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Yoga and Meditation as a Therapeutic Intervention in Oxidative Stress and Oxidative DNA Damage to Paternal Genome

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Abstract

Yoga and meditation (encompassing physical postures, breathing practices, relaxation techniques and meditation) is known to modulate neural, endocrine and immune functions at the cellular level through influencing cell cycle control, aging, oxidative stress (OS), apoptosis and several pathways of stress signalling. Individuals with high level of oxidative stress are in great need of safe, inexpensive, non-pharmacologic, accessible, and effective adjunctive therapies to enhance well-being, reduce the burden of such stress and prevent its chronic sequelae. OS is the aetiology in several complex lifestyle diseases (coronary artery disease, hypertension, primary open angle glaucoma, idiopathic male infertility) and autoimmune disorders. Seminal oxidative stress and sperm DNA damage may be the common underlying cause for infertility, recurrent spontaneous abortions, congenital malformations and complex neuropsychiatric disorders in children and in certain childhood cancers. Thus management by antioxidants and simple life style modifications and interventions like meditation and yoga are highly efficacious in management of oxidative stress and its sequelae.

Keywords: Sperm; DNA damage; Yoga; Meditation; Oxidative stress; Lifestyle

Reactive oxygen species (ROS) regulate several physiological functions and play key role in several biological functions. Humans now live in a sea of free radicals with ever increasing exposure to both exogenous and endogenous source of free radicals (electromagnetic radiation, persistence organic pollutants, insecticides, pesticides, high temperature, psychological stress, smoking, excess alcohol consumption, sedentary life style, varicocele, infection and inflammation). Studies from our laboratory on normozoospermic infertile men and couples with idiopathic RSA and couples with more than 2 children with congenital malformations with unexplained aetiology has shown that systemic and testicular oxidative stress and oxidative damage to sperm DNA is the underlying aetiology in all these disorders believed to be idiopathic. Oxidative stress damages all biomolecules like proteins, lipids and carbohydrates and even mt and nuclear DNA. Free radicals are generated as byproducts of mt oxidative phosphorylation and thus target the mt which are both the source and target of free radicals. Supraphysiological free radical levels damage the mt which produce less ATP and more free radicals. Free radicals target both somatic and germ cells but the sperm a highly polarized cell is most vulnerable to oxidative stress by virtue of it losing majority of cytosolic antioxidants during spermiogenesis and being very rich in polyunsaturated fatty acids. Being transcriptionally and translationally inert it has only limited DNA damage detection and repair mechanism.Thus it is most vulnerable to oxidative damage and depends largely on the oocyte post fertilization to remove the damage as it only has OGG1 but lacks APE and XRCC1 . However in contrast oocyte has very low levels of OGG1 but has APE and XRCC1 thus both work in concert to repair the DNA damage. However extensive DNA damage can overwhelm the oocyte repair capacity and lead to persistence of mutagenic lesions in DNA which then are found in every cell of the zygote if not removed prior to first mitotic division.

This can have serious consequences causing pre and post implantation losses, congenital malformations and even childhood cancers. Thus every effort should be made to prevent oxidative stress in testicular and epididymal tissue, since in majority of cases oxidative stress is caused by a host of modifiable factors (smoking, sedentary lifestyle, excess alcohol intake, obesity) simple changes in social habits and adoption of healthy lifestyle can prevent OS and DNA damage. Delaying marriage and having children at an older age may compound the problem further as sperm tends to accumulate damage and has more denovo germ line mutations due to more cell divisions and also because of accumulation of oxidative DNA lesions. Thus in studies from our lab have shown that sporadic cancers like Retinoblastoma usually affect the last born child when the paternal age is beyond 35 years. Recent studies from our lab have also documented that meditation and yoga are highly effective in reducing OS and DNA damage and thereby the mutagenic load carried by sperm DNA.

