International Journal of Science and Research (IJSR)
ISSN: 2319-7064
ResearchGate Impact Factor (2018): 0.28 | SJIF (2019): 7.583

Effect of Yogic Intervention on Markers of Oxidative Stress and Cellular Aging: A Case Report Study

Selvakumar S[1], Lenin M[2], Dayanalakshmi R[3]

[1]Tutor, Department of Physiology, MGMC & RI, Pondicherry, India

[2]Tutor, Department of Biochemistry, Sree Lakshmi Narayana Institute of Medical Sciences, Pondicherry, India

[3]Assistant Surgeon, Govt PHC, Anniyur, Villupuram Dt, Tamilnadu, India

Abstract: ***Objectives: Few studies showed that a brief yoga-based lifestyle intervention was effective in reducing levels of oxidative stress and cellular aging in obese men. The main objective of this case report was to assess the efficacy of yoga based life style intervention on levels of markers of cellular ageing and oxidative stress at baseline (day 0), at the end of active intervention (day 30), and follow-up at day 180. Study design: Single case report from a prospective ongoing study with pre-post design assessing the level of various markers of cellular aging and oxidative stress. Patient: A 36-year-old man with class I obesity (body–mass index [BMI], 28.5kg/m2) presented to the outpatient department of Medicine at MGMC&RI, pondicherry, India, with history of fatigue, difficulty in losing weight, difficulty to perform daily activities. Setting: After examination and appropriate investigations, including physiologic measures such as blood pressure and lipid profile, he was referred to CYTER & Department of Physiology, MGMCRI, Pondicherry, an outpatient facility conducting meditation and yoga-based lifestyle intervention programs for management of chronic diseases. Intervention: A pretested intervention program included asanas (postures), pranayama (breathing exercises), stress management, group discussions, lectures, and individualized advice Yoga intervention programs, Validated and published at CYTER. Results: The results of this case report shows that the activity of telomerase are enhanced and oxidative stress markers, such as reactive oxygen species and 8-hydroxy-2-deoxy-guanosine levels are reduced from baseline (day 0) to day 180. Conclusions: yoga/meditation-based lifestyle modification causes reversal of markers of aging, mainly oxidative stress, telomerase activity, and oxidative DNA damage. This may prevent onset of several lifestyle-related diseases, of which oxidative stress and inflammation are the chief cause. Study suggest that this simple lifestyle intervention practices may delay aging and prolong a youthful healthy life.***

Keywords: Yoga, cellular aging, oxidative stress

1. Background

Yoga, a scientific-spiritual discipline is the ancient heritage of India that has given answers to spiritual and holistic search for perfect health and well being. Modern life is full of stress and stress-related disorders are rampant in today's world. Yoga is panacea for the modern stress epidemic and has been demonstrated to be an answer to stress and stress related disorders (Madanmohan et al, 2002). The yogic lifestyle, yogic diet, yogic attitude and yogic practices help man to strengthen his body and mind and develop positive health. Yoga enables us to withstand stress by normalising the perception of stress, optimising the reaction to it and effectively releasing pent-up stress through various yogic techniques. Yoga has various facets and the main techniques that are useful to modern man are hatha yoga asans and pranayams, dharana and dhyan. These are most effective when practiced in combination and performed consciously and with awareness. Yogasans help to develop strength, flexibility, will power, good health, and stability and when practiced as a whole with the other limbs of yoga, they give the practitioner a stable and unified strong personality. Yoga is an effective and time-tested method for improving health as well as prevention and management of diseases especially psychosomatic and degenerative disorders. Oxidative stress caused by increase in the production of Reactive Oxygen Species (ROS) such as superoxide radicals (O2), hydrogen peroxide (H2O2), hydroxyl radicals (OH), and singlet oxygen. ROS are produced within the cell in the multiple compartments but majority are generated in the mitochondria during ATP production by oxidative phosphorylation contributing to aging and age-related disorders. Our body has complex antioxidant defence mechanism to prevent the deleterious effect of ROS. An imbalance between reactive oxygen species and antioxidants causes oxidative stress (Cathcart, 2004).

