Influence of 1800 MHz GSM-like Electromagnetic Radiation Exposure on Fracture Healing

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Received for publication July 14, 2013; accepted January 15, 2014 (ARCMED-D-13-00375).

Background and Aims. In this study, we aimed to investigate whether 1800 MHz frequency electromagnetic radiation (EMR) has an effect on bone healing.

Methods. A total of 30 Wistar albino rats were divided into two equal groups. Fractures were created in the right tibias of all rats; next, intramedullary fixations with K-wire were performed. A control group (Group I) was kept under the same experimental conditions except without EMR exposure. Rats in Group II were exposed to an 1800 MHz frequency EMR for 30 min a day for 5 days a week. Next, radiological, mechanical, and histological examinations were performed to evaluate tibial fracture healing.

Results. Radiological, histological and mechanical scores were not significantly different between groups (respectively, \( p = 0.114 \), \( p = 0.184 \) and \( p = 0.083 \)), and all of these scores were lower than those of the controls.

Conclusions. EMR at 1800 MHz frequency emitted from cellular phones has no effect on bone fracture healing.

Key Words: Fracture healing, Electromagnetic radiation, Mobile phone, 1800 MHz, GSM.

Introduction

Bone fracture healing is a crucial process with respect to its important socioeconomic and overall quality of life outcomes. Various local and systemic factors can affect fracture healing in positive or negative ways. Fracture healing and bone tissue formation are complex metabolic processes associated with various local and systemic regulators and involve reciprocal interaction of the cellular structures \( 1−5 \). The bone repair process begins with hematoma formation, which occurs after skeletal injury and bone fracture. This process continues with the inflammatory phase followed by the formation of soft and hard callus tissues, which ultimately leads to the remodeling phase \( 6,7 \). However, fracture healing may not necessarily result in such a favorable outcome, and there are always some disruptions. Currently, there are some ongoing studies focused on obtaining more insight into the pathophysiological background of bone healing and the factors that influence the process. It has also been revealed that bone formation and fracture healing involve electrical activity \( 8 \). Some findings related to the possible effects of electrical stimulation or pulse electromagnetic radiation (EMR) on fracture healing have been reported \( 9,10 \). There are many local, systemic or environmental factors that may affect bone formation and fracture healing in positive and negative ways \( 1−7 \). Bone tissue can potentially absorb the environmental EMR, and mobile phones can be one of the environmental sources of EMR \( 11 \).

Several negative outcomes of EMR related to human health, particularly involving the endocrine and nervous
systems, have been reported; these outcomes are a result of the interaction of some peripheral EMR resources such as cellular phones and base stations with living biological structures (12-18). Cellular phone-based EMR frequencies belong to the high frequency band radiofrequency (RF) in the electromagnetic spectrum (12,19,20). High frequency EMR emitted from cellular phones and base stations may have some negative effects on biological tissues, and bone formation/fracture healing can be affected by these peripheral sources (7,20-22). In a study by Yildiz et al. (21) in which EMR at 1 ± 04 mW/cm² power was applied for 30 min a day for 5 days a week over a period of 4 weeks, it was reported that the mean femoral and vertebral bone mineral density (BMD) values of the rats exposed to 900 and 1800 MHz RF EMR were lower than those of the controls; however, this difference was not statistically significant. In another experimental study (11), it was reported that short- or long-term exposure to EMR at a 900 MHz frequency had no significant effect on the bone tissues of rats. Atay et al. (23) showed a decrease in mean BMD of the pelvic ring bone tissues of individuals who stored their cellular phones on or near their belts. Çiçek et al. (24) reported a decrease in fracturing power, bending resistance and total fracture energy in bone tissues of rats exposed to RF EMR at 1800 MHz. Aydogan et al. (25) reported that there was no prominent difference between the controls and the study group based on histopathological scores following 1800 mHz RF EMR exposure in an experimental rat patellar joint cartilage damage model. Furthermore, the effect of high frequency 1800 MHz EMR on fracture healing is still unknown, and there is no published study on this issue in the literature to date. In this study, we investigated whether high frequency EMR at 1800 MHz emitted from cellular phones affects bone fracture healing.

