Animal Reproduction Science xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Animal Reproduction Science

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

Review article

Impact of light irradiation on preservation and function of mammalian spermatozoa

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ARTICLE INFO

Keywords:
Semen
Mammals
Light irradiation
Motility
In vitro
Fertilizing ability

ABSTRACT

Light irradiation has been demonstrated to exert positive effects on gametes, and particularly on sperm. In effect, a high number of studies conducted in several species, including humans, mice, pigs, cattle and sheep, and using different light sources (such as lasers and light-emitting diodes) have demonstrated that photo-stimulation increases sperm motility. In addition, other works have shown that sperm fertilizing ability both *in vitro* and *in vivo* can be increased following light irradiation; there are also some evidences pointing out to an extend of lifespan of preserved semen. Notwithstanding, no study has reported a detrimental effect of visible light on DNA integrity. The mechanisms through which light exerts its effects are not completely elucidated, but mounting evidence gives cell photosensitizers, especially those present in the mitochondria, a vital role. Stimulating these molecules turns into an increase in the production of ATP and Ca^{2+} influx, which contributes to explain the effects of light upon spermatozoa. Additionally, the presence of opsins in spermatozoa as well as the potential influence of light on the conformation of other proteins may also be involved in the sperm response to light. However, there are still a significant number of points that need to be addressed and their elucidation may contribute to increase the utilization of light irradiation for sperm preservation and ART.

1. Introduction: photobiomodulation and phototherapy

Although one would expect that only plants and photosynthetic bacteria present photosensing molecules able to transform light into chemical energy, animal cells also have chromophores. Since the 1980s, irradiation of animal cells with visible light (low level light), also known as photobiomodulation, has been used for medical treatment (phototherapy) in different disciplines, including dermatology, surgery and rheumatology (Goldman et al., 1980; Abergel et al., 1984; Wheeland and Walker, 1986; Trelles and Mayayo, 1987; Desan et al., 2007; Saltmarche, 2008; Avci et al., 2013). As light stimulation increases ATP production, and this is crucial for sperm motility and oocyte maturation, different studies started to investigate the effects of light on gametes and embryonic cells *in vitro*, especially in sperm (Lubart et al., 1992; Bielanski and Hare, 1992; Abdel-Salam and Harith, 2015). In addition to their effects on gametes, light stimulation with low-level lasers has also been found to recover testicular degeneration in rams at different energy densities (wavelength: 808 nm; power output: 30 mW; energy density: 28 J cm^{-2}; Alves et al., 2016).

Accumulating evidence now indicates that light irradiation accelerates mitochondrial respiration and ATP production (Karu,

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https://doi.org/10.1016/j.anireprosci.2018.02.004
Received 1 December 2017; Received in revised form 3 February 2018; Accepted 6 February 2018
0378-4320/

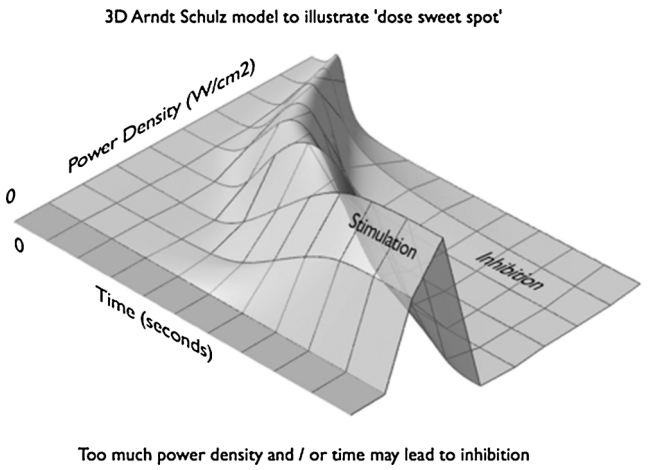

Fig. 1. The Arndt-Schulz curve. The three-dimensional model shows the biphasic response to light stimulation, which relies on irradiance and time of exposure, and could explain why short wavelength increases ROS generation and has antioxidant effects at long wavelength. Reproduced from Huang et al. (2011), under the terms of the Creative Commons Attribution-Non-Commercial 3.0 License.

