### Study of the Cardiovascular Effects of Exposure to Electromagnetic Field

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**Abstract:** This study was conducted to throw light on electromagnetic radiofrequency (EMR) emitted from cell phones which was accused of causing a number of negative health effects in the form of influencing on the heart and circulatory system.

110 adult albino rats, of both sexes, weighing 180- 200 gms were used in the present study. Animals were allocated into two main groups: group I, including rats exposed to cell phone EMF for 4 weeks; and group II, including rats exposed to EMF for 8 weeks. Each group was further subdivided into four subgroups, a control group and three subgroups exposed to EMF for either 1h/day, 2hrs/day or 3hrs/day, exposure being carried out six days/ week, at fixed time of the day. All rats were subjected to measurement of the systolic blood pressure on the day prior to the day of sacrifice, ECG recording, assessment of cardiac weights, absolute& relative, and MDA level in cardiac tissue, as well as determination of plasma renin activity, plasma total antioxidant capacity and plasma calcium level. Specimens from the apex of the heart were subjected to histopathological examinations.

Obtained results revealed that systolic blood pressure was significantly increased in all EMF-exposed rats compared to their respective controls. The heart rate, deduced from the ECG tracings, was non-significantly altered in all groups exposed to EMF for 4 weeks and in the 8 weeks-1hr/day exposure group, but was significantly reduced in rats exposed to EMF for 2hrs or 3hrs/day for 8 weeks. The ECG recording of rats exposed to EMF for 4 weeks revealed a significantly higher R voltage in the group exposed for 3hrs/day, a significant increase in ORS duration in the groups exposed for 2hrs and 3hrs/day and significant prolongation of QT-c interval in the group exposed for 3hrs/day. On the other hand, the ECG recording of rats exposed to EMF for 8 weeks revealed significantly higher R and T voltages, and significantly prolonged P-R and OT-c intervals in the groups exposed for 2hrs or 3hrs/day, the QRS duration being significantly increased in all the 8 weeks- exposed groups. In addition, a significant increase in the absolute and relative weights of the whole heart and of the left ventricle in rats exposed to EMF 2hrs or 3hrs/day for either 4 or 8 weeks was obtained. Plasma renin activity was increased in all exposed rats, the increase being statistically significant in rats exposed to EMF 3hrs/day for 4 weeks, and in all the groups exposed to EMF for 8 weeks. Plasma calcium level was significantly decreased in all the exposed groups except for the group exposed for lhr/day for 4 weeks. The plasma total anti-oxidant capacity was significantly decreased in all exposed groups, for either 4 or 8 weeks, while the MDA level in the cardiac tissue was only significantly elevated in the 8 weeks-3hrs/day exposed group compared to the matched control group. The histopathological examination revealed hypertrophy, fragmentation and vacuolation of the myocardium, which were directly proportional to the exposure time.

On conclusion, long-term exposure to cell phone EMF increases the liability for hypertension reflected on the ECG and cardiac weights which is accompanied by histopathological changes in the myocardium. In addition, an interaction of EMF with biological functions was achieved in the form of increased PRA, decreased plasma total antioxidant capacity and hypocalcemia.

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### 1. Introduction:

Electromagnetic fields (EMFs) permeate our environment everywhere: in our homes, at work, in schools, and elsewhere wherever there are electric wires, electric motors and electronic equipments <sup>(1)</sup>.

The radiofrequency (RF) emitted from the recently introduced digital global system mobile

communications (GSM) is around 900-1800 MHZ.  $^{(2,3)}$ , the emission of radiofrequency waves from the GSM phones being continuous and not in pulses as the old analog mobile phones  $^{(4)}$ .

Although the amount of electromagnetic energy due to cell phones is quite small in comparison to other radiofrequency sources, the increased use of wireless mobile phones worldwide (3.8 billion mobile users) has focused interest on its possible side effects, and the potential health impacts <sup>(5)</sup>.

The biological effects of exposure to EMF from mobile phones were reported to be variable, depending on many factors including duration of exposure, distance from the various sources, species and tissues as well as the conditions of exposure  $^{(6,1,7)}$ .

A variety of negative health effects have been attributed to exposure to radiofrequency electromagnetic field (RF-EMF) from mobile phones, such as cold and flu-like symptoms and electromagnetic hypersensitivity  $^{(8,9)}$ , reduced sperm quality and therefore male infertility  $^{(10,11,12)}$ , memory and sleep problems (13), behavioral changes in children who had been exposed prenatally to  $\widetilde{RF}^{(14)}$ , the development of brain tumors (15,16) as well as inner ear damage with long-term use (17). Also, autonomic control of the heart was altered (18,19) and the carcinogenic potential of RF radiation was achieved (20)

Recently, it was reported that RF radiation from mobile phones could alter intracellular signaling pathways through changes in  $Ca^{2+}$  permeability across cell membranes and cellular calcium levels <sup>(21)</sup>.

