidant balance. The antioxidant capacity varies depending on the duration and persistence of these attacks (ELF-MF) (6). Researchers have followed a fall in the level of serum paraoxonase trauma patients. This situation may be the result of oxidative damage (18). Paraoxonase, antimicrobial, anti-diabetic, anti-oxidative and anti-inflammatory effects are reported by researchers (19). Human serum PON1 esterase enzymes that have lipophilic antioxidant features. This enzymes play a role in reducing oxidative tension. PON1, in particular, is an significant endogenous free radical scavenging system in humans (20,21). In the study performed by Çakır and his colleagues, they left 50 and 100 days of very low frequency electromagnetic field exposure on rats for 3 hours daily. As a result, they stated that the time of increased exposure caused a significant decrease in the mean platelet volume (22). Electromagnetic fields can have many effects on the cell. These can be counted as ionic changes from molecular distortions in the cell (23). Researchers have suggested that these areas may increase apoptosis and lipid peroxidation in studies of the electromagnetic field on the rat heart (24). The acute effects of these areas have provided some evidence that rats cause a sensation in their brains. It has been assumed that the antioxidant balance in the brain of very low frequency electromagnetic fields may have changed (25). Nevertheless, there was some works, the results of the current study showed that ELF magnetic fields do not affect the histology of some organs, their lipid peroxidation, p53 immunoreactivity, sperm counts, and some trace elements (except Mn2+) in rats (26). Researchers have noted that long-term, very low-frequency magnetic field exposures do not alter apoptosis, and 100 and 500 µT ELF MF exposures may cause toxic effects in the brain as they reduce antioxidant balance and increase oxidative stress (27). We observed that our work may alter the paraoxonase 1 activity as a result of the formation of oxidative damage due to the effect of the electromagnetic field created in the environment. In our study, 26 and 52-day exposures were found to show a statistically significant change in comparison with control groups.

One of the limitations of our current study is that the high voltage value is not high and the other limitation is the evaluation of only one parameter.

Serum paraoxonase value varies with the increase of oxidative damage. In our study it is consistent with these findings. As a corollary, our study suggests that the exposure to ELF-EMF produced by the high voltage line may cause a decrease in paraoxonase 1 activity. Such kind of a change may be related with the increase that the electromagnetic field caused in oxidative stress. We've noticed that short-term exposures, compared to long-term ones, may lead to lower paraoxonase 1 activity. Our study shows that electromagnetic fields, which are formed by high-voltage lines, can change the paraoxonase activity and that more detailed work on this field is needed.

Annotation: This study was presented as a poster at the congress 6th World congress of oxidative stress, calcium signaling and TRP channels, Isparta, Turkey, 2016

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REFERENCES

1. Morabito C, Steimberg N, Rovetta F, Boniotti J, Guarnieri S, Mazzoleni G, et al. Extremely low-frequency electromagnetic fields affect myogenic processes in C2C12 myoblasts: role of gap-junction-mediated intercellular communication. BioMed Res Int. 2017;2017:2460215.

2. Wdowiak A, Mazurek PA, Wdowiak A, Bojar I. Effect of electromagnetic waves on human reproduction. Ann Agric Environ Med. 2017;24(1):13-18.

3. Khaki AA, Zarrintan S, Khaki A, Zahedi A. The effects of electromagnetic field on the microstructure of seminal vesicles in rat: a light and transmission electron microscope study. Pak J Biol Sci. 2008;11(5):692-701.

4. Wang H. and Zhang X. Magnetic fields and reactive oxygen species, Int J Mol Sci. 2017;18(10):2175.

5. Poprac P, Jomova K, Simunkova M, Kollar V, Rhodes CJ, Valko M. Targeting free radicals in oxidative stress-related human diseases. Trends Pharmacol Sci. 2017;38(7):592-607

6. Seifirad S, Farzampour S, Nourbakhsh M, et al. ELF-EMF on PON1 serum activity and lipid peroxidation metabolites in rat. J Diabetes Metab Disord. 2014;13:85.

7. Kowalska K, Socha E and Milnerocwicz H. The role of paraoxonase in cardiovascular diseases. Ann Clin Lab Sci. 2015;45(2):226-233.

