Environmental Research 163 (2018) 71–79

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Genotoxic and carcinogenic effects of non-ionizing electromagnetic fields

Adem Kocaman*, Gamze Altun, Arife Ahsen Kaplan, Ömür Gülsüm Deniz, Kıymet Kübra Yurt, Süleyman Kaplan

Department of Histology and Embryology, Medical Faculty, Ondokuz Mayıs University, Samsun, Turkey

ARTICLE INFO

Keywords:
Electromagnetic field
Frequency
Carcinogenic
Genotoxic

ABSTRACT

New technologies in electronics and communications are continually emerging. An increasing use of these electronic devices such as mobile phone, computer, wireless fidelity connectors or cellular towers is raising questions concerning whether they have an adverse effect on the body. Exposure to electromagnetic fields (EMF) is frequently suggested to have adverse health effects on humans and other organisms. This idea has been reported in many studies. In contrast, the therapeutic effects of EMF on different organs have also been reported. Research findings are inconsistent. This has given rise to very profound discrepancies. The duration and frequency of mobile phone calls and the association observed with various health effects has raised serious concerns due to the frequency with which these devices are used and the way they are held close to the head. The present review assesses the results of *in vitro*, *in vivo*, experimental, and epidemiological studies. The purpose of the study is to assess data concerning the carcinogenic and genotoxic effects of non-ionizing EMF. The major genotoxic and carcinogenic effects of EMF, divided into subsections as low frequency effects and radiofrequency effects, were reviewed. The inconsistent results between similar studies and the same research groups have made it very difficult to make any comprehensive interpretation. However, evaluation of current studies suggests that EMF may represent a serious source of concern and may be hazardous to living organisms.

1. Introduction

With the impact of the globalization, the world has entered a time of change and development. This is leading to rapid population growth and energy consumption (Asumadu-Sarkodie and Owusu, 2016). Fast growing wireless broadband and communication technologies have become the main source of global pollution by creating threats to the environment and human life, while at the same time providing concrete solutions to the emerging needs of globalization (Milner et al., 2012). Today, with the widespread use of electric devices, electromagnetic fields (EMF) have become a particularly important global phenomenon, and one that is creating concerns and worries among many people (Miclaus and Calota, 2010; Stather, 1997).

EMF consists of both electric and magnetic fields of force (Phillips, 2013). It was first discovered during the 19th century (Berkson, 2000), however, it has been present since life first emerged, due to its generation *via* natural phenomena (Sher, 1997). All living things are continuously exposed to EMF from natural sources at levels between 25 μT and 65 μT (Gould, 1984). In addition to natural sources of EMF, living organisms are also exposed to EMF generated by human-made sources, such as cell phones, cell phone base stations, radio stations, computer screens and many other electrical devices widely used in daily life (Berg, 1992).

The question of whether exposure to EMF is beneficial or hazardous is still the subject of much debate. This debate is encouraging research to determine whether or not it is safe to live with constant exposure to EMF (Kheifets and Ritz, 2006). Numerous studies have shown the impact of EMF on animals, tissues (Aydin and Akar, 2011; Sonmez et al., 2010), and the functional features of cells (Koch et al., 2003; Liburdy et al., 1993), but the findings are still considered preliminary. In contrast, many studies have reported therapeutic effects of EMF on various organs and body systems, including reversal of cognitive impairment in Alzheimer's disease (AD) (Arendash et al., 2010), stimulation of the repair mechanism in bone and cartilage (Bai et al., 2013; Haddad et al., 2007; Trock et al., 1994), wound healing, and nerve regeneration (Mohammadi and Mahmoodzadeh, 2015).

Some of the main features of EMF are its frequency and wavelength, both of which interact with living organisms in different ways (Grimes and Grimes, 2002; Panagopoulos et al., 2002). The biological effects of EMF depend on the frequency or wavelength. The purpose of this review is to summarize and analyze existing studies that describe the association between EMF and their carcinogenic and genotoxic effects on living organisms. A secondary aim is to contribute to the current debate on the possible impacts of EMF, and whether or not EMF exposure is dangerous to humans.