With regard to the cardiovascular effects of EMF emitted by cell phones, EMF might interfere with work of cardiac pacemakers and other implantable medical devices like cardioverter defibrillators <sup>(22,23,24)</sup>. Mobile phones were reported to cause a rise of blood pressure of 5-10 mm Hg each time of exposure, and it was suggested that cell phone-EMR could induce constrictive effect on blood vessels <sup>(25)</sup>. Also, cell phones could increase the blood pressure (BP) and heart rate (HR) among healthy adults <sup>(26)</sup>. In addition, an increase in blood pressure in rats upon exposure to mobile phone EMF was detected <sup>(27)</sup>. Moreover, an increase in foetal and neonatal heart rate and decrease in cardiac output were found during subjecting pregnant women to cell phones <sup>(28)</sup> Furthermore, it was suggested that EMF emitted by cell phones would influence the autonomic tone, thus modifying the function of the circulatory system <sup>(29)</sup>. However, other study mentioned that changes in heart rate and in arterial blood pressure were independent of the EMF resulting from the use of 900 MHz mobile phones (30)

This study aimed to throw more light on the cardiovascular impact of RF-EMF emitted from mobile phones, and to probe the effect of changes in duration of exposure on the resulting effects.

### 2. Materials and Methods Animals:

The current study was carried out on 110 albino rats, of both sexes, weighing 180-200 gms. Rats were

purchased from the Research Institute of Ophthalmology (El-Giza), and maintained in the Physiology Department Animal House under standard conditions of boarding and feeding, with free access to water.

Animals were allocated into 2 main groups of equal rat number, based on the duration of exposure to the electromagnetic field (EMF): group I, including rats exposed to EMF for 4 weeks, and group II, including rats exposed to EMF for 8 weeks.

Each group was further subdivided into 4 subgroups:

\*Control group {group  $I_C$  (n=13) and group  $I_C$  (n=13)}, including rats not exposed to the cell phone EMF, and kept in the animal house until the day of sacrifice.

\*One hour/day-exposed group {group  $I_1$  (n=14) and group II<sub>1</sub> (n=14)}, including rats exposed to the cell phone EMF 1hr/day, 6 days/week for either 4 weeks or 8 weeks. [Total exposure time for group  $I_1$ =24 hours, and for group II<sub>1</sub>=48 hours].

\*Two hours/day-exposed group {group  $I_2$  (n=14) and group II<sub>2</sub> (n=14)}, including rats exposed to the cell phone EMF 2hrs /day, 6 days / week for either 4 weeks or 8 weeks. [Total exposure time for group I<sub>2</sub>=48 hours, and for group II<sub>2</sub>=96 hours].

\*Three hours/day-exposed group {group  $I_3$  (n=14) and group II<sub>3</sub> (n=14)}, including rats exposed to the cell phone EMF 3hrs /day, 6 days / week for either 4 weeks or 8 weeks. [Total exposure time for group I<sub>3</sub>=72 hours, and for group II<sub>3</sub>=144 hours].

### **Exposure Technique:**

Test rat groups were exposed to radiofrequency electromagnetic field (RF-EMF) of 1800 MHz frequency band mobile phone (Nokia 1208 model), which, according to the GSM, operates with microwave carrier frequencies in the range 900-1800 MHZ <sup>(31,32)</sup>. The exposure was done in special plastic cages, the cell phone being placed under the cage at a distance 0.5 cm below the undersurface of the cage <sup>(33,34)</sup>, and the cell phone was kept in the ringing position, receiving calls from another phone during hours of EMF exposure, but in silent mode, during the whole time of exposure. The intensity of the EMF radiated from the cell phone was 2.2 milli Gauss (10<sup>-</sup> Tesla) at the center of the exposure cage, as measured by Gauss/Teslameter, 4048, USA (Courtesy of the Biophysics Department, Faculty of Science, Ain Shams University).

RF-EMF exposure was carried out at a fixed time of the day.

### Methods:

On the day prior to the day of sacrifice, the systolic blood pressure of all the control and test

animals was measured, using rat tail blood pressure monitor (Harvard apparatus) (*Courtesy of the Physiology Department, Faculty of Medicine, Cairo University*).

On the day of sacrifice, overnight fasted rats were weighed and anaesthetized with i.p. injection of pentobarbitone sodium, in a dose of 40 mg/kg B.W. Rats were subjected to ECG recording, using the ECG recorder Cardimax FX-2111(Fukuda Denshi Co., Ltd., Japan). All leads were established by subcutaneous needle electrodes. From lead II - ECG tracing, the heart rate, the voltages of P, R and T waves, as well as the QRS duration and the durations of P-R and Q-T intervals were calculated. Corrected QT interval (QT-c) was calculated according to Goldschlager and Goldman<sup>(35)</sup>:

$$QT-c = \underbrace{ \begin{array}{c} Q-T \text{ interval (in seconds)} \\ \hline \\ R-R \text{ interval (in seconds)} \end{array} }$$

After the ECG monitoring, an incision was made in the anterior abdominal wall, and the abdominal aorta was exposed and cannulated. A blood sample was collected in a tube containing EDTA, that was centrifuged at 10000 rpm for 10 minutes, and the supernatant plasma used for determination of plasma renin activity. A second blood sample was collected in a heparinized tube, centrifuged at 3000 rpm for 15 minutes, and plasma obtained was used for measurement of plasma calcium level and total antioxidant capacity.

