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The impact of non-ionizing electromagnetic radiation emitting devices on the male reproductive system

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ABSTRACT

With today's technological advances, people spend more and more time using various devices that emit non-ionizing radiation (NIR), such as mobile phones, laptops or WiFi networks. Nowadays, the role of these devices in the human lifestyle seems to make exposure to NIR unavoidable. This exposure, especially when prolonged, has been reported as one of the possible lifestyle factors contributing to reduced fertility, especially in men. The aim of the study was to analyse the current state of knowledge on the impact of NIR emitted by modern devices on the functioning of the male reproductive system and to identify possible mechanisms behind it. The research method used was a literature review on the PubMed platform. A total number of 35 articles from years 2007-2024 were analysed.

According to the scientific literature, exposure to NIR may affect spermatozoa through thermal and non-thermal mechanisms, the most important of which appears to be increased production of reactive oxygen species (ROS), which leads to oxidative stress and cellular damage in the reproductive system. NIR exposure can adversely affect semen parameters such as sperm motility, viability and concentration, alter hormonal mechanisms regulating reproduction and induce morphological changes in reproductive tissues. However, studies conducted in this context often provide inconsistent results, hence the exact effect of NIR on the male reproductive system remains unknown. Therefore, further research is needed to accurately determine the effects of NIR on male fertility and to provide appropriate health recommendations.

Key words: non-ionizing radiation, male reproductive system, infertility, mobile phone, oxidative stress

INTRODUCTION

Modern technological advances mean that people spend more and more time using a wide range of different devices such as mobile phones, laptops and wireless WiFi networks. These devices are known sources of electromagnetic radiation and their ubiquity in today's world makes exposure to the radiation they emit seem unavoidable. It is not surprising, therefore, that there has recently been growing concern about their long-term effects on human health.

Radiation is a wave of energy with the characteristics of both electric and magnetic fields. It can be divided into non-ionizing radiation (NIR) and ionizing radiation (IR), the latter including gamma rays, X-rays and alpha particles.

On the other hand the NIR spectrum includes electromagnetic waves between 1 Hz and 300 GHz frequency. It can be further subdivided into extra-low frequency waves (ELF), which includes frequencies between 1 Hz and 300 Hz, and radio frequency radiation (RFR), including frequencies between 3 kHz and 300 GHz. ELF is emitted by power lines and electrical appliances, while mobile phones, FM radios, microwave ovens, radars, etc. are sources of RFR. Unlike IR, NIR is not energetic enough to directly break chemical bonds and damage DNA, thus exposure to it is much less dangerous than exposure to IR. [1] However, based on available research NIR is capable of damaging tissues through indirect mechanisms such as oxidative stress or temperature increase. [2]

The increasing use of modern devices and exposure to NIR emitted by them has been reported as one of the lifestyle factors that could potentially contribute to the increasing decline in fertility observed in recent years, particulary affecting men. [3] Infertility is now a major problem, affecting approximately 8-12% of couples worldwide and the male factor is estimated to be the cause of 30-50% of all infertility cases. [4] [5]

In the context of the relationship between NIR and male reproductive health, another concern is the common practice of carrying a mobile phone close to the pelvis, e.g. in a trouser pocket. This places the source of NIR in the close proximity to the testicles, which makes them primarly exposed to the radiation and therefore potentially more susceptible to the adverse effects of NIR. [6]

BIOLOGICAL INTERACTIONS OF NIR

Absorbed NIR affects cells and tissues, causing chemical and physical changes within their components, resulting in changes in their function. [7] The severity of these adverse effects depends on the amount of energy absorbed by the tissues. It is influenced by a number of factors related to the characteristics of the radiation, such as power density, frequency or intensity and the dielectric properties of the exposed tissues such as conductivity, permittivity, size and geometry. [8]

The biological effects of NIR absorption can be divided into thermal and non-thermal effects. Thermal effects involve an increase in the local temperature in the NIR-exposed tissue due to the conversion of radiant energy into heat, whereas non-thermal effects have no effect on the local temperature. [8]

