

Review Article

Exposure to electromagnetic fields induces pathophysiological changes and oxidative stress in the cardiovascular system

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Abstract: This study aimed to highlight on the influence of exposure to electromagnetic fields (EMFs) on the cardiovascular system in humans and experimental animals, from the recent articles regarding the cardiovascular effects of exposure to EMFs. EMFs might produce a variety of adverse in vivo effects such as heart problems, chest pain, and cardiovascular system disorders. Previous studies showed that an association between elevated magnetic field exposure and mortality of employer in electric utility industry jobs from arrhythmia-related causes and acute myocardial infarction influence heart rate variability by changing autonomic balance. EMF exposure can affect structure and function of cardiovascular system and may facilitate myocardial infarction by nuclear changing of cardiomyocytes. Exposure to EMFs induced pain or pressure in the chest area, heart palpitations, and/or an irregular heart beat. The symptoms resemble a heart attack and thus contribute to even more anxiety. Also, exposure to EMFs caused highly significant increases in the activities of serum creatinine phosphokinase, lactate dehydrogenase and aspartate amino-transferase enzymes, and decreases in plasma calcium level and total anti-oxidant capacity. Rats exposed to EMF showed increases in blood pressure, the absolute and relative whole heart and left ventricular weights. On the other hand, the heart rate was significantly reduced in rats exposed to EMF. The ECG recording of experimental animals exposed to EMF showed a significantly higher R and T voltages, increase in QRS duration, and prolonged P-R and QT-c intervals. A serious histopathological changes in the heart were seen in experimental animals exposed to EMFs, these changes includes increases the number of apoptotic cells, dark brown stain muscle fiber nuclei, marked cell vacuolation, hyperemia muscle fiber degeneration, distortion of some cardiac myocytes, mononuclear cellular infiltration and histological structure of the myocytes spaces were seen. Ultra structural of the myocardial tissue and sarcomere in experimental animals exposed to EMFs showed that lose of area in sarcomeres, irregular structural of myocardial cells, and ruptures of sarcomeres, lose of mitochondria cristae, blebs of mitochondria. It can be concluded that exposure of human and experimental animals to EMFs have been a negative effect on the heart and blood vessels by causing a histopathological changes and disturbances in the functions of the organs of the cardiovascular system.

Keywords: Cardiovascular system, EMF, Heart function, Histopathology, Ultrastructure, ECG, Oxidative stress.

INTRODUCTION

The use of electrical devices has gradually increased throughout the last century, and scientists have suggested that electromagnetic fields (EMF) generated by such devices may have harmful effects on living creatures [1]. The natural electromagnetic sources are includes sun, some distant stars, atmospheric discharges like thunder, or human body, and unnatural or human made sources are includes printers, vacuum cleaners, cellular phones, hair dryers, refrigerators, washing machines, kettles microwaves, cables that carry electrical currents, television and computers, electrical home gadgets, radio and television base stations, mobile phone base stations and phone equipment, home wiring airport, and transformers [2-6]. The most frequent sources of non-ionizing radiation

(NIR) are mobile phones and cell towers which emit microwave radiation (MWR). They emit radiofrequency electromagnetic waves (RF-EMW) [7-9]. WiFi routers emit a beacon signal that is continuous as long as the device is activated. When information is either uploaded or download, the radiation levels increase both at the router and at the computer. The same is true for cordless phones and wireless baby monitors [10]. Any electrical device can be a source of electromagnetic field (EMF). Radiofrequency (RF) energy is a type of nonionizing radiation that is not strong enough to cause ionization of atoms and molecules [11, 12]. Low level of EMF can emit by cellular phones, so because of global using of this device; estimation of the unforeseen risks from mobile communication has become a social and ethical

problem. As electromagnetic wave (EMW) enters the tissue, its speed and wavelength changes depending upon the electrical properties of the tissue environment. EMW has two types of effects; thermal and nonthermal [1, 13, 14].