### Handling of the Hearts:

After blood collection, all hearts, from both control and test groups, were isolated, washed in saline, dried by filter paper, cleaned of fat and fibrous tissue, and then weighed as a whole in 5-Digit-Metler balance (Sartorious AG, BL-210S), and the weight expressed as absolute value (in mg). Then, the atria were separated together, the right ventricular wall was peeled evenly and the remaining was the left ventricle plus the septum, and each of these cardiac chambers was weighed and their absolute weights recorded (in mg.). The relative heart (or chamber) weight / body weight (mg/gm) was calculated for each specimen. A cut section of left ventricle was weighed and stored frozen at -80°C for subsequent MDA determination in the cardiac tissue. Specimens of the apices of the hearts were subjected to histopathological examination.

Determination of Plasma Renin Activity (PRA) was performed by radioimmunoassay according to

the method described by Malvano et al. <sup>(36)</sup>, using kits supplied by DiaSorin, USA. PRA was calculated as ng angiotensin I generated /ml/hour.

**Determination of Plasma Calcium level** was determined according to the method described by Cali et al. <sup>(37)</sup>, using a colorimeter (Unico, 7200 series, Shanghi, China) at wave length 570 nm. The colorimetric kit was supplied by Teco Diagnostics, Anaheim with.

**Determination of Total Antioxidant Capacity in Plasma** was performed according to the method described by Koracevic et al. <sup>(38)</sup>, using kits supplied by Biodiagnostic- Egypt, and depending on colorimetric technique (by using spectrophotometer of Unico, 7200 series, Shanghi, China) at wave length 505 nm.

### **MDA Determination in the Cardiac Tissue**

Cardiac tissues, stored frozen at -80°C till the day of MDA determination, were homogenized according to Eissa et al. <sup>(39)</sup>, using the homogenizer Karl Kolb (scientific technical supplies D-6072, Dreieich, West Germany). The homogenization buffer (pH 7.2) consisted of 0.32 mmol/L Sucrose, 20 mmol/L N-2 hydroxyethyl piperzine N-2 ethan sulfonic acid (HEPES), 0.5 mmol/L Ethylene diamine tetra-acetic acid (EDTA). 1 mmol/L 1. 4 Dithio DLthreitol (DTT), 1 mmol/L Phenvl methane sulfonvl floride (PMSF)(Sigma). One ml buffer was added for each 0.1 gm tissue. After homogenization, samples were centrifuged at 3000 rpm for 10 min., and MDA in the supernatant was determined according to the technique of Esterbauer and Cheeseman<sup>(40)</sup>, in which MDA in the sample reacts with thiobarbituric acid in the reagent, and the produced color read at wave length 535 nm. The obtained concentrations of MDA were then divided by 1000, the results being expressed in µmol/ gm wet tissue.

#### **Histopathological Examination:**

Specimens from the apices of the heart were fixed in 10% buffered neutral paraformaldehyde solution. Tissues were sectioned at  $5\mu m$ , stained with H&E and examined using light microscope <sup>(41)</sup>.

### Statistical analysis:

Student's "t" test for unpaired data was used to assess the statistical significant differences between groups. All statistical data and statistical significance were performed by using SPSS statistical package (SPSS Inc.) version 16.0.0. A probability of P < 0.05 was considered as significant.

### 3. Results:

### **Changes in Heart rate and Systolic Blood Pressure:**

As shown in Table 1 and Fig. 1-A; the heart rate, deduced from the ECG recording, was significantly reduced in the 8 weeks-2hrs and 3hrs/day EMF-exposed groups (groups  $II_2\&II_3$ ) compared to their matched control group (P <0.005 and <0.05 respectively).

On the other hand, in table 1 and fig.1-B, the systolic blood pressure was significantly increased in all EMF-exposed groups compared to their respective controls (P <0.001 for all). The systolic blood pressure was significantly higher (P< 0.005) in the 8 weeks-3hrs/day exposed rats (group II<sub>3</sub>) compared to the corresponding 4 weeks-3 hrs /day exposed group (group I<sub>3</sub>).