Materials and Methods

Animal Model

A total of 30 adult Wistar albino male rats aged between 4 and 6 months and weighing 256 ± 20 g were included in this study. The animals were obtained from the Animal Research Laboratory of the Medical Faculty of Suleyman Demirel University (SDU). Before the initiation of the experimental part of the study, written approval consent was granted from the local Ethics Committee of SDU School of Medicine. Male rats were preferred for this study because they have no short periodic or cyclic hormonal changes, which occur in females (26), and they have been commonly used in animal models of experimental orthopedic surgery. Rats were equally and randomly divided into two groups as follows: Group 1 (controls, n = 15) and Group 2 (exposed to 1800 MHz EMR, n = 15). The rats were kept under ideal humidity and circadian rhythm conditions (temperature: 22 ± 2°C, 12 h light-dark cycle, humidity: 30-70%). They had access to standard pellets (rat diet) ad libitum. The animals were not restricted in terms of activity and/or loading-stress during the experiment. Only Group 2 animals were exposed to EMR, whereas Group 1 controls were not; both groups were housed in the same room.

EMR Application Setting

An RF generator (Set Elec. Co. 900/1800 Lab.Test Transmitter, Model 8050 GX, Istanbul/Turkey), which can produce outputs between 0 and 4 W at 1800 MHz, was used to produce the signals at cellular phone working frequency. RF EMR was applied to the rats using half-wave dipole antennas at 1800 MHz. At the SDU Electronic and Communication Engineering Research Laboratory, the power intensity and the EMR near the dipole antenna were measured while the RF generator was operating at the 2 W level; the whole rat body SAR value was theoretically calculated as 0.008 W/kg. Rats near the dipole antenna were exposed to EMR at a 1.04 mW/cm² power intensity. SAR values and theoretical analysis calculations were based on the method described by Gajsek et al. (27,28).

Surgical Method

All rats were food deprived for 12 h prior to the operation. Prophylactic cephalosporin sodium (Sefazol® [15 mg/kg]; Mustafa Nevzat İlaç Sanayii A.Ş. Istanbul, Turkey) was administered i.m. 2 h before the surgical intervention. Ketamine HCl (Ketalar® [10 mg/kg]; Pfizer İlaçları Ltd. Şti, Istanbul, Turkey) and xylazine HCl (Alfazyne® [0.25 mg/kg]; Ege Vet Hayvan. Tic. Ltd. Şti, İzmir, Turkey) were i.p. injected for general anesthesia. Manually induced fractures and intramedullary fixation methods were applied as previously described (22). We preferred the intramedullary fixation approach because it is a standard method (29). Moreover, it is very easy to remove intramedullary rods prior to histological and/or biomechanical procedures. Right tibial bones were transversely broken with finger pressure based on the three-points principle. After this procedure, the right posterior regions of the legs were cleaned with antiseptic solution, covered with sterile green dressings and prepared for the operation. A 1.5-cm long incision was made on the anterior of the right knee. Using a scope, the fracture line was ligated and stabilized using the intramedullary fixation method with 0.5-mm-thick K-wires, which were inserted from the proximal tibia and passed through the intramedullary route. The incision site was closed with running 4-0 prolene. The fractures were classified according to their appearance based on a previously described method with modifications (22). The good condition was defined as one fracture line located between the proximal 1/3 and the distal 2/3 of the bone, and the bad condition was defined as partial, multisegmental fractures or fractures with articular involvement. Fractures that were
defined as “good” \((n = 26)\) were included in this study, whereas “bad” fractures \((n = 4)\) were excluded.

**EMR Exposure**

Rats were then placed into plastic tubes that were approximately the same length as the animals to prevent movement, and RF EMR was applied by using half-wave dipole antennas at 1800 MHz frequency, which were directly connected to the RF generator (adjusted output power: 2 W; mean power intensity: 1.04 mW/cm²; whole body mean SAR value: 0.008 W/kg). Rats were kept at 5 mm from the dipole antenna. Additionally, a monitor panel at a 100 dB isolation level was placed to avoid unsolicited interaction between the 900 and 1800 MHz frequencies (Figure 1). Animals in Group 2 were exposed to 1800 MHz EMR for 30 min a day 5 days a week over a total of 8 weeks. Group 1 rats were kept in plastic tubes under the same conditions as those of Group 2, but they did not receive any EMR. The experimental setup procedure and application were based on the method described by Chou et al. (30). The radiation conditions were controlled using spectrum analyzer probes and a satellite receiver meter (Promax, Barcelona, Spain) as well as a Portable RF Survey System (HI-4417, Holaday Industries Inc., Eden Prairie, MN) and probes.