* Corresponding author.
E-mail address: adem.kocaman@omu.edu.tr (A. Kocaman).

https://doi.org/10.1016/j.envres.2018.01.034
Received 21 September 2017; Received in revised form 14 January 2018; Accepted 23 January 2018

In the first section, EMF and its main ranges are explained. Frequencies and wavelengths are described and differences set out. Then, non-ionizing range is divided into subsections based on frequency. Within the subsections, existing experimental and epidemiological studies are reviewed in terms of genotoxic and carcinogenic effects.

2. Classification of EMFs

EMF is produced by electrically charged objects and may be defined as a combination of electric fields (EF) and magnetic fields (MF). Electromagnetic waves are carried by particles known as photons (quanta) (Feynman, 1974). EMF exhibits its characteristic features *via* the interrelated parameter of wavelength and frequency. Frequency is measured in terms of number of oscillations per second (hertz) and wavelength describes the distance between one wave and the next, measured in meters. As the frequency increases, the wavelength becomes shorter and carries more energy compares to lower frequency waves (Hackmann, 1994).

EMF can be divided into two main types depending on the energy levels of electromagnetic waves. If electromagnetic waves contain enough energy per quantum to ionize molecules, they can break the bonds between molecules and cause chemical reactions (Sher, 1997). These waves are known as *'ionizing radiation'* and have the potential to damage living cells, causing cancer, tumors and genetic damage (Sukhoviia et al., 1975). High ultraviolet, X-rays and gamma rays are some forms of ionizing radiation. If the quanta energy levels are insufficient to break molecular bonds, these electromagnetic waves are known as 'non-ionizing radiation'. Low and extremely low frequency (ELF) radiofrequency (RF) microwaves and visual light are some forms of non-ionizing radiation. Common man-made sources of non-ionizing radiation include microwave ovens, computers, wireless networks, cell phones, and power lines.

3. Effects of non-ionizing radiation frequencies

3.1. Extremely low frequency effects

Frequencies up to approximately 300 Hz (Hz) are known as extremely low frequency (ELF), and are part of the non-ionizing radiation range of the electromagnetic spectrum. The fields emitted by power lines, railways, and electrical devices at home and in the workplace are in the ELF range. The effects of both EF and MF on biological systems are highly controversial. Recent studies have focused on the illumination of their potential genotoxic, carcinogenic, and neurological effects. The effects of ELF on genotoxicity and carcinogenicity are summarized (Table 1). This section therefore includes studies summarizing the genotoxic and carcinogenic effects of ELF.

3.1.1. Genotoxicity

The absence of an accepted general mechanism that explains how EMF affects biological systems poses a great challenge in interpreting experimental data from EMF studies. The effect mechanism of EMF on DNA and RNA is still unknown. As the energy level of non-ionize EMF is not sufficient to break the intermolecular chemical bonds, the intracellular effects of EMF appear indirectly. The most prominent of these indirect ways is the effect of free radicals. When the number of free radicals is increased in the cell, structures such as DNA, RNA, protein, and membrane lipids are damaged due to the oxidative stress (Cassien et al., 2015; Dinu et al., 2016; Dizdaroglu and Jaruga, 2012; Lagouge and Larsson, 2013; Storr et al., 2013). It has been shown that EMF triggers the increase of free radical in the cell by the Fenton reaction (Lai and Singh, 2004). Through the Fenton reaction, hydrogen peroxide, the oxidative respiratory product in the mitochondria, is converted to free hydroxyl molecules *via* catalysis with iron (Floyd, 1981; Henle et al., 1996).