### **ECG Changes:**

As shown in table 2 and Figs 2-4, rats exposed to EMF for 4 weeks, the ECG revealed significant (P <0.02) increase in R voltage in the 3 hrs/day exposure group as well as significant (P <0.05 for both) increase in QRS duration in the 2 hrs and 3 hrs/day exposure groups and significant (P <0.05) prolongation of QT-<sub>C</sub> interval in the 3 hrs/day exposure group compared to their matched control values. On the other hand, the ECG tracing of rats exposed to EMF for 8 weeks revealed significant increase (P <0.005, <0.002, <0.01 and <0.01 respectively) in R wave and T wave voltages in both the 2 hrs and 3 hrs /day exposure groups, together with significant increase in ORS duration in all exposed groups (P < 0.005 for group II<sub>1</sub>, < 0.005 for group  $II_2$  and <0.001 for group  $II_3$ ) and significant prolongation of P-R and QT-<sub>C</sub> intervals in the 2 hrs and 3 hrs/day exposure groups (P <0.01, <0.001, <0.05 and <0.02 respectively).

Compared to the 4 weeks exposure groups, the ECG of the corresponding 8 weeks exposure groups revealed significant (P <0.05 for both) increase in the P wave and T wave voltages in the 2 hrs/day exposure group, as well as significant (P <0.001 and <0.002 respectively) prolongation of P-R interval and increase of T voltage in the 3 hrs/day exposure group.

## Changes in Absolute and Relative Cardiac Weights:

In table 3, rats exposed to EMF for 4 weeks, the absolute weight of the whole heart and its relative weight to body weight were both increased significantly (P <0.001 and < 0.05 for group I<sub>2</sub> and <0.001 for both for group I<sub>3</sub>) in the 2 hrs and 3 hrs /day exposure groups compared to the matched control values. Likewise, the absolute left ventricular weight and its relative weight to body weight were both significantly (P <0.001 and <0.01 for group I<sub>2</sub>)

and <0.001 for both for group  $I_3$ ) increased in the 2 hrs and 3 hrs/day exposure groups compared to the control group.

In rats exposed to EMF for 8 weeks, the relative whole heart to body weight as well as absolute and relative left ventricular weight were all significantly increased whereas the absolute and relative right ventricular weight was significantly reduced in the 2 hrs/day exposure group compared to the control values (P <0.001 for WH/BW, <0.01 for the absolute LV weight, <0.001 for LV/BW, <0.001 for absolute RV weight and <0.01 for RV/BW). The absolute and relative whole heart weight, and the absolute and relative left ventricular weight were significantly increased and the absolute right ventricular weight was significantly decreased in the 3 hrs/day exposure group compared to the control group (P < 0.05 for whole heart weight, <0.001 for WH/BW, <0.005 for left ventricular weight, <0.001 for LV/BW and <0.05 for the absolute right ventricular weight).

Compared to the corresponding 4 weeks exposure groups, the relative whole heart and left ventricular weights were both significantly higher and absolute right ventricular weight was significantly reduced in the 2 hrs/day exposure group (P <0.01 for WH/BW, <0.01 for LV/BW and <0.02 for absolute right ventricular weight).

### Changes in Plasma Renin Activity (PRA):

In table 1 and fig.1-C, compared to the respective control values, PRA was significantly (P <0.01) increased in the 4 weeks-3 hrs/day EMF-exposed rats and in all groups exposed to EMF for 8 weeks (P <0.02 for groups II<sub>1</sub> & II<sub>2</sub> and <0.002 for group II<sub>3</sub>). PRA was significantly (P<0.005) higher in the 8 weeks-1 hr/day exposed rats compared to the corresponding 4 weeks-1 hr/day exposed group.

### Changes in Plasma Calcium:

In table 1 and Fig.1-D, compared to the matched controls, plasma calcium level was significantly reduced in all EMF-exposed groups except for the 4 weeks-1hr/day exposed group (P <0.05 for group I<sub>2</sub>, <0.02 for group I<sub>3</sub>, <0.05 for group II<sub>1</sub>, <0.005 for group II<sub>2</sub> and < 0.002 for group II<sub>3</sub>).

# Changes in Plasma Total Antioxidant Capacity and Cardiac Tissue MDA:

As shown in table 1 and fig.1-E, the plasma total anti-oxidant capacity was significantly decreased in all exposed rats compared to their respective control groups (P <0.005 for groups  $I_1 \& I_2$  and <0.001 for all the other groups).

In the 8 weeks exposed groups, cardiac tissue MDA level showed an increase, which was only statistically significant in the 8 weeks-3hrs /day

exposed group, compared to the matched control group (P < 0.01) (Table 1; Fig. 1-F).

### **Histopathological Changes:**

As shown in fig.5-a, b & c, the wall of the apical region of the left ventricle of the control groups revealed regularly arranged cardiac muscle fibers, appearing branching, anastomosing and running in various directions. The myocardial cells were attached end to end. The nuclei appeared central and vesicular, and the sarcoplasm appeared acidophilic and striated. In transverse section, the cardiac myocytes appeared more or less comparable in size with noticeable myofibrillar content.

