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INHIBITORY EFFECT OF CELL PHONES AGAINST HUMAN BREAST CANCER AND MYELOID LEUKEMIA CELLS GROWTH IN CULTURE MEDIA

KÜLTÜR ORTAMINDA İNSAN MEME KANSERİ VE MİYELOİD LÖSEMİ HÜCRELERİNİN PROLİFERASYONUNA KARŞI CEP TELEFONLARININ İNHİBİTÖR ETKİSİ

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Abstract

Objective: There is current news that emerges regarding the relationship between the magnetic effects of cell phones and some types of cancer. In spite of the studies carried out, the level of evidence of this news is low, and also the relationship between the magnetic effects of cell phones and other types of cancer is not certain except for brain cancer. In this study, it is aimed to examinethe effects of magnetic field of cell phones on the samples of breast cancer human myeloid leukemia cell growth.

Methods: In the study, breast cancer MCF-7 and leukemia K562 cell lines were used as the source of cancer cells. During the six-day cell culture, cancer cells were subjected to the effects of cell phone by using a telephone call program (Automated outbound call software). The system made 6 calls for 1 minute for each call once in 144 minutes from a fixed line. The number of cultured cells and proliferation capacities of the two types of tumor cells in the control and experimental groups were assessed.

Results: The number of cancer cells, which were subjected to the effects of cell phone as a result of the culture of tumor cells, was found lower when compared with control group (7500000 ± 100000 vs 6625000 ± 225000 for MCF-7; 15412500 ± 112500 vs 13700000 ± 250000 for K562; $P < 0.05$ for both). In MTT test, it was found out that two types of cell proliferation were inclined to slow down with the effect of cell phone.

Conclusion: The results can be translated that cell phone may inhibit neoplastic transformation, and this observation may promote to initiate new clinical studies both for healthy people and for patients with cancer.

Keywords: Cancer cells, Magnetic fields, Cell phone, Proliferation

Öz

Amaç: Cep telefonlarının manyetik etkileri ile bazı kanser türleri arasındaki ilişkiye dair güncel haberler bulunmaktadır. Yapılan araştırmalara rağmen bunların kanıt düzeyi düşüktür. Ayrıca cep telefonlarının manyetik etkilerinin beyin kanseri dışında diğer kanser türleri ile ilişkisi kesin değildir. Bu çalışmada, insan meme kanseri ve miyeloid lösemi hücre örneklerinin proliferasyonu üzerinde cep telefonlarının manyetik alanının etkilerinin incelenmesi amaçlanmıştır.

Yöntem: Çalışmada kanser hücresi kaynağı olarak meme kanseri MCF-7 ve lösemi K562 hücre dizileri kullanıldı. Altı günlük hücre kültürü sırasında kanser hücreleri, bir telefon arama programı (otomatik giden arama yazılımı) kullanılarak cep telefonunun etkilerine maruz bırakıldı. Sistem sabit hattan 144 dakikada bir her aramada 1'er dakika süreyle 6 arama yaptı. Kontrol ve deney gruplarındaki iki tip tümör hücresinin kültürlenen hücre sayısı ve çoğalma kapasiteleri değerlendirildi.

Bulgular: Tümör hücrelerinin kültürü sonucunda cep telefonu etkisine maruz kalan kanser hücrelerinin sayısı kontrol grubuna göre daha düşük bulundu (7500000 ± 100000 vs 6625000 ± 225000 MCF-7 için; 15412500 ± K562 için 112500 vs 13700000 ± 250000; her ikisi için $P < 0,05$). MTT testinde iki tip hücre çoğalmasının cep telefonunun etkisiyle yavaşlamaya meyilli olduğu tespit edildi.

Sonuç: Sonuçlar, cep telefonunun neoplastik dönüşümü engelleyebileceği şeklinde tercüme edilebilir ve bu gözlem hem sağlıklı insanlar hem de kanserli hastalar için yeni bir klinik çalışma başlatmayı teşvik edebilir.

