Assessment of the role of specific absorption rate of mobile phones on the induction of microwave-induced survival adaptive responses after exposure to lethal doses of gamma radiation

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ABSTRACT

***Background*:** Whether exposure to common electromagnetic fields affects human health adversely has been a controversial issue. The main goal of this study was to assess the role of 900 MHz microwave radiations with different specific absorption rates (SARs), emitted from some widely used cell phones, on the induction of adaptive response in male Balb/c mice after receiving a lethal dose of gamma radiation. ***Materials and Methods*:** This study was conducted on 120 male Balb/c mice. The animals were divided into groups of 20 mice each (6 groups). Group one (the control group) received neither microwave radiation nor the lethal dose of gamma radiation. Group two was exposed only to the lethal dose of 8.8 Gy. The mice in group three were first exposed to low SAR 900 MHz microwave radiations emitted from a cell phone for six hours (3 hours in the morning and 3 hours in the afternoon) for 5 days and then were exposed to a lethal dose of 8.8 Gy on day six. The mice in group 4 were treated as those in group 3 but with a moderate SAR and the mice in group 5 were also treated as those in groups 3 and 4 but with a high SAR. The mice in group six were exposed only to high SAR 900 MHz microwaves. ***Results*:** All groups were monitored for 12 days and their daily mortality rates were recorded. The results showed that there was a statistically significant difference between group two (the animals exposed only to lethal dose of gamma radiation) and the groups with a pre-exposure to microwave radiations before receiving the lethal dose. ***Conclusion*:** To the best of our knowledge, this is the first study that investigates the role of SAR on the induction of microwave-induced survival adaptive response. It can be concluded that 900 MHz microwaves emitted from cell phones, regardless of their SAR can induce adaptive responses which make the animals more resistant to subsequent lethal doses of ionizing radiation. These findings also confirm our preliminary findings obtained in a previous study.

Keywords: *Adaptive response, non-ionizing radiation, microwave, GSM mobile phone, survival.*

INTRODUCTION

Widespread use of cell phones has prompted researchers to further investigate the bio-effects of exposure to electromagnetic fields (EMFs) at different levels. Based on current reports, in spite of uncertainty about the bio-effects of prolonged use of cell phones, hundreds of millions throughout the world make use of cell phones [1]. Although the range of cell phone frequencies is wide (100-2000 MHz), the Global system for Mobile Communication (GSM) mobile phones emit radiations with a frequency of 900 MHz [2]. In spite of controversy over the effects of microwaves emitted from cell phones, mutagenic and carcinogenic effects of electromagnetic radiations have been reported in some studies [3, 4]. Therefore, scientists are encouraged to perform more and more studies on the effects of radiofrequency radiation emitted from cell phones and mobile base stations on human health [5]. Despite the findings of some studies that cell phone users have reported more subjective symptoms, Mortazavi, *et al.* (2007), in a study on 518 students, did not find any increase in the frequency of such symptoms in cell phone users in comparison to occurrence of the same symptoms in non-users [6]. A review of the latest studies reveals that effects of microwaves radiated from cell phones on human cognitive activities is still ambiguous and the experts' opinions on this issue are divided [7].

Widespread studies have shown that when cells are exposed to low doses of ionizing radiations and DNA damaging agents such as ultraviolet rays (UV), alkylating agents, oxidants and heat, such cells get more resistant to high doses of those agents and, in some cases, to similar agents. The induction of adaptive response was first reported by Samson and Cairns. These researchers found that Escherichia Coli (*E. coli*) bacteria which had been exposed to low doses of alkylating agents were less susceptible to high doses of the same and similar agents [8]. Following this significant finding, it was argued that whether ionizing radiations also induce the same effects. Olivieri *et al.* in 1984, found that human lymphocytes exposed to tritium-*labelled thymidine* became resistant to cytogenetic damages resulting from high doses of X-rays. Olivieri's finding known as radioadaptive response was very important at that time since he found that this radioadaptive response led to a 50% decrease in the frequency of chromosome aberrations in lymphocytes pre-exposed to adapting doses compared to those only exposed to a subsequent high dose [9]. In 2009, it was found that initial irradiation of cells in culture medium with radiofrequency radiation induced an adaptive response which increased the resistance of these cells to mytomycin C [10]. Mortazavi *et al.* recently found that laboratory animals pre-exposed to radiofrequency radiation were less susceptible to subsequent lethal effects of high doses of ionizing radiation [11, 12]. Cao *et al.* also showed that, compared with the animals exposed to gamma radiation alone, mice pre-exposed to RF at 120 W/cm^2 and then subjected to 8 Gy and 5 Gy gamma irradiation revealed a significant increase in survival time and a significant reduction in hematopoietic tissue damage, respectively [13]. This study aimed to investigate the role of SAR on the induction of microwave-induced adaptive response.