The cardiac muscle specimens of rats exposed to EMF for 1hr and 2 hrs/day for 4 weeks exhibited

congestion of blood vessels without apparant affection of cardiac myocytes (Fig.6-a). In rats exposed for 3hrs/day for 4 weeks as well as in all the 8 weeks exposure groups, apparent hypertrophy of many of the cardiac myocytes, with deeply acidophilic sarcoplasm and vesicular nuclei, (Fig.6b&c), was detected, accompanied by mononuclear cellular infiltration of the cardiac muscle (Fig. 7-a). However, distortion of some cardiac myocytes, together with some areas of complete degeneration and fragmentation of the cells was observed (Fig.7b). Loss of the regular arrangement of the cardiac myocytes was observed in the 8 weeks-2 hrs and 3 hrs /day exposure groups (Fig.8-a), together with marked cell vacuolation, particularly in the 8 weeks-3hrs/day EMF-exposed group (Fig.8-b).

Table (1): Changes in heart rate (beats/min), systolic blood pressure (mmHg), plasma renin activity (ng/ml/hr), plasma calcium level (mg/dL) total antioxidant capacity in plasma (mM/L) and cardiac tissue MDA level ( $\mu$ mol /gm wet tissue) in the different studied groups.

		HR	Systolic	Plasma Renin	Plasma	Plasma Total	MDA in	
		(beats/min)	Blood	Activity	Calcium	Antioxidant	Cardiac	
	Group		Pressure	(ng/ml/hr)	Level	Capacity	Tissue (µmol	
			(mmHg)		(mg/dL)	(mM/L)	/gm wet tissue)	
	Control gr.	396	122.46	102.79	10.42	2.66	0.71	
		±7.58	±2.48	$\pm 15.48$	±0.2	±0.02	±0.07	
		(14)	(13)	(11)	(11)	(13)	(12)	
	1hr exposure gr.	408	153.71	117.22	10.04	2.45	0.65	
		±15.05	±2.41	±18.7	±0.17	±0.03	±0.06	
		(14)	(14)	(12)	(12)	(14)	(11)	
4 week	Р	NS	<0.001	NS	NS	<0.005	NS	
Exposure	2hr exposure gr.	394	168.07	147.85	9.91	2.44	0.66	
Groups		±22.02	±0.99	$\pm 17.88$	±0.17	±0.03	$\pm 0.07$	
		(14)	(14)	(13)	(14)	(14)	(8)	
	Р	NS	<0.001	NS	< 0.05	<0.005	NS	
	3hr exposure gr.	404	176.36	168.36	9.87	2.09	0.67	
		±15.12	±1.89	±23.58	±0.15	$\pm 0.1$	±0.03	
		(14)	(14)	(13)	(14)	(14)	(10)	
	Р	NS	<0.001	<0.01	< 0.02	<0.001	NS	
	Control gr.	446	118	128.22	10.31	2.67	0.43	
		±16.31	±4.32	±15.42	±0.17	±0.01	±0.08	
		(14)	(13)	(13)	(13)	(13)	(9)	
	1hr exposure gr.	455	152.79	187.26	9.87	2.38	0.65	
		±15.88	±3.21	±12.52	±0.12	±0.02	±0.09	
8 week		(14)	(14)	(13)	(14)	(14)	(10)	
Exposure	Р	NS	<0.001	< 0.02	< 0.05	<0.001	NS	
Groups	P*	<0.05	NS	<0.005	NS	NS	NS	
	2hr exposure gr.	376	171.29	189.4	9.69	2.36	0.68	
		±15.37	±3.18	$\pm 14.11$	±0.14	±0.03	±0.13	
		(14)	(14)	(13)	(14)	(14)	(9)	
	Р	<0.005	<0.001	< 0.02	< 0.005	<0.001	NS	
	P*	NS	NS	NS	NS	NS	NS	
	3hr exposure gr.	395	187.79	209.3	9.56	2.06	0.81	
		±17.84	±2.88	±13.89	$\pm 0.11$	±0.07	±0.15	
		(14)	(14)	(13)	(12)	(14)	(9)	
	P	<0.05	<0.001	< 0.002	< 0.002	<0.001	<0.01	
	P*	NS	< 0.005	NS	NS	NS	NS	

In parenthesis is the number of rats studied in each group.

P: Significance by LSD at P <0.05 from control group.

P\*: Significance by LSD at P <0.05 of 8 week groups from respective 4 week groups.

NS: Not significant. gr.: group.

Values are expressed as means  $\pm$ SEM.

