Review

Lifestyle and testicular dysfunction: A brief update

Ashok Agarwal a,*, Nisarg R. Desai a, Riccardo Ruffoli b, Angelo Carpi c

a Center for Reproductive Medicine, Glickman Urological and Kidney Institute and Obst/Gyne and Women’s Health Institute, Cleveland Clinic, Cleveland, OH, USA
b Department of Human Morphology and Applied Biology, University of Pisa, Italy
c Department of Reproduction and Ageing, University of Pisa, Italy

Received 23 June 2008; accepted 1 July 2008

Abstract

The incidence of testicular cancer, cryptorchidism and defective spermatogenesis is increasing probably due to environmental and lifestyle-related factors. The aim of this review is to briefly describe and comment on the principal lifestyle factors. The recent findings that the electromagnetic waves following the use of the cell phone and the prolonged exposure to the noise stress cause relevant testicular dysfunction in man or animals reinforce the hypothesis of the importance of lifestyle-related factors.

© 2008 Elsevier Masson SAS. All rights reserved.

Keywords: Lifestyle; Testicle; Spermatogenesis

1. Introduction

The incidence of testicular cancer, cryptorchidism and defective spermatogenesis is increasing [1]. Genetic factors are supposed to play a marginal role [1,2]. The principal hypotheses suggest that testicle is damaged by environment and lifestyle-related factors either at perinatal or at puberty time. Concerning the factors which may affect the adult tests, the environmental hormone disruption hypothesis lacks the epidemiological evidence [2] and the effects of tobacco, alcohol and sedentary work have not been well documented. Heat exposure, ionizing radiations, dibromochloropropane, estrogens and anabolic steroids are definite important damaging factors [1,2]. The occurrence of the above reported diseases, disorders or factors in the developmental age and the fact that Sertoli cells are key regulators of germ cells and Leydig cells’ development provide a rational basis for their association [1]. However, recent data suggest the occurrence of new types of lifestyle-related damaging factors.

The aim of this brief report is to describe and comment on the recently reported effects of acoustic waves in animals and of the electromagnetic waves related to the use of cell phone in man.

2. Lifestyle-related factors

In Table 1 the principal lifestyle factors with the potential to affect human male sperm production and fertility have been summarized.

3. Scrotal temperature and effect of lifestyle

It is well known that testicular temperature within scrotum is 1–2 °C lower than core body temperature and increase in testicular temperature can affect spermatogenesis. However, recent changes in lifestyles make testes more susceptible to heat. Exposure to hot occupational environment (bakers, welders, foundry workers), sedentary work habits, traveling in car for long time during commute to and from work, tight clothing, all these can disrupt regulation of intrascrotal temperature and can lead to increase in testicular temperature [8,2].
**Table 1**

Principal lifestyle-related factors

<table>
<thead>
<tr>
<th>Mechanism/factor</th>
<th>Lifestyle-related factor</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heat</td>
<td>Dresses, hot and thermal baths</td>
<td>[1,2]</td>
</tr>
<tr>
<td>Estrogens</td>
<td>Contraception (body image)</td>
<td>[1,2]</td>
</tr>
<tr>
<td>Androgens</td>
<td>Body image and performance</td>
<td>[1,2]</td>
</tr>
<tr>
<td>Alcohol&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Various</td>
<td>[3,4]</td>
</tr>
<tr>
<td>Smoking&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Various</td>
<td>[3,4]</td>
</tr>
<tr>
<td>Ionizing radiations</td>
<td>Excessive radiological screening</td>
<td>[5]</td>
</tr>
<tr>
<td>Tadalafil&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Sexual intercourses</td>
<td>[6]</td>
</tr>
<tr>
<td>Prolonged urban automobile driving</td>
<td>Reported in taxi drivers (extended to other drivers?)</td>
<td>[7]</td>
</tr>
</tbody>
</table>

<sup>a</sup> Increase in XY frequency in sperm affects already poor semen quality.

<sup>b</sup> Increase in sperm disomy.

<sup>c</sup> A single dose reduces sperm motility in young infertile patients.

### 4. Smoking

It is well established that smoking has a detrimental effect on male reproductive system. Saleh et al. demonstrated cigarette smoking leads to increase in reactive oxygen species (ROS) level and decrease in ROS-TAC score [9]. They reported high level of leukocytes in smokers and suggested that oxidative stress is due to ROS generation by activated leukocytes [9]. Various compounds of cigarette smoke (i.e., polycyclic aromatic hydrocarbons) and smoking metabolites may act as chemotactic stimuli and thereby induce an inflammatory response, recruitment of leukocyte and subsequent generation of ROS [9,10]. In a recent study, Gaur et al. showed that motility is one of the first sperm parameters affected and asthenozoospermia may be an early indicator of reduced semen quality in light smokers [11]. They reported significantly high teratozoospermia in heavy smokers compared to non-smokers [11]. Studies have shown that maternal smoking affects reproductive parameters of their offspring (male) during adolescence [10,12].