MATERIALS AND METHODS

Animal model

In this study, 120 adult 25-30 g male Balb/C mice were used. These young (2 months of age) animals were obtained from the animal laboratory of SUMS (Shiraz University of Medical Sciences). All animals were kept in a standard condition (temperature 23±2 °C, 12 h light and 12 h darkness and free access to food and water). The mice were divided into six groups of 20 mice each. The mice were kept in compartments (cages), with no more than 10 mice in each cage.

Grouping and RF exposure

According to table 1, animals were divided into six groups. Animals that received RF

Table 1. Grouping of the animals and the interventions (adapting and challenge doses) applied in each group.

Time / Group	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
Group 1 (No MW→No LD)	No MW	No MW	No MW	No MW	No MW	No LD
Group 2 (No MW→LD)	No MW	No MW	No MW	No MW	No MW	LD (8.8 Gy GR)
Group 3 (Low SAR MW→LD)	6 Hours of MW Irrad	6 Hours of MW Irrad	6 Hours of MW Irrad	6 Hours of MW Irrad	6 Hours of MW Irrad	LD (8.8 Gy GR)
Group 4 (Medium SAR MW→LD)	6 Hours of MW Irrad	6 Hours of MW Irrad	6 Hours of MW Irrad	6 Hours of MW Irrad	6 Hours of MW Irrad	LD (8.8 Gy GR)
Group 5 (High SAR MW→LD)	6 Hours of MW Irrad	6 Hours of MW Irrad	6 Hours of MW Irrad	6 Hours of MW Irrad	6 Hours of MW Irrad	LD (8.8 Gy GR)
Group 6 (High SAR MW→No LD)	6 Hours of MW Irrad	6 Hours of MW Irrad	6 Hours of MW Irrad	6 Hours of MW Irrad	6 Hours of MW Irrad	No LD

MW: 900 MHz Microwave Radiation LD: Lethal Dose GR: Gamma Radiation
SAR: Specific Absorption Rate Irrad: Irradiation

exposure, had two daily irradiation sessions; 3 h in the morning and 3 h in the afternoon [12] for five days.

As materials such as glass and plastic do not significantly absorb microwaves, in our study the mice were kept in standard plastic restrainers during RF exposure. To guarantee an identical exposure, animals' restrainers were placed in a circle equidistant from the mobile phone antenna. The distance between the antenna of the mobile phone and animal's head was 5 cm.

1. Low SAR cell phone: Samsung D880 (0.2 W/Kg)
2. Medium SAR cell phone: HTC touch 2 (0.83 W/Kg)
3. High SAR cell phone: Nokia E51 (1.4 W/ Kg)

SAR rating was based on methods used in our previous experiments [14]. The cell phones were in the talk mode during the exposure.

Irradiation with the lethal dose

In this study, the survival rate for 12 days was monitored, that is, after exposure to the lethal gamma dose of 8.8 Gy as the LD 50/6 [12, 15], the number of surviving mice was recorded. A Theratron 780c cobalt radiotherapy machine was used (SSD = 90 cm, dose rate = 50.1 cGy/ min, field size = 35×35 cm^2, irradiation time = 17.56 min). After exposure to the lethal dose, the mice were returned to the animal lab at Shiraz University of Medical Sciences and were kept in standard conditions. The survival rates of the animals were monitored for the following 12 days.

Statistical Analysis

Kaplan-Meier's survival analysis was used for assessing the survival rate in each group. A dead animal was counted as 0, whereas live animals were defined as 1.

RESULTS

In the first group (the control group: no exposure to RF and gamma radiation), two death events were reported throughout the duration of the study (12 days). The mice in the second group, which had been exposed to only the lethal dose of gamma, no death events were reported for the first 2 days. From the third day till the 12^{th} day of the study, 2 mice died. No death events were reported for the mice in the third group, which had been exposed to 900 MHz microwaves emitted from the cell phone with low SAR until 4 days after receiving the

lethal gamma dose. The first death was reported on the fifth day. For mice in the fourth group, as for those in the third group, the first death event was reported on the fifth day. For the mice in the fifth group, which had been exposed to 900 MHz microwaves from the cell phone with high SAR, as those in groups 2, 3, and 4, no deaths were reported until 4 days after exposure to the lethal gamma dose. In this group, the first death case was also reported on the fifth day. For the mice in the sixth group, which had been exposed only to microwaves with high SAR from the cell phone (no exposure to lethal dose of gamma), no death events were reported for the 12 days. Figure 1 shows the survival rates of the animals during study time.