The testicles are an organ particularly susceptible to the thermal effects of NIR absorption. It is well known that they are an organ highly sensitive to temperature increases, as the temperature of the scrotum must be maintained at 2-4 °C below the core body temperature to ensure effective spermatogenesis. Otherwise heat stress develops in the testes, which leads to DNA damage, changes in the expression of genes regulating spermatogenesis and increased apoptosis of reproductive cells, resulting in reduced fertility. [9]

On the other hand, non-thermal effects of NIR exposure include processes such as the disruption of cellular calcium transmission and, more importantly an increase in the production of reactive oxygen species (ROS), which then can lead to oxidative stress. At the cellular level, they are thought to cause DNA damage, inhibition of cell growth and protein misfolding. [10]

ROS and oxidative stress

ROS are highly reactive compounds that contain oxygen atoms with an unpaired electron, such as superoxide anion ($O_2^{\bullet -}$) and hydroxyl radical ($^{\bullet}HO$), or have a single chemical bond between the two oxygen atoms, such as hydrogen peroxide (H_2O_2). They are naturally produced in small amounts at the cellular level as by-products of mitochondrial aerobic metabolism. In addition, a certain amount of ROS is necessary to maintain tissue homeostasis, however in excessive concentrations, these molecules are highly toxic and can cause cellular damage. [11]

Exposure to NIR can contribute to excessive ROS generation through a process called the Fenton reaction. This is a chemical reaction in which a hydroxyl radical is formed from mitochondrial hydrogen peroxide in the presence of iron. The higher the metabolism of a cell (as in the case of reproductive cells), the more hydrogen peroxide is produced as a by-product, making the cell more susceptible to the effects of NIR. [12]

However, living cells can protect themselves from ROS overgeneration. Cellular antioxidant mechanisms maintain ROS levels within normal range. These systems consist of molecules that can reduce the production of ROS or scavange them. They include antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT) or glutathione peroxidase (GPx), and also antioxidant molecules such as glutathione (GSH), vitamin E or vitamin C. [13]

When cellular production of ROS exceeds the compensatory capacity of antioxidant systems, a condition called oxidative stress occurs. This imbalance between ROS and antioxidants leads to cellular damage through lipid peroxidation, DNA structure disruption and changes in protein configuration. ROS-mediated DNA damage includes double-strand breaks, mutations and replication errors, which result in genomic instability and cell death, while changes in protein configuration lead to loss of their physiological function. At the same time, lipid peroxidation produces highly reactive products such as acrolein, malondialdehyde or 4-hydroxynonenal. These compounds can further react with other molecules, such as proteins or nucleic acids, increasing their damage. [14]

THE EFFECTS OF NIR ON THE MALE REPRODUCTIVE SYSTEM

Reproductive cells are particularly susceptible to the adverse effects of both ionizing and non-ioniznig radiation, because biological processes occur in them at a very high rate. They undergo numerous cel divisions and therefore grow rapidly, and the higher the growth rate of the cell, the greater the risk of incorporating potential errors that may occur in the biosynthesis of various cellular molecules as a result of radiation exposure. [15] Damaged reproductive cells lose their function, which can lead to reduced fertility or even infertility.

The available literature on the effects of NIR on the male reproductive system consists mainly of experimental animal studies, while human data is limited to retrospective observational studies and in vitro semen studies. However, the results of these studies are often contradictory and the exact effect of NIR on the male reproductive system remains controversial. Some studies show that NIR can damage sperm cells, while others report no effect or an insignificant effect. These differences may be due to the different conditions used

in each experiment, such as the frequency or intensity of the radiation, the duration of exposure or the method of administration of NIR to the animal body. They are the reason why it is difficult to make robust comparisons between studies. However, the balance of evidence seems to suggest that NIR may have adverse effect on spermatoza, therefore it is important to increase our knowledge in this area. [16]

ANIMAL STUDIES DATA

Animal studies, mostly in rodents, suggest possible adverse effects of NIR exposure on the male reproductive system. The pooled results of the meta-analysis by *Yu et al. (2021)* suggest that exposure to mobile phone radiation may impair motility and reduce sperm viability in rats. [17] The mechanisms behind these effects are not fully understood, however recent studies suggest the involvement of processes such as increased cellular oxidative stress in the reproductive system, increased sperm cells apoptosis, histopathological changes in the reproductive organs and endocrine disruption. [18]