Anahtar Kelimeler: Kanser Hücreleri, Manyetik Alan, Cep telefonu, Proliferasyon

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Introduction

With a view to maintain life in a healthy way, there should be a balance between the reproduction and death of the human cells that form the living being. During life, some cells assign their duties to some other cells. The cells that should die according to genetic programming are destroyed in a certain order.[1] To set an example for cell death during natural course of life, it can be assumed as the disappearance of some structures, which emerge while the living being is growing mature in ovum or mother's womb, in maturation process. To give another example, cell death might be the disappearance of overstimulated immune cells to avoid damaging familiar cells.[2-4]

As a result of the stimulus such as hormones, some chemical substances and radiations coming from environment when the natural course continues, DNA damage can occur in cells. If the cell cannot repair DNA damage, the cells carrying abnormal characters disappear in a programmed way (apoptosis). In this way, hazardous possibilities such as the spread of damaged cells and cancer genesis are prevented.[4,5]

There is a weak side of the cells that have the potential of fast reproduction and accelerated cycle. This weak point is that they are quite sensitive to environmental effects. These environmental effects can cause abnormal maturation of cells and deviations in their differentiation processes. These deviations result in some unwanted events such as disabilities, damages in tissues and organs, and genetic diseases.[6,7]

Some technological devices such as cell phone, which have been ever increasingly produced and used in recent years, result in electro-magnetic pollution by producing electro-magnetic waves. The observations and studies carried out up until now indicate that electro-magnetic waves may increase the frequency of brain cancer formation.[6,8] However, the effects of electro-magnetic waves on the other types of cancer are not certain. The possible effects of electro-magnetic waves on cells were also examined in laboratory environment; however, the effects of electro-magnetic waves on cancer cells are limited.[9-11] The observations should be supported with sufficient laboratory studies. In the first instance, knowing these effects can make people more sensitive regarding the protection of people from magnetic effects. Also, it can shed light on the formation mechanisms of some types of cancer and draw the attention of patients receiving cancer treatment.

In this study, it was aimed to examine the effect of cell phones on the growth of cancer cells of different embryonic layers, epidermal and mesenchymal origin in culture, and thus at drawing the attention on both fast-dividing cells demonstrating malign character.

Methods

Study design

The study was planned as an experimental study and carried out in the Hematology Research Laboratory, Başkent University Adana Turgut Noyan Application and Research Center. In the study, breast cancer cells were used as an example for the cancer cell of epidermal origin, while human myeloid leukemia cells were used as an example for the cancer cells of mesenchyma layer origin. The K562 (German Collection of Microorganisms and Cell Cultures (Braunschweig, Germany) cell line was obtained for our previous studies and stored in the freezer was also used for this study. The MCF cell line was obtained from the Ministry of Agriculture and Forestry Alum Institute. The samples of both types of cancer cells were cultured into six cell culture plaques. Three of these plaques were subjected to the magnetic field of cell phone during the cell culture, while the other three were set as control plaques. In this way, study groups with three plaques were constituted.[12]

After six-days cancer cell culture and before applying 3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide (MTT) test used to determine cytotoxicity/cell viability, culture plaques were monitorized in inverted microscope (Nikon EclipseT100, Tokyo, Japan) when they were viable. After then, MTT test was conducted and the proliferation capacities of the cells in each culture plaque were observed.[13] And then, the number of cells present in each plaque and similarly the condition of viability of the cells were analyzed.