		P wave	PR	R voltage	QRS	T wave	QT-c
Group		Voltage	interval	(μV)	duration	voltage	Interval
	-	(μV)	(msec.)		(msec.)	( <b>µV</b> )	(msec.)
	Control gr. (13)	107.69	46.15	584.62	30.77	207.69	217.15
	_	±5.21	±2.67	$\pm 38.97$	$\pm 2.88$	±12.46	±8.57
	1hr exposure gr.	114.29	44.29	607.14	34.29	214.29	240.79
	(14)	±6.27	±2.28	$\pm 50.78$	±2.51	±12.21	±11.53
4 week	Р	NS	NS	NS	NS	NS	NS
Exposure	2hr exposure gr.	107.14	47.14	635.71	37.86	217.86	237.93
Groups	(14)	±10.29	±2.66	±35.71	±1.14	±17.86	±9.81
	Р	NS	NS	NS	<0.05	NS	NS
	3hr exposure gr.	103.57	44.29	728.57	37.86	192.86	246.29
	(14)	±6.34	±2.28	±46.21	$\pm 3$	±4.85	$\pm 8.68$
	Р	NS	NS	<0.02	<0.05	NS	<0.05
	Control gr. (13)	115.38	43.08	546.15	23.85	207.69	226.31
		±6.66	$\pm 2.08$	±24.33	±1.4	±11.1	±10.06
	1hr exposure gr.	132.14	50	592.86	32.86	221.43	247.07
	(14)	±8.46	±2.77	±19.51	±1.63	±13.58	±8.23
8 week	Р	NS	NS	NS	<0.005	NS	NS
Exposure	<b>P</b> *	NS	NS	NS	NS	NS	NS
Groups	2hr exposure gr.	132.14	52.86	664.29	33.57	260.71	255.71
	(14)	±11.25	±2.66	$\pm 41.41$	±2.25	±15.88	±7.63
	Р	NS	<0.01	<0.05	<0.005	<0.01	<0.05
	P*	<0.05	NS	NS	NS	<0.05	NS
	3hr exposure gr.	121.43	57.14	742.86	37.14	260.71	259.29
	(14)	±8.64	±2.86	±45.35	±1.25	±15.88	$\pm 7.81$
	Р	NS	<0.001	<0.002	<0.001	<0.01	<0.02
	<b>P</b> *	NS	<0.001	NS	NS	<0.002	NS

### Table (2): Changes in ECG waves and segments in the different studied groups.

In parenthesis is the number of rats studied in each group.

Values are expressed as means  $\pm$ SEM.

P: Significance by LSD at P <0.05 from control group.

P\*: Significance by LSD at P <0.05 of 8 week groups from respective 4 week groups.

NS: Not significant.

gr.: group.

Group		BW	WH	WH/BW	At	At/BW	RV	RV/BW	LV	LV/BW
	-	(g)	(mg)	(mg/g)	(mg)	(mg/g)	( <b>mg</b> )	(mg/g)	(mg)	( <b>mg</b> / <b>g</b> )
	Control gr.	196.92	511.95	2.607	33.43	0.171	66.09	0.336	411.93	2.095
	(12)	±3.34	$\pm 8.95$	±0.047	$\pm 4$	±0.022	±2.7	±0.014	$\pm 8.92$	$\pm 0.042$
	1hr exposure gr.	209.5	558.57	2.674	40.18	0.205	63.55	0.304	456.84	2. 185
	(10)	±3.53	±12.01	±0.075	±6.12	±0.031	±3.91	±0.182	±11.76	$\pm 0.063$
4 week	Р	NS	NS	NS	NS	NS	NS	NS	NS	NS
Exposure	2hr exposure gr.	216.25	653.24	3.017	32.31	0.148	65.94	0.304	554.99	2.565
Groups	(8)	±3.37	$\pm 38.1$	±0.164	$\pm 5.07$	±0.022	±5.1	±0.022	±33.52	$\pm 0.148$
	Р	NS	<0.001	<0.05	NS	NS	NS	NS	<0.001	<0.01
	3hr exposure gr.	191.3	627.5	3.281	29.37	0.153	61.57	0.324	536.56	2.804
	(10)	±6.27	±26.91	±0.083	$\pm 7.03$	±0.036	±3.96	±0.022	±23.61	$\pm 0.071$
	Р	NS	<0.001	<0.001	NS	NS	NS	NS	<0.001	<0.001
8 week Exposure Groups	Control gr.	203.33	548.94	2.739	39.67	0.197	75.51	0.376	437.52	2.183
	(9)	±9.75	±12.03	±0.116	±3.4	±0.017	±4.56	±0.025	±9.32	±0.09
	1hr exposure gr.	208.5	600.64	2.935	33.18	0.164	71.62	0.342	495.84	2.43
	(10)	±10.11	±19.62	±0.155	$\pm 3.51$	±0.021	±5.57	±0.023	±18.69	±0.151
	Р	NS	NS	NS	NS	NS	NS	NS	<0.05	NS
	<b>P</b> *	NS	NS	NS	NS	NS	NS	NS	NS	NS
	2hr exposure gr.	168.33	593.23	3.598	34.32	0.207	47.96	0.285	509.96	3.106
	(9)	±11.18	±20.17	±0.176	±4.42	±0.027	$\pm 6.8$	±0.032	$\pm 14.87$	±0.168
	Р	<0.002	NS	<0.001	NS	NS	<0.001	<0.01	<0.01	<0.001
	<b>P</b> *	<0.001	NS	<0.01	NS	NS	<0.02	NS	NS	<0.01
	3hr exposure gr.	175.56	611.29	3.531	32.6	0.186	58.74	0.331	519.94	3.014
	(9)	±5.86	±17.83	±0.196	±4.17	±0.024	±6.16	±0.029	±22.51	±0.211
	Р	<0.02	<0.05	<0.001	NS	NS	<0.05	NS	<0.005	<0.001
	<b>P</b> *	NS	NS	NS	NS	NS	NS	NS	NS	NS