1989; Gao and Xing, 2009). Strikingly, the first studies indicated that light effects were more apparent when photobiomodulation was applied on cells under stressing conditions, such as incubation in a starvation medium with low levels of oxygen or Ca^{2+} (Karu, 2008; Gao and Xing, 2009; Ankri et al., 2010). Moreover, cell response to light stimulation is biphasic and follows, as suggested by Lubart et al., (2006), an Arndt-Schultz curve (Fig. 1). Thus, low doses produce stimulating effects, moderate doses have no-effect and high doses exert cytotoxic effects. In the case of reactive oxygen species (ROS), photo-stimulation at short wavelength increases ROS generation (ascending part of the curve) and at long wavelength exerts an antioxidant effect.

The purpose of this work is to review the effects of light stimulation on the function, fertilizing ability and storage of mammalian sperm. The article also refers succinctly to the sperm of non-mammalian species and to the use of lasers in Assisted Reproductive Technology (ART). Finally, we also try to summarize the hypotheses that could explain how irradiation with visible light affects sperm cells.

2. Effects of light irradiation on mammalian spermatozoa

2.1. Sperm motility

Almost all studies that have evaluated the impact of light irradiation on spermatozoa have focused on motility and other kinematic parameters, and have found a positive effect. However, there are differences between studies and species. Table 1 aims at summarizing most of the contents discussed in this section.

In humans, one of the first studies that evaluated the effects of light stimulation on sperm motility was that of Sato et al. (1984). These authors exposed human sperm to laser irradiation (Krypton Laser red light, $\lambda = 647$ nm) at different intensities (4 J cm^{-2}, 8 J cm^{-2} and 32 J cm^{-2}) and found that the percentage of total motile spermatozoa increased, especially when the intensity was 32 J cm^{-2} (raise was about 8–10%). In contrast, these authors reported no effect on velocity, thus suggesting that laser irradiation mainly induced the non-motile spermatozoa to move rather than to increase their kinematic parameters. With regard to infrared irradiation, Lenzi et al. (1989) combined two different intensities and two different frequencies as follows: 5 mW and 2 Hz; 5 mW and 2200 Hz; 30 mW and 2 Hz; 30 mW and 2200 Hz, and observed an increase in the percentage of progressively motile spermatozoa, linearity (LIN), amplitude of lateral sperm head displacement (ALH), and a decrease in tail beat frequency (BCF). These differences between irradiated and non-irradiated samples were more apparent after 4–22 h of irradiation. In another work, Firestone et al. (2012) irradiated human sperm from patients with different sperm quality (normozoospermic, asthenospermic and oligoasthenozoospermic) with infrared wavelength ($\lambda = 905$ nm; energy density = 50 mW cm^{-2}; 1.5 J cm^{-2}) for 30 s. After incubating samples for 30 and 120 min at 37 °C, light stimulation at 905 nm was found to significantly increase total sperm motility, straight line velocity (VSL) and LIN. The extent of that increase was higher in oligoasthenozoospermic patients, which led these authors to suggest that photo-stimulation could be used to improve sperm motility in those patients (Firestone et al., 2012). These results matched with another study that observed that irradiation of human sperm from asthenozoospermic patients with 830-nm gallium-aluminum-arsenide (GaAlAs) laser (output power = 100 mW; aperture size = 0.67 cm^2; energy density = 4 and 6 J cm^{-2}) maintained better their progressive motility after 45 and 60 min of irradiation at 37 °C (Salman Yazdi et al., 2014). Preece et al. (2017) also reported that red light stimulation with a diode laser ($\lambda = 633$ nm; energy density = 5.66 mW cm^{-2}) for 35 min increased the motility of frozen-thawed human spermatozoa.

In addition to the use of lasers as light-source, the effects of photo-stimulation on the sperm motility of asthenozoospermic patients (humans) were also evaluated in response to light emitting diode (LED). Ban Frangez et al. (2015) irradiated spermatozoa with different wavelengths (energy densities are within brackets): a) 850 nm (2.16 mW cm^{-2}), b) 625, 660 and 850 nm