Cell Culture

RPMI-1640 (Stem Cell Technology, Vancouver, Canada) was used as the medium for the cultures. 10% fetal bovine serum, L-glutamine and antibiotic were added into feed lot. The cells frozen for the culture were resolved in water bath at a temperature of 37°C and prepared for the culture. After the count, cell solutions were transferred to 75 cm^2 culture flasks (BD, Le Ponte d'claix, France) as 100.000 cell/10 mL. The culture flasks incubated in environment with 5% CO2, 95% moisture and at temperature of 37 °C for 6 days. The process mentioned above was performed with control groups first, repeated for experimental groups with cell phone after. 1 mL sample (after trypsinization for MCF-7) was taken from the plaque on the last day of the culture for control and experimental groups and this sample was used for cell count and viability.[13,14]

Cell Count, Viability Test and MTT Test

By taking 10 µL of the obtained cell solution, the cells were counted under the light microscope (Olympus BX51, Tokyo, Japan) using the Thoma cell counting chamber (Arat et al., 2008). Acridine Orange (Sigma, A6014, Germany) viability assay was used to measure the viability of cells. Examined under a fluorescent microscope (Nikon, Eclipse E600, Tokyo, Japan). Green cells were considered viable, while orange cells were considered dead.

In the MTT test, 5000 cells/100 microliter per well were seeded in 96-well culture plates for each group. Control groups of both cell lines were analyzed first, and then test groups with mobile phone were analyzed. Culture plates were incubated for 96 hours at 5% CO2, 95% humidity and 37 °C. At the end of the experiment 10 µL (5 mg/mL

concentration) MTT solution for each was added into all of these wells. It was left for incubation of four hours again. In the end of incubation, DMSO was added into each well and left for incubation in the mixer for 15 minutes. And then, it was read in plate ELISA reader at a wavelength of 570 nm (reference wavelength is 630 nm).[13]

Creating Electromagnetic Effect

In order to create electromagnetic field during the study, the relationship between human being and cell phone was imitated. To this end, 1800 MHz GSM (Vodafone, Hong-Kong, China) device used frequently among people was used. The cell phone was placed in carbon dioxide incubator, in which cell culture was carried out, in a way that it can have contact with culture plaques.

With a view to provide standard calls, a fixed telecom line connected with a computer and analog modem was used. In the project, 6 calls for 1 minute for each, once in 144 minutes were made from fixed line in order to obtain data and use the cell phone (GSM; global system for mobile communication) device in the call process through "Automated Outbound Call Software" present in the web site titled "http://www.nch.com.au/ivm/outbound.html". The calls were recorded.

The cell phone was charged every morning between 8.00 o'clock and 9.00 o'clock. If it is considered that the cells caught infection during the culture of the tumor cells (according to their appearance and smell), these cells would be excluded from the study. It was also planned that if there is any difficulty in measurements and analyses technically, the study would be repeated. With a view to carry out the project, permission was received from Başkent University Adana Application and Research Center Directorate.

Statistical Analysis

In the statistical analysis of data, GraphPad Prism vs 9.0.0 (GraphPad Software, San Diego, CA, USA) program was used. The effect of the cell phone in study groups that contained both types of tumor cells was assessed by noting the number of cells obtained after the culture and their values read in ELİSA device and the percentages of viable cells. Student's t test was used in comparing the continuous measurements between the groups. A value of $p < 0.05$ was considered statistically significant.

Results

Cells of a million were initially seeded in each culture flask. Adequate growth was observed after 6 days in cell cultures generated with control groups and experimental groups of cell lines. Technical problems such as color change and odor did not occur in the culture plates.

Table 1 and Figure 1 shows the number of cells obtained after cell culture in control and test groups. The number of cells, which were subjected to the effects of cell phone as a result of the culture of tumor cells, was found lower when compared with the control group. This difference was found statistically significant both for MCF-7 breast cancer cells and K562 leukemia cells (7500000 ± 100000 vs 6625000 ± 225000 for MCF-7; 15412500 ± 112500 vs 13700000 ± 250000 for K562; $P < 0.05$ for both).