Table (3): Changes in body weight, absolute cardiac weights (mg) and relative weights (mg/g) of whole heart (WH), atria (At), right ventricle (RV) and left ventricle (LV) and in the different studied groups.

In parenthesis is the number of rats studied in each group.

Values are expressed as means ±SEM. N

NS: Not significant. gr.: group.

P: Significance by LSD at P <0.05 from control group.

P\*: Significance by LSD at P <0.05 of 8 week groups from respective 4 week groups.



**Fig.(1):** Heart rate  $(1_A)$ , systolic blood pressure  $(1_B)$ , plasma renin activity  $(1_C)$ , plasma calcium level  $(1_D)$ , plasma total antioxidant activity  $(1_E)$  and cardiac MDA level  $(1_F)$  in the different studied groups. a: Significance by LSD at P<0.05 from respective control group.

b: Significance by LSD at P<0.05 of 8 week groups from respective 4 week groups.

4 weeks Control group	21 21 21
4 weeks -2 hrs/day exposure group	 
4 weeks -3 hrs/day exposure group	Mullhhleldeldeldeldeldeldeldeldeldeldeldeldeld

**Fig.(2):** ECG tracings of rats exposed to EMF for 4 weeks (prolonged QRS duration in 2 hrs/day group and higher R voltage & prolonged QRS duration in 3 hrs/day groups relative to control group).



**Fig.(3):** ECG tracings of rats exposed to EMF for 8 weeks (prolonged QRS duration in 1 hr/ day group, decreased heart rate, prolonged PR interval, prolonged QRS duration and higher R and T voltage in 2 hrs and 3 hrs / day groups).

a

a



QT-<sub>C</sub> interval



**Fig. (5):** Photomicrograph of control rat cardiac muscle showing regularly arranged cardiac muscle fibers (**5-a**), nuclei appeared central and vesicular and their sarcoplasm appeared acidophilic (**5-b**). The cardiac myocytes in transverse section appeared more or less comparable in size with noticeable myofibrillar content (**5-c**).



**Fig.(6):** photomicrograph ,in 1hr &2hr.4week exposed rats , showing congestion of blood vessels and extravasation of RBCs \* (**6-a**), in 3hr .4w & all exposed subgroups in 8 w group showing hypertrophy of many of the cardiac myocytes with deeply acidophilic sarcoplasm and vesicular nuclei (L.S) (**6-b**) &(T.S) (**6-c**).



**Fig.(7):** photomicrograph in 3hr .4w & all exposed subgroups in 8 w group showing mononuclear cellular infiltration (7-a) and distortion of some cardiac myocytes, together with some areas of complete degeneration and fragmentation (7-b).



**Fig.(8):** Photomicrograph showing loss of the regular arrangement of the cardiac myocytes being most prominent in 2 hrs & 3 hrs subgroups in the 8 weeks group (8-a) ,and marked cell vacuolation in the different groups in particular. in 8 weeks -3hrs EMF-exposed groups (8-b).

### 4. Discussion:

Exposure to cell phone EMF caused significant increase in the systolic blood pressure in all test groups, the pressure being higher with prolonged exposure, together with decreased heart rate only in the groups exposed for longer periods. The observed increase in blood pressure, in the present study, could be the result of increased plasma renin activity (PRA), which was increased in all the exposed groups, though the increase was only statistically significant in the 4 weeks-3hrs/ day exposed group as well as all the groups exposed to the cell phone EMF for 8 weeks.

Also, the absolute and relative whole heart and left ventricular weights were increased, particularly in the groups exposed to EMF for longer periods indicating hypertrophic changes. The increased blood pressure encountered in this study could explain the changes in absolute and relative cardiac weights. Earlier, it was stated that one of the early and most common consequences of chronic hypertension is left ventricular hypertrophy (LVH), and that the renin-angiotensin system contributes to the development of LVH in hypertension<sup>(42,43)</sup>.

The observed increase in blood pressure agrees with the earlier study which reported that mobile phones caused a rise of blood pressure of 5-10 mmHg each time of exposure <sup>(25)</sup>. Also, a recent study demonstrated that blood pressure in rats was increased through hours after exposure to mobile phone EMF <sup>(27)</sup>. The present findings

disagree, however, with another study which stated that exposure to mobile phone EMF did not affect

significantly the blood pressure, heart rate or cardiac electrical activity <sup>(44)</sup>.