Elevated oxidative stress in the reproductive system

Oxidative stress is widely recognised as one of the potential factors responsible for reproductive disorders. Recent studies indicate that NIR may cause excessive ROS generation after exposure, resulting in increased oxidative stress in the semen of exposed rodents. [18][19]

Oxidative stress can damage sperm cells, which are particularly susceptible to these particles due to relatively low levels of cytoplasmic antioxidants and high presence of polyunsaturated fatty acids (PUFA) in their cell membrane. ROS can interact with the PUFA and cause their peroxidation, which results in cell membrane damage and reduced sperm viability, which may contribute to reduced fertility. [19]

In a study by *Liu et al. (2015)*, adult male rats were exposed to NIR at a frequency of 900 MHz for 2 hours per day. After 50 days, the researchers measured ROS levels and total antioxidant capacity (TAC). The exposed group showed a 46.21% increase in ROS levels and a 28.01% decrease in TAC volume compared to the control group. These results are consistent with previous experimental studies in rats. In addition, the authors observed a significantly increased percentage of apoptotic cells in the flow cytometry and significant changes in the expression of genes regulating apoptosis in favour of pro-apoptotic factors in the semen of the exposed group. They suggested that oxidative stress caused by NIR exposure may induce apoptotic processes in spermatoza, which may lead to reduced fertility in exposed males. [20]

Apoptosis

Apoptosis, also known as programmed cell death, is an important process in the correct remodeling and maturation of tissues. It enables the orderly removal of unnecessary or damaged cells, protecting the body from excessive cell proliferation and maintaining tissue homeostasis.

The process of apoptosis is initiated and executed by zymogenic proteases called caspases, hence measuring their activity in the sample can be used as an indicator of apoptosis. Typically, caspase -3 acts as an executor, while caspase -8 and -9 activate signalling pathways inducing the process. Apoptosis can be initiated by a variety of intracellular stimuli, such as DNA or cytoskeletal damage and impairment of macromolecule biosynthesis.

According to *Kesari et al. (2012)*, the sperm of rats exposed to NIR was characterised by a significant increase in caspase-3 activity in comparison to the control group. This may

indicate that NIR exposure can induce apoptosis in spermatoza. In addition, the same study showed disturbed sperm morphology in the exposed group, as visualized by transmission electron microscopy. The authors linked the morphological changes to the increase in apoptotic processes. Changes observed included disruption of microtubule structures such as the axoneme and cytoskeleton, as well as the distortion of the acrosome from the head membrane. Rearrangements in the cytoskeleton and axoneme may lead to reduced sperm motility, while deformation of the acrosome may hinder the penetration of the ovum, potentialy leading to reduced fertility. [21]

Histopathological changes in the reproductive organs

In relation to histopathology of the male reproductive system and exposure to NIR, *Gautam et al. (2024)* demonstrated morphological changes in the epididymis and seminiferous tubules in the testes of exposed adult rats. The epididymis is an organ that stores sperm and provides an optimal environment for spermatoza to acquire motility and the ability to fertilize, while the seminiferous tubules are the structures in which the process of spermatogenesis takes place. The seminiferous tubules of the study group were characterised by reduced diameter, irregular shape and increased cytoplasmic vacuolization compared to the control group. [22]

On the other hand, many studies report Leydig cells as the most susceptible to the effects of NIR exposure. These are the interstitial cells in the testicles that are responsible for the secretion of 95% of male testosterone. Testosterone is a hormone recquired to initiate and maintain spermatogenesis, and as such is critical for the proper functioning of this process. Therefore, potential Leydig cells damage may contribute to infertility due to inefficient spermatogenesis. Numerous changes in normal structure were observed in the Leydig cells of the rodents exposed to NIR. These included: mitochondrial swelling, vacuolization of the cytoplasm, reduced lipid bodies, light staining of the remaining lipid bodies and their excessive cavitation. These results suggest a negative effect of NIR expousure on Leydig cells structure, but the significance of these changes is not fully understood and requires further carefully designed studies. [23]

Endocrine disruption

Normal hormonal regulation is essential for the proper functioning of the male reproductive system. Hypothalamic gonadotropin-releasing hormone (GnRH) causes the release of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) in the anterior pituitary gland. Subsequently LH stimulates Leydig cells to synthesize and release testosterone, while FSH acts on Sertoli cells, causing them to secrete androgen binding protein, inhibin and activin. Disorders in this hormonal regulation may be one of the factros affecting male fertility.