As shown in table 2, the survival rates in animals that received both adapting (low SAR RF) and challenge dose (lethal dose of 8.8 Gy of gamma radiation) and the animals receiving only the challenge dose (lethal dose of 8.8 Gy of gamma radiation) were 60% and 7.5%, respectively. This difference was statistically significant (p=0.000). On the other hand, the survival rates in animals that received both adapting (medium SAR RF) and challenge dose (lethal dose of 8.8 Gy of gamma radiation) and the animals receiving only the challenge dose

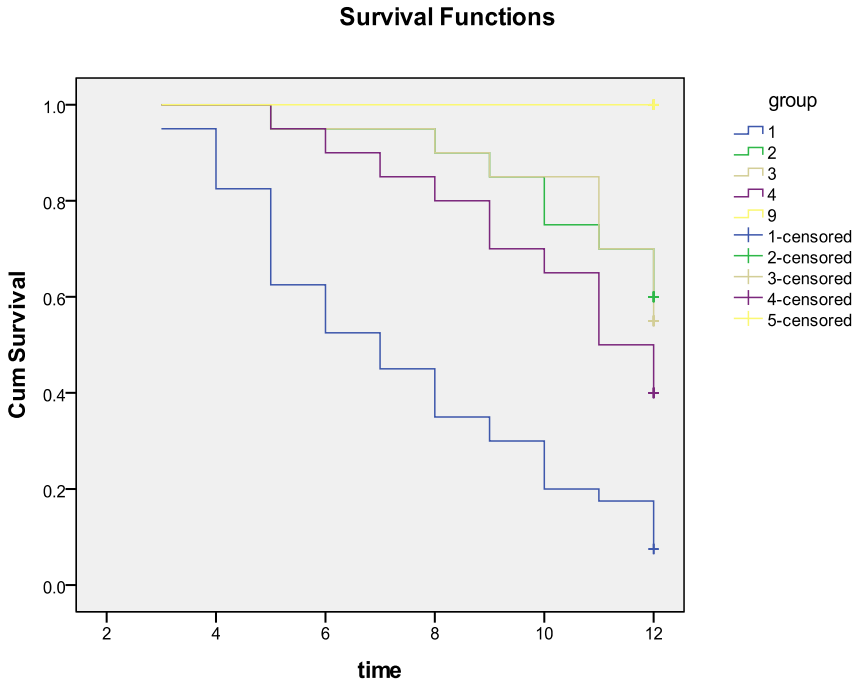

Figure 1. The survival rates of the animals during study time.

Table 2. Survival rates in different groups of animals 12 days after exposure to the lethal dose of 8.8 Gy of gamma radiation.

Intervention (Exposure to RF for 5 days)	Survival Rate after 12 Days		P-Value Log Rank (Mantel-Cox)
	MW→LD	Group 2 No MW→ LD	
Group 3 (Low SAR MW→LD)	60%	7.5%	0.000
Group 4 (Medium SAR MW→LD)	55%	7.5%	0.000
Group 5 (High SAR MW→LD)	40%	7.5%	0.001
Overall (3 Groups) (MW→LD)	51.6%	7.5%	0.001

(lethal dose of 8.8 Gy of gamma radiation) were 55% and 7.5%, respectively. This difference was also statistically significant (p=0.000). Finally, the survival rates in animals that received both adapting (high SAR RF) and challenge dose (lethal dose of 8.8 Gy of gamma radiation) and the animals receiving only the challenge dose (lethal dose of 8.8 Gy of gamma radiation) were 40% and 7.5%, respectively. This difference was also statistically significant (p=0.001). After pooling the results of groups 3-5, the survival rates in animals that received both adapting (RF) and challenge dose (lethal dose of 8.8 Gy of gamma radiation) and the animals receiving only the challenge dose (lethal dose of 8.8 Gy of gamma radiation) were 51.6% and 7.5%, respectively. Again, the difference was statistically significant (p=0.001).