![Figure 1. Schematic view of the EMR application process.](image)

![Figure 2. (A) Control group, postop 8 weeks. Score: 7. (B) EMR-1800 MHz Group, postop 8 weeks. Score: 7. (A color figure can be found in the online version of this article.)](image)
Radiological Evaluation

Following the administration of sevoflurane via inhalation, animals were placed in a prone position and their extremities were fixed to the surface. Conventional A-P direct radiographs were taken (tube distance = 50 cm, energy level = 44 kV, 1.25 mA/s) at a suitable angle to obtain radiographs including the fractured lower extremity. Control radiographs were taken 1 day following the operation to evaluate the fracture and stabilization status. The formation of callus tissue was followed by taking subsequent radiographs during the 2nd, 4th, 6th and 8th weeks (Figures 2A–B). At the end of the study, three specialists who were blinded to the radiographs and experimental groups evaluated the results based on a previously described radiographic scoring system (22,26). Radiographs were included in the evaluation when the scorings by the two specialists were the same.

Histopathological Evaluation

Right tibial bones of the rats were excised with the callus tissues and were separated from the surrounding soft tissue. All specimens were placed into 10% neutral buffered formalin solution for fixation. A routine tissue processing procedure was performed after the decalcification process was completed. Specimens were then embedded in paraffin blocks; 6-μm-thick sections were longitudinally cut with a microtome by centering the fracture line, stained with hematoxylin-eosin and examined under a light microscope (Figures 3A–B). The stained slides were evaluated by three specialists who were blinded to the study groups according to the method described by Huo et al. (31). The protocol described by Deibert (32) was preferred as the histopathological evaluation method. Cells were counted with a microsquared slide. The mean percentages of the chondrocytes, osteocytes and fibroblasts located in the middle of the fractures in three squares were calculated.

Mechanical Evaluation

This evaluation was performed according to a previously described method (22). The fracture was evaluated on two planes (antero-posterior/medio-lateral) with respect to motility and was scored as follows: 0—Non-union (movement present in both planes); 1—Moderate union (movement present in one plane); and 2—Complete union (the lack of any movement). The specialists involved in this study evaluated the union tissues in the tibial fracture sites (Figures 4A–B). In addition to the established radiological and histological results, we also performed manual examinations and evaluations. When the evaluations from the specialists were not consistent, another researcher involved in the study provided the final decision on the evaluation of the results. Statistical Analysis: SPSS 11.0 for Windows (SPSS Inc. Chicago, IL) statistical analysis software was used for the statistical calculations. Normal distribution of our data was evaluated using Kolmogorov-Smirnov test. Mann-Whitney U test was used for group comparisons, and p values <0.05 were considered statistically significant. The results are expressed as the mean ± standard deviation.
Results

In the beginning of the study, four rats with bad fracture conditions (two from the control group and two from the EMR group) were excluded from the study. During the study, one rat from the control group and three rats from the EMR group died. Additionally, three rats from the control group and two rats from the EMR group were excluded because the obtained histological slides could not be clearly examined. There was no sign of wound infection or osteomyelitis in the animals. The established results at the end of the study are as follows:

Radiological Evaluation Results

A total of 22 direct radiographs (12 from the control group and 10 from the EMR group) were evaluated. The mean and standard deviation values are given in Table 1. There was no statistically significant difference between the EMR and control groups (\( p = 0.114 \)), and the results from the EMR group were worse than the controls (Table 1).

Histopathological Evaluation Results

Nine slides from the control group and eight slides from the EMR group were examined. Mean and standard deviation of the scores are given in Table 1. There was no statistically significant difference between the EMR and control groups (\( p = 0.184 \)), and the results from the EMR group were worse than the controls (Table 1).

Mechanical Evaluation Results

A total of 22 tibial bones (12 from the control group and 10 from the EMR group) were evaluated. There was no statistically significant difference between groups based on the manual evaluation (\( p = 0.083 \)), and the scores from the EMR group were lower than the controls (Table 1).