Table 1. The number of cells obtained after cell culture in control and experimental groups

Study groups		Number of Cells Day 6	
		MCF-7	K562
Control	N	3	3
	SD	100000	112500
	Median	7500000	15412500
	Bottom	7400000	15300000
	Top	7600000	15525000
Test Groups	N	3	3
	SD	225000	250000
	Median	6625000	13700000
	Bottom	6400000	13450000
	Top	6850000	13950000
	P value	0.0035	0.0004

In spite of the difference in the number of cells, the viability rates in control and experimental groups did not change (94.3±0.6 % for control group; 95.6±0.6 % for experimental group, $p > 0.05$). Table 2 and Figure 2 show the proliferative capacity of the cells cured in control and experimental groups which were exposed to MTT test.

Examining the absorption values of the samples which were taken from wells by carrying out MTT test in culture plaques and read in ELISA, it was determined that as a result of they were subjected to the effects of cell phones in the culture environment, the proliferative capacities of both MCF-7 breast cancer cells and K562 leukemia cells were inclined to be lower when compared to the controls. However, this difference was statistically significant only for K562 cells ($p< 0.05$).

Table 2. The proliferative capacity of the cells cured in control and experimental groups which were exposed to MTT test

Study groups		% Proliferation	
		MCF-7	K562
Control	N	3	3
	SD	3,781	3,392
	Median	100	100
	Bottom	96,22	96,61
	Top	103,8	103,4
Test Groups	N	3	3
	SD	0.9778	2.056
	Median	94.98	93.32
	Bottom	94	91.26
	Top	95.96	95.38
	P value	0.09	0.043

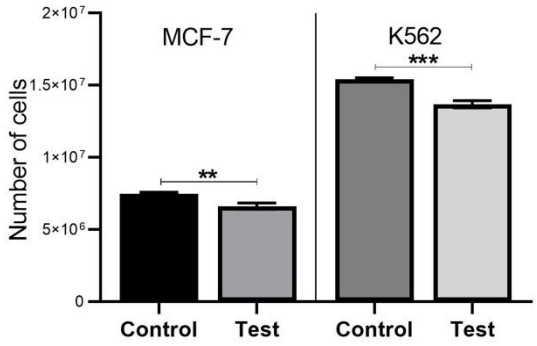

Figure 1. The number of cells obtained after cell culture in control and experimental groups

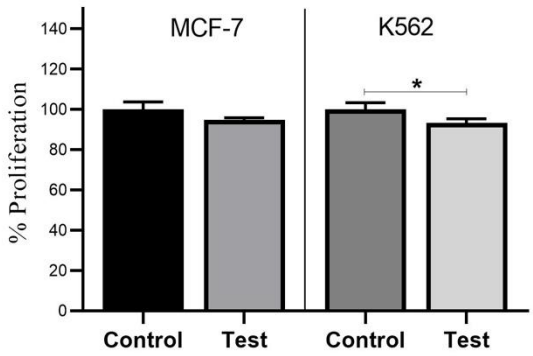

Figure 2. The proliferative capacity of the cells cured in control and experimental groups which were exposed to MTT test

Discussion

Each living being might be damaged as a result of the environmental effects in the place it is present. Chemical effects such as pesticides, roughly, biological effects such as microbes and physical effects such as accidents can be counted among these effects. With the developments in technology, the importance of electromagnetic pollution among these physical effects is gradually increasing day by day. And cell phones have been the technological devices which produce magnetic pollution and commonly used among people. They have become an integral part of daily life.[10,15]

There is much news of media, newspapers in particular, regarding the harmful effects of cell phones on human health.[9-11] The most important of this news in scientific terms can be counted as the INTERPHONE study which includes 5115 people with the participation of 13 countries.[16] Brain cells are the cells that have slow proliferative capacity and thus, their renewal ability is restricted. The results of the studies indicate mostly that cell phones may cause brain tumors stemming from brain cells.[16-18] It is also asserted that the harmful effects of cell phones to brain cells may originate from the heat effect occurring when they are kept close to brain, except for magnetic field.[17]