Aging is the progressive loss of metabolic and physiologic functions. In this narrow sense, aging may be defined as the life history of the individual, expressed in the cumulative burden of oxidative stress and inflammation. Broadly, the aging process may be divided into two groups: aging associated with damage accumulation and developmentally programmed aging. However, an emerging hypothesis insists over the free radical theory that is damage accumulation theory of aging. In a recent study yoga and meditation reduces the level of oxidative DNA damage accumulation biomarker (8-OHdG) up to normal (Kumar et al, 2015). There are 3 markers of cellular aging – oxidative stress, DNA damage and decline in telomerase activity (Kumar et al, 2015). Oxidative stress is a distress that generates a sea of chemical and hormonal reactions in the body by free radicals and it damages both, mitochondrial and nuclear DNA (Swetha et al, 2014). Due to adaptive response to this oxidative stress, various body systems such as the immune system may be affected. Oxidative damage preferentially damages telomeric DNA and accelerates telomere loss, whereas antioxidants decelerate it. Telomeres are complex DNA repeats found at chromosome ends that ensure genomic stability. Telomeres shorten after each cell division; therefore rate of shortening and the telomere length are index of mitotic-cell age (Shammas, 2011).Telomerase is main cellular protein responsible for telomere maintenance and elongation. Telomere shortening is counteracted by the

cellular enzyme telomerase (Ornish et al, 2008). Telomerase adds telomeric repeat sequences to the chromosomal DNA ends, preserving not only telomere length, but also healthy cell function and long-term immune function (Yadav et al, 2005). Telomeres and telomere associated proteins plays an important role in aging process and that accelerated telomere erosion is associated with metabolic and inflammatory diseases associated with aging (Kong et al, 2013). In most cases direct link between telomere shortening and constant high level of oxidative stress observed in various diseases (Bernadotte et al, 2016). In human, reduction in telomere length is an ideal prognostic marker for disease risk and its progression (Bisoffi et al, 2006). Few findings suggest that telomeres are prone to damage by oxidative stress due to the presence of high numbers of guanine residues (Harman et al, 2013) and also, it was proposed previously that the oxidative damage to the nitrogen bases have been contribute severely to the process of aging and senescence. ROS can accelerate telomere shortening and their increased levels are responsible for oxidative cellular damage in nuclear and mitochondrial DNA, either directly or indirectly and also hinders the repair process of oxidative bases of DNA. It have been implicated in organismal ageing and countless reports of association of oxidative damage and ageing process. In contrast to the genomic DNA, the telomeric DNA was proposed to be deficient in the repair process and this may be due to the insufficient level of telomerase in the aging cells (Kumar et al, 2015).It has been shown that DNA damage accumulates with age, potentially because of increased production of ROS and/or a decline in DNA repair capacity with age (Chen et al, 2007). Studies suggest that telomere attrition is modifiable, as substantial variability exists in the rate of telomere shortening that is independent of chronological age (Prescott et al, 2012). Therefore, variability of telomere length may be partially explained by lifestyle practices, including dietary patterns (Sun et al, 2012). As accelerated telomere attrition may underlie many chronic diseases, identifying modifiable factors that affect telomere dynamics is important factor. There are evidences suggests that one of the pathways through which chronic stress may impact health is through accelerated cell aging, as indexed by the length of the telomeric DNA at the end of chromosomes (Parks et al, 2009). Chronic psychological stress and mood disorders are linked to shorter telomere length (Puterman et al, 2010) and dampened telomerase activity (Epel et al, 2004). Longer leukocyte telomeres are related to exercise (Puterman et al, 2010), healthy diet, including greater intake of antioxidants such as vitamins C, E, D (Richards et al, 2007) and a healthy lifestyle index consisting of greater intake of fruits and vegetables, and less dietary fat (Mirabello et al, 2009).Regular physical activity has been associated with decreased levels of oxidative stress and inflammation, and it helps to prevent chronic disease (McTiernan, 2008). Obesity and sedentary behaviours may potentially influence telomere length (Valdes et al, 2005).Long term yoga practitioners who has been practicing yoga for several months to years may positively affect the genome expression profiles in immune cells in circulation (Qu et al, 2013).