DISCUSSION AND CONCLUSION

The findings of this study revealed that there were statistically significant differences between group 2, which was exposed only to lethal dose of gamma radiation, and the other groups (group one, the control group with no exposure to any irradiation, and groups 3, 4, 5, and 6 which had been exposed to radiofrequency radiations for 6 h for 5 days before being exposed to lethal gamma dose). This indicates that radiofrequency radiation (900 MHz microwaves emitted from cell phones) can induce adaptive response. These findings are in line with the very limited recently published reports that indicated the possibility of the induction of adaptive response after pre-treatment with microwave radiation [13, 16-19]. Sannino et al. have previously reported that pre-exposure of peripheral blood lymphocytes collected from human volunteers to non-ionizing RF radiation (900 MHz, at a peak specific absorption rate of 10 W/kg for 20 h) increases their resistance to a challenge dose of mitomycin C (100 ng/ml at 48 h) [16]. Later, they confirmed their previous results and showed that the timing of adapting dose exposure of radiofrequency plays an important role in the process of adaptive response induction [17]. On the other hand, Chinese researchers have recently shown that pre-exposure of mice to non-ionizing 900 MHz RF induced adaptive response and thus reduced the hematopoietic tissue damage from a subsequent challenge dose of ionizing radiation [18].

It can be argued that 900 MHz microwaves from cell phones might play the role of a trigger in the cells. In other words, the microwaves can induce an adaptive response and develop protection against genetic damages resulting from ionizing radiations so that they can prevent the creation of micronuclei [10]. Another factor can be the effect of enzymes, which have a part in the repair of damages to DNA, particularly polymerase enzymes which react during the DNA breakage by free radicals produced by mitomycin C [20-22]. Other studies have suggested that the stimulation of the immune system plays a part in the induction of adaptive response after exposure to low doses of ionizing irradiations or substances such as mitomycin [23]. It can be argued that such substances act as "radiation vaccines" in the body and consequently activate the immune system to resist against higher doses. The issue can also be discussed from a defense mechanism aspect. When the cells are exposed to low doses of ionizing irradiations and the chromosome damage occurs, apoptosis becomes active and this prevents the cell from developing cancer [24, 25]. In this process, the cells with irreparable chromosome damage are destroyed.

Other researchers have stepped further from the cellular level and have studied adaptive response at a molecular level. They have argued that there is a relationship between the metabolic production of reactive oxygen species (ROS) and the induction of adaptive response [26]. ROS are the activated species of oxygen that cause chromosome damages. According to some published reports, repair of the damaged DNA in the natural cells is affected by the alterations in the ROS mechanism. In other words, when the level of ROS increases due to ionizing radiations, the repair control system of DNA rises as well. In normal conditions and without ionizing radiations in which the level of ROS is low, the repair

rate decreases. A further factor which might have a part in the creation of the adaptive response is the activation of glyoxalase system. This system consists of a set of enzymes whose function is to detoxify methyglyoxal aldiodoes produced in the metabolism [27]. The role of this system has been studied in bacteria and eukaryotes [28]. Some studies have indicated that the glyoxalase system which exists in the liver and spleen of mice and has a biochemical role, when exposed to ionizing radiation (e.g. adaptive dose), is stimulated and has a protective role [29].

Another important point in this study was the lack of the effect of SAR on the induction of adaptive response. As was pointed out above, no statistically significant difference was found between groups 3, 4, and 5 which had been exposed to 900 MHz microwaves with low, moderate and high SAR before exposure to lethal gamma dose, respectively. Although all of the above-mentioned factors have been reported for the induction of adaptive response, it cannot definitely be said whether these factors induce adaptive response or they themselves are the result of other factors. Regarding the discussed points, what makes finding the main cause of the adaptive response observed in this study difficult is that we do not exactly know the mechanism of the action of 900 MHz radiofrequency radiation emitted from cell phones on the induction of adaptive response. Do the thermal effects induced by radiofrequency radiations in the cells cause more cell resistance? Do 900 MHz non-ionizing microwaves from cell phones and ionizing radiations or substances such as mitomycin C function in the same way since we observed similar results in the induction of adaptive response against the ionizing radiation?

Regarding the final similar results in the use of ionizing and non-ionizing radiation as adaptive doses, can we ignore the effect of ionization in the induction of adaptive response? Do multiple mechanisms play a part in the induction of adaptive response? In other words, do low-dose ionizing radiations and radiofrequency radiations each separately activate a specific kind of mechanism but with similar effects? All these questions can be formulated as some hypotheses which require exact and extensive studies to find their answers.

Conflict of interest:
None Declared

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