8. Litvinov D, Mahini H. and Garelnabi M. Antioxidant and anti-inflammatory role of PON1: implication in arteriosclerosis diseases. N Am J Med Sci. 2012;4(11):523–532.

9. Memişoğulları R. and Orhan N. Paraoxonase and cancer, e-ISSN1309-3878 Konuralp Medical Journal. 2010;2(2):22-26.

10. Ferré N, Camps J, Prats E, Vilella E, Paul A, Figuera L, et al. Serum Paraoxonase activity: a new additional test for the improved evaluation of chronic liver damage. Clin Chem. 2002;48(2):261-268.

11. Wolf FI, Torsello A, Tedesco B, et al. 50-Hz extremely low frequency electromagnetic fields enhance cell proliferation and DNA damage: possible involvement of a redox mechanism. Biochim Biophys Acta. 2005;1743(1-2):120-129.

12. Focke F, Schuermann D, Kuster N, et al. DNA fragmentation in human fibroblasts under extremely low frequency electromagnetic field exposure. Mutat Res. 2010;683(1-2):74-83.

13. Tiwari R, Lakshmi NK, Bhargava SC, & Ahuja YR. Epinephrine, DNA integrity and oxidative stress in workers exposed to extremely low-frequency electromagnetic fields (ELF-EMFs) at 132 kV substations. Electromagn Biol Med. 2015;34(1):56-62.

14. Selek S, Coşar N, Koçyiğit A. et al. PON1 activity and total axidant status in patients with active pulmonary tuberculosis. Clin Chem. 2008;41:140-144.

15. Aslan M, Nazligul Y, Horoz M, et al. Serum paraoxonase-1 activity in Helicobacter pylori infected subjects. Atherosclerosis. 2008;196:270-274.

16. Abdi S. Effects of static and electromagnetic fields on human serum paraoxonase-1 activity in vitro. J Bas Res Med Sci 2018;5(2):21-26.

17. Çelik MS, Akpolat V, Işık B, Çelik MY, Yavaş MC. et al. ELF-EMF on serum PON1 and MDA levels, Int Arch Med. 2014;6(1):1-4.

18. Korkmaz İ. et al. The relationship between oxidative stress, paraoxanase and injury severity in blunt trauma patients, J Clin Anal Med. 2013;4(3):196-9.

19. Aggarwal G. et al. Toward understanding the catalytic mechanism of human paraoxonase 1: site-specific mutagenesis at position 192. PLoS ONE. 2016;11(2).

20. Bodolay E, Seres I, Szodoray P, et al. Evaluation of paraoxonase activity in patients with mixed connective tissue disease. J Rheumatol. 2008;35:237-43.

21. Erdem FH, Karatay S, Yıldırım K, et al. Evaluation of serum paraoxonase and arylesterase activities in ankylosing spondylitis patients. Clinics (Sao Paulo). 2010;65:175-9.

22. Çakir DU, Yokuş B, Akdağ MZ. et al. Alterations of hematological variations in rats exposed to extremely low frequency magnetic fields (50 Hz), Arch Med Res. 2009;4:352-356.

23. Kıvrak EG, Yurt KB, Kaplan AH. et al. Effects of electromagnetic fields exposure on the antioxidant defense system. Journal of Microscopy and Ultrastructure. 2017;5(4):167-176.

24. Kiray A, Tayefi H, Kiray M, et al. The effects of exposure to electromagnetic field on rat myocardium. Toxicol Ind Health. 2013; 29: 418-425.

25. Koylu O, Gürbilek M, Çiçekbaşı AE, et al. The effects of electromagnetic fields on the level of MDA that's known as A carsinogenic compound, in the rats' brain tissue and plasma. Journal of Turkish Clinical Biochemistry. 2005;3(1):027-033.

26. Akdağ MZ, Dasdağ S, Akşen F. et al. Effect of ELF magnetic fields on lipid peroxidation, sperm count, p53, and trace elements. Med Sci Monit. 2006;12(11):366-371.

27. Akdag MZ, Dasdag S, Ulukaya E, et al. Effects of extremely low-frequency magnetic field on caspase activities and oxidative stress values in rat brain. Biol Trace Elem Res. 2010;138:238-249