Yoga's eminence for stress reduction has fortified its popularity in recent years, and data from various randomized trials suggest that use of yoga and meditation reduces symptoms of anxiety and stress. Recent studies suggest that this is possibly mediated by decreasing cellular oxidative stress, including oxidative DNA damage. However, there is paucity of literature on the effect of yogic techniques on physiological functions in general and oxidative stress parameters and oxidative DNA damage in particular. Moreover, none of study had shown the effect of yoga in elderly population on oxidative DNA damage and cellular aging. In view of this, we planned to undertake a systematic study to evaluate role of yoga as simple and therapeutic life style intervention to increase the quality of life by investigating total antioxidant capacity, 8-hydroxy-2'-deoxyguanosine (8-OHdG) and markers of cellular aging as telomere length and telomerase activity.

Therefore, the hypothesis is that yoga/meditation may enhance cellular longevity and delay the aging process by reducing oxidative stress, decelerating telomere loss and telomere-driven replicative senescence, which is primarily a stress response. To validate this hypothesis, this study assessed biochemical markers of cellular aging, oxidative stress at baseline (day 0), at the end of active intervention (day 30), and follow-up at day 180 in an obese patient.

2. Objectives

The objective of this case study was to assess the efficacy of this intervention in reducing the levels of biochemical markers of cellular ageing, oxidative stress at baseline (day 0), at the end of active intervention (day 30), and follow-up at (day 180).

3. Material and Methods

Case history

A 36-year-old man with class I obesity (body–mass index [BMI], 28.5kg/m2) presented to the outpatient department of Medicine at MGMC&RI, pondicherry, India, with history of fatigue, difficulty in losing weight, difficulty to perform daily activities. After examination and appropriate investigations, including physiologic measures such as blood pressure and lipid profile, he was referred to CYTER & Department of Physiology, MGMCRI, Pondicherry. After obtaining informed written consent, this patient was enrolled in a yoga-based lifestyle intervention at CYTER. The meditation/yoga-based lifestyle intervention at CYTER is a pretested 30-day program held for approximately 1 hour a day. The program includes a series of physical postures (asana), breathing exercise (pranayama) and meditation for approximately 1 hour. Special focus is given on coping with stress and anxiety. Each day's program ends with relaxation through shavasana (a relaxation technique) or meditation. After completing this 30-day active intervention under direct supervision of a qualified yoga instructor at CYTER, the patient was advised to continue the same practice for at least the next 180 days at home. He was regularly followed-up in person by a yoga instructor for adherence during this period. The patient was advised to ingest a normal Indian vegetarian diet during the intervention period. The laboratory assessments were done at baseline (day 0), at the end of active intervention (day 30), and at follow-up (day 180). The markers of cellular aging were assayed by measuring the activity of telomerase. Telomerase activity was determined

by using a telomerase assay kit, as per manufacturer's protocol. The peripheral blood mononuclear cells were obtained by gradient density centrifugation by use of Ficoll-Paque method. Peripheral blood mononuclear cells were stored at -80^{0}C until used for assay. Markers of oxidative stress (reactive oxygen species [ROS]) were measured by estimating the luminol-dependent chemi-luminescence with luminometer in integrated mode for 10 minutes. Oxidative DNA damage (8-hydroxy-2-deoxy- guanosine [8-OhdG]) was measured by enzyme-linked immunosorbent assay as per manufacturer's protocol.