Studies concerning the effect of NIR on the reproductive hormone regulation in male laboratory animals provide mixed results. Many of them report a significant decrease in plasma testosterone levels in exposed animals, but there are also studies that find no effect of NIR exposure on testosterone concentration. [24][25] Other hormones that could potentially be affected by exposure to NIR are FSH and LH. However, in this case the effects of exposure are also not well understood and the results of the studies are contradictory. In general, the effect of NIR on LH and FSH levels seems to depend on the parameters of the radiation wave and the exposure time. Prolonged exposure to NIR at 900 MHz frequency caused an increase in plasma LH and FSH levels in adult male rats. In addition, at the same NIR intensity, a

decrease in plasma inhibin b and an increase in activin b were observed, which together with the observed damage to Leydig cells suggests an impairment of testicular function without alteration of the pituitary gland. On the other hand, prolonged exposure to NIR at 1800 MHz frequency caused a decrease in plasma LH and FSH levels, suggesting damage to the hormonal axis in the pituitary or hypothalamus. In addition, short-term exposure (30 minutes per day for 20 days) did not cause endocrine disruption in the exposed animals. In conclusion, the effect of NIR on the hypothalamic-pituitary-gonadal axis remains controversial and requires further evaluation. [26]

Exposure time and distance from the NIR source

The results of recent animal studies suggest that only prolonged exposure to NIR causes adverse effects in the male reproductive system. In a study by *Yu et al. (2020)*, 135 adult male rats were randomly divided into 3 groups according to the duration of NIR exposure (50, 100 and 150 days respectively). They were further divided into another 3 groups consisted of 15 animals each. The first group lived in cages without any intervention, the second group was put in customised containers without NIR exposure, while the last group was kept in customised containers and exposed to NIR. No significant changes in semen parameters were observed in any of the 50-day groups. On the other hand, the 100-day groups showed a statistically insignificant decrease in sperm viability and motility while the 150-day groups showed a significant decrease in these parameters and also abnormal sperm morphology. At the same time, no significant changes or differences were found in the semen collected from all groups not exposed to NIR at any of the time intervals. [27]

Other studies have reported replicable results. *Oh et al. (2018)* showed reduced spermatogonia and Leydig cell counts in adult male rats exposed to NIR. The extent of this reduction was positively correlated with the duration of exposure. In addition, the groups placed further away from the NIR-emitting device showed less severe adverse effects than those placed closer, while the physical parameters of the radiation and the exposure time remained the same. These results may indicate that the degree of adverse effects of NIR exposure also depends on the distance between the testicles and the radiation source. [28]

HUMAN STUDIES DATA:

The results of animal studies and the increasing use of NIR-emitting devices suggest that one of the factors that may contribute to the growing problem of male infertility is the adverse effect of NIR on the sperm and testicular function. Indeed, human studies have identified long-term mobile phone use as a possible cause of deterioration in sperm parameters such as motility, viability, concentration and morphology, which may result in reduced fertility. However, the literature concerning NIR and human sperm is limited and often provides conflicting conclusions. For example, some of the studies report reduced motility and no effect on sperm concentration, while others show no correlation between NIR exposure and human sperm quality. However, given the observed decline in sperm parameters in recent decades and the simultaneously increasing use of devices such as mobile phones, it is reasonable to determine the exact relationship between NIR exposure and male reproductive health. [29]

The available literature evaluating the effects of NIR on the human male reproductive system includes semen in vitro sperm studies as well as retrospective observational studies.