Cardiac muscle cells are especially differentiated to transmit electrical stimuli, with myocardial cells enabling the heart to contract, sinoatrial and atrioventricular nodule cells creating the electrical stimulus, and endocardial cells spread the ventricles inward. These heart cells have four important physiological features: inducibility, contractibility, autonomy, and transmissibility [1, 15]. Because of its inducibility, changes in the contraction and rhythm of the heart can result from external stimuli. It is possible for EMF to affect heart function by influencing these physiological features [1]. Development of various heart diseases and daily exposure with EMF, hypothesized an association between exposure to magnetic fields and acute cardiovascular disease [12]. At greater EMF strengths or shorter exposures, the ability of the body to develop compensation mechanisms is reduced and the potential for heart-related effects increases [1]. The main effects of electromagnetic fields have increased body temperature. High temperatures and cause damage to internal body organs, vessels, internal bleeding causes. In fact, one of the mechanisms that cause cell damage, which is why hypothermia [9, 16, 17]. With the impact of EM fields, body atoms and molecules may lose the electrical balance between them, biochemical activities may be affected and electrical structure in the communication of cells and tissues may be disrupted [18, 19]. The EMF penetrate the human body and act ions on all organs, altering the cell membrane potential and the distribution of ions and dipoles [20-23]. Chemical and physical processes at the atomic level are the bases of reactions between biomolecules in an EMF, since the field can magnetically affect the chemical bonds between adjacent atoms with consequent production of free radicals [23-26].

Students in schools with WiFi are complaining of headaches, dizziness, nausea, vomiting, insomnia, blurred vision, difficulty concentrating, weakness, and heart palpitations. In the same area, 4 students had sudden cardiac arrests during exercise class within a 2-year period. When other students moved to a different school his symptoms disappeared [10]. Acute cardiovascular changes in humans deliberately exposed to RFEMF are documented in studies relating to magnetic resonance imaging (MRI) and, at higher levels, of RFEMF used to deliberately destroy myocardial tissue in cardiac ablation therapy [27]. Some people who are electrically hypersensitive complain of pain or pressure in the chest area, heart palpitations, and/or an irregular heartbeat, accompanied by feelings of anxiety that develop rapidly. The symptoms resemble a heart attack and thus contribute to

even more anxiety [10]. People who lived closest to the antennas of mobile phone base stations experienced the following symptoms more often than those who lived further away: cardiovascular problems, loss of appetite, headaches, dizziness and nausea, fatigue, feeling of discomfort, movement difficulties, depression, sleep disturbance, hearing disruptions, visual disruptions, difficulty concentrating and memory loss, irritability, and skin problems [10, 28]. Studies have shown that mammalian and human cells that electromagnetic radiation generated free radicals cause oxidative stress and impaired antioxidant system and genotoxic effect [9, 29].

Effects of EMF on Heart function

Olson and David, [30] reported an elevation in CK, LDH and GOT after exposure to radiofrequency. Zhang *et al.*, [31] reported that, electromagnetic shield applied to volunteers showed a highly significant effect on serum level of creatinine phosphokinase. Yuan *et al.*, [32] have seen increased levels of LDH in the serum of volunteers occupationally exposed to very high frequency radiations. These observations indicate that exposure to the radiofrequency radiation increases cell death and changes the homeostasis of the tissue [33]. Peppes *et al.*, [34] showed the significant positive correlations between angiographic findings, and peak serum myocardial enzyme levels (CPK, AST, and LDH), and inflammatory biomarkers were identified. Therefore, due to result in this study the effect of radiation increased cardiac enzymes in the exposed group and can be suggested that cardiovascular disease increased in this group. Also, Aberumand *et al.*, [9] reported that male white mice exposed to the phone calls 10 times, each time for 10 minutes per day for one month showed that creatine phosphokinase, LDH, AST and high-density lipoprotein which reflect cardiac function were increased and a different pathological damage in the heart in the group exposed mobile ray compared to control group. The mobile radiation is harmful effects on enzyme activity and tissue. Exposure to electromagnetic fields is responsible for changes in enzyme and can effected on healthy. In additon, Jeong *et al.*, [35] reveals an association between elevated magnetic field exposure and mortality of employer in electric utility industry jobs from arrhythmia-related causes and acute myocardial infarction (AMI). Also, Savitz *et al.*, [36] recorded that a higher mortality due to arrhythmia or acute myocardial infarction in workers who are exposed to high magnetic field for a longer time. Roshangar *et al.*, [37] concluded that EMF exposure can affect structure and function of cardiovascular system and may facilitate myocardial infarction by nuclear changing of cardiomyocytes.

This may be due to that magnetic fields interact with moving charges in cells and change their velocities [38]. However, Cell membranes have been identified as a primary site of interaction with the low frequency fields [39]. Therefore, the alterations in these

charges and molecules consider the first step in the production of biological effects as magnetic field interact with moving charges and change enzymatic activity [40]. In addition, EMF may regulate the rate and the amount of product of biochemical reaction possibly through free radical mechanism including direct influence on enzyme action [24].