Discussion

EMR has become an important health problem based on the increasingly widespread use of cellular phones; previous studies have suggested harmful effects of RF waves on human health (11–18). Cellular phone-based EMR frequencies belong to the high frequency band RF area of the electromagnetic spectrum. Many types of mobile phones operate at 900 MHz or 1800 MHz and produce electromagnetic fields (7,11,12,19–22). Negative effects of 1800 MHz
EMR on biological tissues have been reported in epidemiological, clinical and experimental studies that were conducted to determine the effect of radiofrequency EMR emitted from cellular phones operating at the high frequency band (15–18,33–35). However, some studies reported that EMR emitted from cellular phones may have no serious effects on health (36–38). Bone tissue is a potential route for the absorption of hazardous environmental energy such as RF EMR emitted from cellular phones (7,11,20–22). There are few studies regarding the possible effect of RF EMR from cellular phones on bone tissue or the fracture healing process (20–25,39). However, the effect of high frequency 1800 MHz EMR on fracture healing is still unknown and to date there has been no such study in the literature. In our study in which 1800 MHz EMR was used, we used radiological, mechanical and histological methods to investigate the bone fracture healing following exposure to EMR with a power intensity of 1.04 mW/cm² and 0.008 W/kg SAR values established from 1800 MHz cellular phones and/or similar sources for 30 min/day for 8 weeks.

There is a limited number of studies on the effects of cellular phone-based EMR on fracture healing. In a study by Aslan et al. (22) in which a rat tibial bone fracture model was used, it was reported that bone fracture healing was very negatively affected by 900 MHz EMR exposure. Based on somewhat contrasting results, Kalender et al. (39) found that 900 MHz EMR exposure has no significant effect on fracture healing, although the mean histopathological scores of the exposed group were worse than the controls. In the current study, we also observed that 1800 MHz EMR exposure had no significant effect on bone fracture healing, although the mean radiological, histological and biomechanical scores were worse in the exposed group than in the controls.

Results from our study and the other studies mentioned above may be affected by various factors such as the materials used, the experimental animal model, the applied methodology, EMR type, frequency, power fidelity, and exposure duration/dose. Studies using different frequency ranges and diverse methods typically yield different results. Additionally, there is no consensus in the literature on which EMR type, frequency, duration and dose has negative or therapeutic effects based on the results from studies performed using low and high frequencies and the effects of EMR on bone and other tissues (7—10,40—42). Furthermore, the effects of EMR emitted by cellular phones and base stations on human health are due to the frequency, SAR and power of the radiation (11,19—22,43).

It has been previously reported that high-frequency EMR leads to biological tissue damage by affecting the biochemical mechanisms or by inducing heat; this represents a limitation in our study (44—46). We did not measure the systemic temperature or the temperature at the local fracture sites in the groups. These data would allow us to rule out a temperature effect as the basis for the findings. Another limitation of our study is the small number of samples. Additionally, we did not perform any scintigraphic or quantitative computerized tomography imaging and biochemical analysis. Perhaps more detailed data on the effect of EMR on the stages of bone fracture healing and callus tissue formation could be gathered by performing scintigraphic and quantitative tomographic imaging; in addition, bone turnover markers determined by biochemical analysis could provide valuable additional information for our study. Whole body exposure, which was performed based on the calculation of the whole body mean SAR value using the method described by Gajsek et al. (24,25), was used because cellular phones are used near the head region while talking and are carried at the belt level or in pockets at other times; therefore, this method considers the effect of cellular phones on the whole body instead of calculating the SAR values for only bone tissues. The duration and dose of the EMR application were based on the threshold values determined and approved by The International Commission on Non-Ionizing Radiation Protection (19,26,47).

As a result, we conclude that RF EMR at 1800 MHz emitted from cellular phones has no significant effect on bone fracture healing. Bone is a potential tissue for the absorption of environmental hazardous energy, and RF electromagnetic waves originating from cellular phones can produce EMR, which may affect bone tissues. It is obvious that the EMR magnitude, duration and frequency can lead to some differences in the observed impact on the tissues and can therefore yield different results. We hope that the results produced in this study are valuable when the prevalence of cellular phone usage in the world and the problems encountered during the fracture healing process are taken into consideration. We also hope that these results can shed light on future studies; however, we also think that more comprehensive studies are required in this field to elucidate the underlying mechanisms of the observed effects.

Acknowledgments

We thank Prof. Dr. İsmet Doğan (Biostatistic), Prof. Dr. M.Fehmi Özgüner (Physiology), Associate Prof. Selçuk Çömlekçi (Electronic & Communication Engineering) and Assistant Prof. Dr. Ahmet Özden (Radiology). This study was supported by the SDU Research Projects Management Unit (project number 1141-TU-05).

References

1800 MHz; GSM-like EMR and Fracture Healing