### 5. Effect of environmental toxicants and endocrine active compounds

#### 5.1. Role of lead

Main sources of lead are deteriorated lead-based paints and resulting dust and soil contamination. Other minor sources are plumbing system with lead pipes and lead-gazed ceramic pottery [13]. Lead can cause oxidative stress by interfering with antioxidant enzymes and also by its effect on cell membrane polyunsaturated fatty acids (PUFA) [14]. Various animal and human studies reported lead can cause adverse effect on male reproductive organs [15–17].

#### 5.2. Role of phthalates

Phthalates are constituents of many consumer plastic products. Oral exposure is the major route of exposure in general population. In 1998, Santhosh et al. reported increase in lipid peroxidation in cultures of rat hepatocytes due to exposure to DEHP [di-(2-ethylhexyl) phthalate] [18]. Later on, in 2002 Kasahara et al. demonstrated oral administration of DEHP causes increased generation of ROS in rat testes. They suggested that this may be due to induction of cytochrome c release from germ cell mitochondria [19].

Discussion of all environmental toxicants and endocrine active compounds is out of context of this article.

### 6. Effect of cell phone on male fertility

The frequency of cell phone radiation ranges between 850 and 1900 MHz. As energy carried by cell phone radiation [radiofrequency electromagnetic waves (RF-EMW)] is extremely low compared to ionizing radiation, i.e., X-rays (frequency, $10^{10}$–$10^{18}$ MHz), they do not cause ionization of molecule. However, exposure to RF-EMW causes a number of effects on biological systems [20–28]. Results of various studies demonstrating effects of cell phone radiation on male fertility are conflicting due to heterogeneity of data and research methods [20,29–41].

Recently, epidemiological studies, including one from our center, have proposed cell phone usage may cause decrease in sperm parameters [29,30,34,37,41]. Most remarkable finding of our study was significant association of cell phone usage with reduced sperm motility in men using cell phone >4 h/day vs. men not using at all (67.80 ± 6.16% vs. 44.81 ± 16.30%, $p < 0.0001$) [29]. In a recent cross-sectional study, Baste et al. studied infertility among military men employed in the Royal Norwegian Navy [30]. They reported odds ratio (OR) of 1.86 for infertility (95% confidence interval (CI): 1.46–2.37) among military personnel who self-reported exposure to RF-EMW relative to those who reported no work near RF-EM (electromagnetic) field [30].

Chronic exposure of RF-EMW can affect mitochondrial genome and nuclear β-globin locus of epididymal spermatozoa [30] causing increased expression of adhesion protein on spermatozoa [42]. Dasdag et al. demonstrated a decrease in mean seminiferous tubule diameter after exposure of rats ($n = 18$) to cell phone radiation [32]. However, these results could not be reproduced in a follow up study [33].

Various animal studies demonstrated production of oxidative stress after cell phone exposure [16,39,43,44]. Animal models are not a good candidate for the purpose to study effect of RF-EMW on human reproductive system, because their testicular dimensions are smaller and during experiment animals have a different level of exposure compared to human testes in real life (i.e., carrying cellular phone in trouser pocket or clipped on trouser belt) [45,46]. However, as a supporting evidence to animal studies, Friedman et al. have suggested production of free radical due to cell phone radiation may be due to stimulation of mammalian cell plasma membrane NADH oxidase [24].

Studies on in vitro effect of RF-EMW on human sperm are conflicting [35,36]. Erogul et al. studied ($n = 27$) the effect of cell phone radiation for 5 min on neat semen of human volunteer. They demonstrated significant decrease in rapid progressive motility (Grade A, $p = 0.0007$), an increase in...
slow progressive motility (Grade B, \( p = 0.0007 \)) and an increase in percentage of immotile sperm (Grade D, \( p = 0.0003 \)) [35]. However, Falzone et al. found no effect on purified mature spermatozoa (exposure duration 1 h) [36]. We have recently demonstrated for the first time that RF-EMW exposure can cause oxidative stress in ejaculated human semen (duration 1 h, specific absorbance rate (SAR) 1.46 W/ kg, temperature of 20 °C). We found significant increase in reactive oxygen species (ROS) level and decrease in ROS- TAC score (reactive oxygen species-total antioxidant capacity) after cell phone exposure.

7. Effect of noise on testicular functions

It is well established that stress can cause increased level of glucocorticoids and leads to decrease in testosterone level [47]. Recently, Ruffoli et al. demonstrated chronic noise stress leads to accumulation of lipofuscin in mouse testis and subsequent decrease in testosterone production [48]. This was in support of previously established finding that administration of corticosterone causes production of free radical formation in the mitochondria of the Leydig cell and free radical generation is known to stimulate lipofuscin formation [49,50]. Therefore, lifestyle and work environment involving high level of noise exposure may be detrimental to testicular function [48].

8. Conclusion

Many acquired factors can damage human testicular function. Some of them are lifestyle related and are associated to a high probability of testicular damage. New lifestyle-related risks recently described seem to derive from cell phone electromagnetic radiations and chronic noise stress.

References