Data from in vitro sperm studies

In vitro studies appear to be the best available method to determine the effects of NIR on human sperm. In vivo experiments in which humans would be exposed to NIR are not feasible due to their unethical nature, while epidemiological studies and animal model studies have their limitations. In the era of widespread use of modern technology, it is extremely difficult, if not impossible, to select a group of people who do not use any devices at all as a control group in a well-designed epidemiological study. On the other hand, the animal model cannot be directly extrapolated to humans for a number of reasons. Rodent testicles are much smaller than human testicles, they can also move freely between the scrotum and the abdominal cavity through the inguinal canal and often whole-body exposure of the animal to NIR cannot be avoided. [30]

Hassanzadeh-Taheri et al. (2021) investigated the effects of NIR on sperm samples obtained from healthy donors. Each of the samples was divided into 2 equal volumes, one of which was then exposed to NIR and the other was the control group. Compared to the unexposed group, a significant decrease in sperm motility and viability was observed in the study group. [31] Similar results have been reported in other in vitro studies. One proposed reason for the observed decrease in semen quality associated with the adverse effects of NIR is the increased ROS production and consequent oxidative stress resulting from exposure to this type of radiation. [32]

The effect of NIR on mitochondria appears to be responsible for increased ROS production and oxidative stress. Mitochondrial membrane potential and DNA can be damaged by the negative effects of NIR on the electron transport chain. Radiation disrupts the proper metabolism of this complex, resulting in increased ROS generation. More importantly, sperm cells are particularly susceptible to oxidative stress due to their small cytoplasmic volume and limited antioxidant concentration. [33] For this reason, they may be one of the main targets of the effects of absorbed NIR.

Data from human observational studies

According to a meta-analysis by *Kim et al.* (2021), which focused mainly on observational studies in humans, chronic use of mobile phone may adversely affect sperm parameters. NIR emitted from mobile phones contributes to reduced sperm motility, viability and concentration. Moreover, these effects seem to increase with the duration of mobile phone use. However, a significant proportion of the studies analysed were retrospective observational studies, based on the participants' reported duration of mobile phone use. This could be a source of bias in the results of the meta-analysis, as human memory is not able to store all information with high accuracy. [34]

The results of the observational studies are consistent with in vitro studies regarding the effect of NIR on the sperm mitochondria. A case-control study of patients from the Department of Dermatology and Andrology in Ismailia, Egypt suggests that mitochondrial NAD^+-dependent isocitrate dehydrogenase (NAD^+-IDH) is one of the potential targets of NIR emitted by mobile phones. The authors studied semen samples from 90 randomly selected men with idiopathic infertility after excluding smoking, chronic diseases and occupational exposure to NIR. The samples were divided into 4 groups according to the duration of mobile phone use reported by the participants. The results showed that NAD^+-IDH activity in the ejaculate was significantly increased in the group with the longest mobile phone use (≥4 h/day), compared to the control group. Its activity was also negatively correlated with sperm cells motility. NAD^+-IDH is an enzyme that can be found only in the mitochondrial matrix,

therefore its increased activity in sperm may indicate mitochondrial membrane damage. This enzyme is involved in the Krebs cycle, catalysing the decarboxylation of isocitrate to α-ketoglutarate in the presence of NAD^+. It therefore plays an important role in the production of cellular ATP. Since sperm motility is mainly dependent on the synthesised ATP, a decrease in its production may be the cause of reduced sperm motility. This suggests that exposure to NIR may cause damage to the enzymatic pathways in sperm mitochondria, resulting in asthenozoospermia, which is a major male factor in reduced fertility. [35]

CONCLUSIONS:

Current evidence suggests that prolonged exposure to NIR emitted by devices such as mobile phones may be a potential risk factor of male subfertility. However, studies in this area often reach different conclusions, and the exact mechanisms behind the effect of NIR on the male reproductive system are not fully understood. In addition, most of the scientific data on the subject has been obtained using an animal model that cannot be directly extrapolated to humans. Nevertheless, in the era of continuous technological progress and the growing problem of infertility, it seems important to icrease our knowledge of the effects of NIR on reproduction through further well-designed studies. This will make it possible to reduce potential adverse health effects and possibly develop appropriate health and prevention recommendations.

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