In addition, the R wave and T wave voltages as well as the P-R and  $QT_{-C}$  intervals were all increased in the groups exposed for longer periods while the QRS duration was prolonged in almost all groups. The increased R wave voltage observed in the 4 weeks-3hrs/day exposed group and in the 8 weeks-2hrs & 3hrs /day exposed groups could be due to the increased thickness of the left ventricular wall. This left ventricular hypertrophy, evident also from the histopathological examination, could explain the higher T wave voltage observed in the 8 weeks-2hrs & 3hrs /day exposure groups.

The present study revealed, also, reduction in the heart rate in the 8 weeks-2hrs &3hrs/day exposed groups (groups II<sub>2</sub>&II<sub>3</sub>), i.e. occurring in rats subjected to longer durations of exposure to EMF. This reduced heart rate could possibly be explained by an increase in parasympathetic tone in these rats. In a previous study, the parasympathetic tone was suggested to be increased, while the sympathetic tone was lowered in humans during cell phone call, thus modifying the functioning of circulatory system <sup>(29)</sup>. Further, the reduced heart rate could be due to the associated increase in plasma renin activity. High concentration of renin-angiotensin II was reported to lead to significant baroreceptor- mediated bradycardia <sup>(45)</sup>.

The prolonged P-R interval observed in the present study in groups  $II_2$  and  $II_3$  could be explained by the increased tone of the parasympathetic system, or possibly as a result of the encountered hypocalcaemia which cause diminished conduction velocity in the heart (46)

The significantly prolonged  $QT_{-C}$  interval in the groups with prolonged exposure to EMF could be attributed to the associated increased renin activity that was reported to remodel the cardiac ion channels, resulting in prolongation of ventricular repolarization and thus prolongation of  $QT_{-C}$  interval <sup>(47)</sup>.

The observed significant hypocalcaemia associated with exposure to EMF occured as a result of alteration of intracellular signaling pathways resulted from RF radiation exposure through changes in Ca<sup>2+</sup> permeability across cell membranes <sup>(21)</sup>. It has been reported that calcium positive ions strengthen cell membranes because they bind together the negatively-charged phospholipid molecules, and that electromagnetic radiation could lead to the replacement of calcium with monovalent ions that weakens the membrane and makes it more likely to tear and form pores <sup>(48, 49)</sup>. Thus, the observed hypocalcemia, in this study, might be one of the mechanisms by which EMF interacts with biological tissues that RF radiation from cell phone could alter.

The present findings also revealed significant decrease in plasma total antioxidant capacity in all exposed groups. As, acute exposure to RF fields of cell phones could modulate the oxidative stress and free radical generation by enhancing lipid peroxidation and reducing the activation of SOD and GSH-Px, free radical scavengers <sup>(50)</sup>. Further, RF-EMF exposure was reported to cause production of extracellular superoxide <sup>(51)</sup>. So the decrease in plasma total antioxidant capacity encountered in this study might be the result of its exhaustion in defending the free radical believed to be generated with RF-EMF.

The significantly increased cardiac MDA content encountered in the present study in the 8 weeks-3hrs/day exposed group, with the longest duration of exposure (144hr), points to the limits of the cardiac antioxidants to cope with the excessive MDA generation due to RF-EMF exposure.

The significant increase in cardiac tissue MDA level with prolonged EMF exposure to from cell phone, in this study, was in agreement with other studies <sup>(52,53)</sup>. It has been suggested that increased total oxidant status levels due to RF radiation emitted from GSM cell phones might play a role in inducing oxidative damage by increasing lipid peroxidation and oxidative stress <sup>(54, 55)</sup>.

The forementioned effect of RF-radiation in generation of free radicals, increased lipid peroxidation and tissue damage could possibly explain the vascular congestion with the shorter duration of exposure, namely the 4 weeks- 1hr & 2hrs/day exposed rats (groups  $I_1 \& I_2$ ). A recent study on rats exposed to cell phone 1hr/day for 4 weeks demonstrated congestion of blood vessels and extravasation of RBCs in the myocardium, together with disruption of few cardiac fibers. These findings were suggested to be due to free radical generation with EMF <sup>(56)</sup>.

The hypertrophic myocardial changes observed in the present study, which were especially related to the longer duration of exposure, could be explained by the associated increased blood pressure in these groups.

### 5. Conclusion:

The results encountered in the present study revealed that long-term exposure to cell phone EMF increases the liability for hypertension reflected on the ECG and cardiac weights, accompanied by histological changes in the myocardium. Also, the associated increased PRA, decreased plasma total antioxidant capacity and hypocalcemia could be suggested as contributing mechanisms reflecting interaction of EMF with biological functions.

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