It was indicated in scientific sources that there may be some differences among individuals in terms of being negatively affected from cell phones.[19] It was reported that age is an important factor and the highest exposure can be seen in children and early adults. A human being's being at home, in workplace, travelling on a bus or a train or being in a rural area while using cell phone can change his/her level of exposure.[4,18] This effect increases in relation to the proximity to base stations and high voltage transmission lines.[19] The distance of cell phones to human body was also found out to be important for magnetic exposure. Even the firms that produce cell phone added warnings in the instructions of the device regarding its harmful effects. These warnings indicate that the device should be kept away from human body about 2.5 cm. It is a known fact that use frequency and duration of cell phones are important regarding exposure. The presence of cell phone radio frequency and other electric household appliances along with cell phone was found important regarding exposure.[18,19]

Cell phones are generally carried in the pockets of shirts which are close to breast region or in back pockets of pants which are close to the area where the bone marrow is intensive. The tumor cells of breast and bone marrow which have neighbor relations with these regions were chosen as the material of the study as the cells which are of ectoderm and mesoderm layers origin and have fast proliferative capacity. The fact that these cells have cell chains that can be obtained commercially provided the opportunity to carry out the study in culture environment. In our study, it was determined that the proliferative capacities of breast and bone marrow neoplasm cells, which were subjected to the effect of cell phone during the culture, slowed down in comparison to the other cells even though it was not certain. The fact that this slowing down was observed in both types of tumor cells stemming from different layers may support the idea that the effect is independent from the type of tumor and formed as a result of a general environmental effect (magnetic field). As mechanism, it is claimed that the inhibitory effect of electromagnetic waves of mobile phones (<300 GHz) on cell proliferation is related to the T-type Ca2+ channel subunit expressed in malignant cells, especially MCF-7 breast cells, and Ca2+ uptake into breast cells is affected by the electromagnetic field and sensitizes tumor cells.[20] Alteration of intracellular Ca2+ level affects apoptosis, proliferation, mitochondrial activity, and gene transcription of cells.[21,22] Another mechanism could be probable epigenetic influence. Further studies are needed on this subject.[23]

In this study, cells in the same number were cultured in each culture plaques. Culture study was carried out on the cells in experimental groups in the same duration, the same environment and conditions. In order to reduce margin of error, each experiment was repeated in three different culture plaques. With a view to test the effect of cell phone, the cell phone was placed in incubator in a way that it was close to the plaques. In the INTERPHONE study, calls were standardized in a way that corresponds to the intensive use duration defined as the use of cell phone more than half an hour in a day and cell phone calls in the same frequency and duration were made.

MTT test, which is an acceptable method for researching the effect of environmental effects on the reproduction of cells, and viability tests were used.[13]

The study has some limitations. First, the period of cell culture and subjection to the effects of cell phone could be kept longer. Second, the electromagnetic field of subjection cannot have a numerical measurement. This measurement could have been possible by using the devices utilized in experiments and creating fixed magnetic field. Third, studies on the mechanism are required, such as apoptosis study. In this study however, the basic thought was to examine the effect of cell phone on cancer cells by simulating the use of cell phone as in daily life.

In conclusion**,** the results obtained in our study support the idea that the proliferative capacities of breast cancer and leukemia cells of different embryonic layer origins can be affected when they are subjected to the effects of cell phone in laboratory environment. The fact that these effects are inclined to slow down the proliferation of cancer cells may encourage researchers for carrying out further studies on mitigating the concerns about tumor genesis.

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Compliance with Ethical Standards

This study does not have a design on biomaterials directly sourced from humans or animals. The study was performed with a commercially available cell line. Therefore, ethical committee approval is not required.

Conflict of Interest

The authors declare no conflicts of interest.

Author Contribution

The project idea was put forward by BB and MA. BB, MA, and EM jointly designed and conducted the laboratory phases of the study. IK provided laboratory support. The writing phase of the study was done by all the authors.

Financial Disclosure

Financial disclosure none.

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