Effect of EMF on heart rate and blood pressure

Belliemi *et al.* [41] found that EMF generated by incubators can alter heart rate variability in newborns specially in pretermes. Study of Andrzejak *et al.*, [42] demonstrated that the mobile phone may influence heart rate variability by changing autonomic balance. Jeong *et al.*, [35] showed 1-day exposure to ELF-EMF suppressed the values of QT intervals in ECG by affecting ventricular repolarization and increased basal HR. During the exposure to radiation from the cordless phone base station, subject experienced a slight increase in heart rate (from 65 to 86 bpm), an irregular heart beat, and changes in the response of the sympathetic and parasympathetic nervous system (SNS and PNS), respectively. This upregulation of the SNS and down regulation of the PNS is an example of the “fight-or-flight” response, indicating physiologic stress. During periods of this type of stress, the body redirects most of the blood and energy from the internal organs to the arms and legs to prepare the organism for fighting or fleeing a stressful situation. Intermittent exposure may not cause a problem but if the exposure is continuous and long-term, the immune system of the body will be compromised and the body will not be able to repair itself, resulting in symptoms that are commonly experienced by those who are electrically hypersensitive. This inability to heal is what then accelerates the symptoms of aging [10]. When students with Wolff-Parkinson- White syndrome are exercising and are exposed to microwave radiation, the combined stress on the heart can lead to supraventricular tachycardia [10, 43]. Mohamed *et al.*, [44] reported that rats exposed to cell phone EMF for 2hrs or 3hrs/day for 4 and 8 weeks showed that the heart rate was significantly reduced. Reduction in the heart rate could possibly be explained by an increase in plasma renin activity and parasympathetic tone in these animals [44]. Andrzejak *et al.*, [42] reported that the sympathetic tone was lowered, while parasympathetic tone was suggested to be increased in humans during cell phone call, thus modifying the functioning of circulatory system. High concentration of renin-angiotensin II was reported to lead to significant baroreceptor-mediated bradycardia [45].

Braune *et al.*, [46] reported that mobile phones caused a rise of blood pressure of 5-10 mmHg each time of exposure. Li *et al.*, [47] found that blood pressure in rats was increased through hours after exposure to mobile phone EMF. Mohamed *et al.*, [44] reported that rats exposed to cell phone EMF for 4 and

8 weeks showed that systolic blood pressure was significantly increased. In all EMF-exposed rats compared to their controls. The observed increase in blood pressure, could be the result of increased plasma renin activity (PRA), which was increased in all the exposed groups. 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 [44, 48, 49]. Mohamed *et al.*, [44] recorded that rats exposed to cell phone EMF for 4 and 8 weeks for either 1h/day, 2hrs/day or 3hrs/day, exposure being carried out six days/ week, at fixed time of the day showed that 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. The hypertrophic myocardial changes could be explained by the associated increased blood pressure in these groups [44]. On the other hand, Soviet researchers reported indications that long term RFEMF may cause hypotension and bradycardia or tachycardia, but these findings have not been replicated elsewhere in humans [27].

Effect of EMF on heart weight:

Mohamed *et al.*, [44] reported that rats exposed to cell phone EMF for 4 and 8 weeks showed that 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.

Effect of EMF on the microscopical structure of the heart:

Previous studies showed that some pathological damages in heart include inflammation, hemorrhage, and congestion [9, 12, 50, 51]. Khaki and Khaki, [12] reported that heart ventricular section from a Wistar male rat exposed to EMF (50 Hz) for 40 consecutive day shows increasing in dark brown stain muscle fiber nuclei, number of apoptotic cells, hyperemia muscle fiber degeneration, and histological structure of the myocytes spaces were seen. Programmed cell death (Apoptosis) is characterized by shrinkage of the cell and the nucleus. The nuclear chromatin is condensed into sharply delineated masses, and eventually breaks up. Mohamed *et al.*, [44] revealed that the cardiac muscle specimens of rats exposed to cell phone EMF for 4 weeks for either 1h/day, 2hrs/day showed that exhibited congestion of blood vessels without apparent affection of cardiac myocytes. 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, were detected, accompanied by mononuclear cellular