It has been suggested that ELF shows its effect on the cell in two steps (Lai and Singh, 2004). In the first step ELF mediates iron metabolism and increases the amount of free iron in the cytoplasm, particularly in the nucleus due to of the presence of numerous numbers of iron pumps within the nuclear membrane (Meneghini, 1997). An increased iron concentration accelerates the formation of free hydroxyl radicals through Fenton reactions. The hydroxyl radicals act on DNA, RNA, cell membrane lipids, and proteins inside of the cell. As a result of lipid damage in the cell membrane (lipid peroxidation), calcium leakage increases into the cell. The increase in calcium ions accelerates the calmodulin-dependent nitric oxide synthesis and triggers the second step (Lai and Singh, 2004). Nitric oxide is more active than hydroxyl radicals to damage DNA and other macromolecules. Nitric oxide triggers iron formation from the ferritin, which increases the amount of iron ions in the cell (Reif and Simmons, 1990). This cycle continues until the cell undergoes apoptosis or necrosis (Fig. 1). It has also been suggested that ELF may act by increasing the formation of hydrogen peroxide, especially in active cells due to their constant mitochondria functions (Phillips et al., 2009).

Effects on the genetic material of the cell are among the best indicators for showing whether ELF has a genotoxic effect on the cell. *In vivo* and *in vitro* ELF studies report different results and propose different mechanisms to explain the genotoxic effects of ELF (Grundler et al., 1992).

One of the most interesting issues is whether ELF creates DNA chain breakage. In one study, hamster lung cells were exposed to 50 Hz ELF to reveal its effects on autophagy mechanism. ELF exposure did not induce double-strand breaks (DSBs) in DNA, but it elevated cell surface modifications and actin filament reorganization. Increased autophagesome formation and LC3-II expression levels were also observed after exposure to 50 Hz ELF in cultured cells. These results indicate that ELF does not directly create DNA damage, however DNA damage is an end product of molecular irregularities resulting from ELF exposure. In addition, the elevation of autophagy might help to balance homeostasis against apoptosis (Shen et al., 2016). Similarly, DNA damage, the cell cycle, and protein expression were investigated in human neuroblastoma cells exposed to menadione and 50 Hz ELF. Menadione treatment increased mitochondrial superoxide production while 24 h (h) exposure to 50 Hz ELF reduced DNA damage and altered cell cycle distribution against menadione-induced genotoxic effects in humans (Luukkonen et al., 2016). Destefanis et al. (2015) investigated the effects of 50 Hz ELF on human lens epithelial cells (LECs) using molecular and immunohistochemical methods. Genotoxicity tests revealed no significant differences between the control and experimental groups. These results suggested that neither short- nor long-term ELF exposure causes any DNA damage in LECs *in vitro*. Feng et al. (2016) reported a protective effect of 50 Hz ELF against apoptosis in human amniotic cells. Cell viability, early apoptosis, mitochondrial ROS and the level of phosphorylated Akt were evaluated. Cells were induced by staurosporine to enter early apoptosis and, as a result of ELF exposure, the level of mitochondrial ROS increased. The team also reported that ELF is able to reverse apoptotic events using the transient mitochondrial ROS release and activation of Akt. A recent study assessing the brain histopathology of freshwater fish exposed to 50 Hz ELF showed that the expression levels of some antioxidant genes expression levels may change in response to ROS as a result of exposure to ELF (Samiee and Samiee, 2017). In a similar manner, menadione was used as a cofactor to reveal the effect of 50 Hz ELF in human neuroblastoma and glioma cell lines. In contrast to the previous study, ELF increased the genotoxic effects, depending on the amount of menadione in co-exposure. 50 Hz ELF exposure increased cytosolic and mitochondrial superoxide production in rat glioma cell lines. Additionally, 50 Hz ELF significantly increased micronuclei formation – which plays a genotoxic role in the carcinogenesis mechanism and AD (Kesari et al., 2016). The effects of 50 Hz ELF have also been investigated to reveal energy re-programming and anti-glycative defence in human neuroblastoma cells. Results