Childhood cancer appears to be an ever growing disease and a leading cause of death worldwide. Recent studies, from our laboratory have supported the view that sperm DNA damage may be the cause of morbidity and mortality in offspring of fathers with oxidative damage to sperm genome. Oxidative stress also affects the methylation pattern of sperm genome causing hypomethylation of repetitive elements causing genome instability and mutability and hypermethylation of tumour suppressor genes which may lead to higher incidence of both gonadal and extragonadal tumours in these men or to cancers in offspring. OS also targets the telomeric DNA accelerating its shortening further compounding the genome instability and may also cause premature aging of the testis. Shorter telomeres may affect spermatogenesis and such men may manifest with oligozoospermia or azoospermia.

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Various studies have demonstrated that the poor lifestyle and social habits contributes in generation of seminal free radicals leading to oxidative stress [1]. Major cause of DNA damage in sperm is oxidative stress [2,3]. Also, as sperm have a very basic DNA damage detection and repair mechanism, therefore a policy of prevention is better than cure would be best to prevent oxidative DNA lesions as the effect of antioxidants is highly variable [4].

In previous studies, we have documented that yoga/ meditation-based lifestyle intervention gradually reduced oxidative DNA damage in sperm over a period of 6 months [4]. In the same report we have also found that, the seminal ROS (reactive oxygen species) levels declined within 10 days practice of meditation and yoga [5,6]. Analysis of sperm transcriptome showed down regulation in levels of genes of inflammatory pathways and antioxidant genes probably due to decline in levels of oxidative stress and upregulation in activity of telomerase genes aiding in maintenance of telomere length [7,8]. This finding is highly relevant because though genetic causes of infertility, RSA and congenital malformations are irreversible but oxidative DNA damage can be minimized by adopting a healthy lifestyle These findings have clinical implications in cases with male factor infertility opting for assisted conception and may reduce pre and post implantation losses following assisted and spontaneous conception and may also improve the rates of spontaneous conceptions in these men and the need to resort to assisted conception. Also, diagnosis of oxidative sperm DNA damage and prompt treatment and counselling to parents about adoption of healthy lifestyle with daily practice of yoga and meditation may also prevent/decrease incidence of childhood cancer and several neuropsychiatric disorders and even autism in children.

We also found that in obese patients the telomerase activity increased significantly following practice of meditation and yoga and may be due to decrease in BMI to normal levels, but interestingly BMI was not reduced non-obese controls after the intervention [9]. These findings indicate that yoga and meditation irrespective of caloric restriction significantly improves health. Yoga and meditation was also associated with upregulation in levels of anti-aging gene, such as SIRTUINS. A recent study from the authors' laboratory (unpublished) found upregulation in levels of after 1 month of practice of yoga and meditation. This is the first study to report uregulations in levels of SIRT1 following meditation and yoga practice independent of caloric restriction. We also found such couples with (idiopathic infertility, rec spontaneous abortion, children with congenital malformation and cancers) to have mild to moderate depression and following this practice of meditation and yoga there was significant decline in cortisol levels and upregulation in levels of endorphins and improvement in quality of life and reduced psychological stress and severity of depression. Thus yoga and meditation is the key to reversing testicular aging as the three hallmarks of aging- OS, DNA damage and shortening of telomeres all show a significant decline post meditation and yoga intervention.

Therefore, in conclusion, meditation/yoga-based lifestyle intervention might result in decline in free radical levels in blood and lower seminal oxidative stress; reduce oxidative damage to both mitochondrial and nuclear genome which culminates in lower mutagenic load in DNA. Decline in oxidative damage in sperm may aid couples opting for assisted conception to conceive spontaneously and may reduce number of couples experiencing pre and post implantation losses, recurrent spontaneous abortion or having children with congenital malformations/cancer. Regular practice of yoga and meditation could also be the key to healthy senescence as it could have a buffering effect on age-dependent DNA damage and repair capacity.

Limitations of the studies

Such studies should now be carried out in different populations and a larger number of individuals.

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