infiltration of the cardiac muscle. However, distortion of some cardiac myocytes, together with some areas of complete degeneration and fragmentation of the cells were observed. Loss of the regular arrangement of the cardiac myocytes was observed in the 8 weeks-2 hrs and 3 hrs /day exposure groups, together with marked cell vacuolation, particularly in the 8 weeks- 3hrs/day EMF-exposed group. Aberumand *et al.*, [9] reported that the cardiac muscle of male white mice exposed to the phone calls 10 times, each time for 10 minutes per day for one month showed that congestion of blood vessels and extravasations of RBCs. In addition, disruption of few fibers and hypertrophy of many of the cardiac myositis with condense nuclei was detected, accompanied by infiltration of inflammatory cells. Oxidative stress through H₂O₂ and the NO donor, N-acetyl-Snitroso- DL-penicillinamide (SNAP), induced apoptosis in ventricular cardiomyocytes isolated from a rat heart [12]. Also, Hanafy *et al.*, [50] reported that the effect of RF-radiation in generation of free radicals, increased lipid peroxidation and tissue damage with vascular congestion that aggregate of blood vessels and extravasation of RBCs in the myocardium, together with the disruption of few cardiac fibers. It is believed that EMF with high energy waves cause the rise of local temperature where these waves contact together and like ionizing rays lead to the formation of free radicals and create their destructive effects. Free radicals attack lipids, changing in their nature and breaking protein bounds cause cell damage [50, 52, 53]. Also, Khaki *et al.*, [54] reported that cellular damage caused by oxidative stress of exposure to electromagnetic radiation can induce apoptosis in various tissues of the body.

Effect of EMF on the ultra structure of the heart

Ultra structural study of the myocardial tissue and sarcomere of Wistar male rat exposed to EMF (50 Hz) for 40 consequence day, were showed that lose of mitochondria, blebs of mitochondria, lose of area in sarcomeres and irregular structural of myocardial cells, sarcomeres were ruptures. Authors suggested that necrosis is present by the quick loss of cellular homeostasis, fast swelling as a result of the accumulation of water, electrolytes and starts with plasma membrane rupture and cause to the disruption of cellular organelles [12].

EMF induce oxidative stress

Reactive oxygen species (ROS) are natural consequences of oxidative cell metabolism. Over production of ROS and imbalance of oxidant/antioxidant system are effective factors in the oxidative stress of cellular structures such as lipids, proteins and nucleic acids [55]. Various environmental factors may intervene in this Phenomenon including longterm exposure to ELF-MF [56]. Free radical scavenging enzymes such as catalase, superoxide dismutase (SOD), glutathione peroxidase (GPX) are the first line cellular defense against oxidative injury [57].

Animal studies conducted significant decrease in total antioxidant activity such as SOD , GPX , vitamins E and A concentrations and increase of MDA (a product of polyunsaturated fatty acid peroxidation and used as an indicator of oxidative stress in cells and tissues) and plasma selenium concentration in erythrocytes and plasma after EMF exposure [58].

Acute exposure to RF fields of cell phones could modulate the oxidative stress and free radical generation by production of extracellular superoxide [59], enhancing lipid peroxidation and reducing the activation of SOD and GSH-Px, free radical scavengers [60]. Mohamed *et al.*, [44] concluded that rats exposed to cell phone EMF for 4 and 8 weeks for either 1h/day, 2hrs/day or 3hrs/day, exposure being carried out six days/ week, at fixed time of the day showed that 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. So the decrease in plasma total antioxidant capacity 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, points to the limits of the cardiac antioxidants to cope with the excessive MDA generation due to RFEMF exposure [61, 62]. 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 [63, 64].

Effect of EMF on ECG

Mohamed *et al.*, [44] reported that 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 QRS duration in the groups exposed for 2hrs and 3hrs/day and significant prolongation of QT-c interval in the group exposed for 3hrs/day. The ECG recording of rats exposed to EMF for 8 weeks revealed significantly higher R and T voltages, and significantly prolonged P-R and QT-c intervals in the groups exposed for 2hrs or 3hrs/day, the QRS duration being significantly increased in all the 8 weeks- exposed groups. The increased R wave voltage observed 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 [44].

Mohamed *et al.*, [44] found that rats exposed to cell phone EMF for 4 and 8 weeks for either 1h/day, 2hrs/day or 3hrs/day, showed that plasma calcium level was significantly decreased in all the exposed groups. Hypocalcemia might be one of the mechanisms by

which EMF interacts with biological tissues that RF radiation from cell phone could alter [60]. The observed significant hypocalcaemia associated with exposure to EMF occurred as a result of alteration of intracellular signaling pathways resulted from RF radiation exposure through changes in Ca²⁺ permeability across cell membranes [65]. 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 [66, 67]. The prolonged P-R interval 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 [44, 68]. 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 [69].

CONCLUSION

It can be concluded that exposure of human and experimental animals to EMFs have been a negative effect on the heart and blood vessels by causing a histopathological changes and disturbances in the functions of the organs of the cardiovascular system. This may be due to that magnetic fields interact with moving charges in cells, change their velocities and altering the cell membrane potential and the distribution of ions and dipoles. The alterations in these charges and molecules consider the first step in the production of biological effects as magnetic field interact with moving charges and change enzymatic activity. EMFs may regulate the rate and the amount of product of biochemical reaction possibly through free radical mechanism including direct influence on enzyme action.

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