Yoga intervention programs:
Validated and published at CYTER (Bhavanani et al, 2015).
Jathis and kriyas (loosening techniques)

Standing asanas
Veera asana
Tada asana
Ardhakati and kati chakra asana
Ardhautkat asana

Sitting asanas
Vakra asana
Paschimottana/purvottana asana
Chatuspadakriya/vyagraha pranayama
Nava kriya

Face prone asanas
Bhujanga asana/bhujangini mudra
Makara asana

Supine asanas
Pawanamukta series
Padauttana series
Sethukriya

Pranayamas
Suka pranayama
Chandra nadi
Pranava
Bhramari
Mudras
Brahma mudra

Relaxation
Savitri pranayama in shavaasana
Marmanasthanam/kaya kriya
Chakra awareness sequence

Table 1: Markers of Cellular Aging and Oxidative Stress at Baseline, End of Active Intervention, and Follow-Up

Variable	Baseline (day 0)	End of active intervention (day 30)	Follow-up (day 180)
Telomerase (IU/cell)	0.81	3.16	36.2
ROS (RLU/min)	1312.086	1184.16	1001.08
8-OHdG (pg/mL)	11,082.46	9765.34	6572.87

8-OHdG, 8-hydroxy 2¢deoxyguanosine; RLU, relative light units; ROS, reactive oxygen species.

Table 2: Physiologic Measures at Baseline and Follow-Up

Variable	Baseline	Day 180	Difference
BMI (kg/m2)	28.5	23.6	-4.9
Systolic blood pressure (mmHg)	136.5	124.2	-14.3
LDL cholesterol (mg/dL)	131.4	88.9	-1.1
HDL cholesterol (mg/dL)	69.8	46.4	-0.6
Total cholesterol (mg/dL)	177.8	127.6	-1.3
LDL/HDL ratio	2.14	1.9	-0.24
Triglycerides (mmol/L)	46.4	42.5	-0.2

BMI, body–mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

4. Results

There was a sustained reduction in oxidative stress markers, such as levels of ROS ND plasma 8- OhdG, Meanwhile there is increased Telomerase activity baseline to day 180 (Table 1). At day 180, BMI had decreased (from 29.5 to 24.7kg/m2), with a significant improvement in all physiologic measurements (Table 2).

5. Discussion

Oxidative stress and inflammation contributes in causation, and progression of several life style related chronic diseases. Yoga/meditation is one such practice that combines a healthy lifestyle with mental peace (Shammas et al, 2011) which is similar to mind–body medicine functioning on the principles of psycho neuroimmunology (Cawthon et al, 2002). A modification in lifestyle and relaxation practices including yoga and meditation were shown to improve clinical profile of patients with various pathologies and enhance immunity (Harman et al 2013). and this benefit was independent of the type of clinical diagnosis.

The present study also shows that these lifestyle interventions (yoga/meditation) may cause a significant decrease in markers of oxidative stress (ROS levels) and this is evident as the oxidative DNA damage marker (8-OHdG) also reduced significantly. The results indicates an enhanced telomerase activity decreased production of ROS and oxidative DNA damage (8- OHdG marker). The present study showed a rise in telomerase activity with a reduction in ROS levels and oxidative DNA damage, which also coupled with the reduction in infammation and stress. Interestingly, this improvement was observed in an exceedingly short duration as early as 30 days of active intervention and was sustained through day 180. Added to it, an interesting improvement in physiologic parameters was observed by day 180. Thus, such cases may show significant decline in oxidative DNA damage following meditation/ yoga practice. This might have a crucial effect in reducing childhood disease and even cancer.

Few findings suggest that telomeres are prone to damage by oxidative stress due to the presence of high numbers of guanine residues (Harman et al 2013). Furthermore, the increased ROS levels are responsible for singles trand breaks in nuclear and mitochondrial DNA, either directly or indirectly and the increased ROS level also hinders the repair process of oxidative bases of DNA. In contrast to the genomic DNA, the telomereic DNA was proposed to be

deficient in the repair process of single-strand breaks19 and this may be due to the insufficient level of telomerase in the aging cells. The results of this study also suggest that the benefits through a positive lifestyle intervention can be evident as early as 30 days even the activity of telomerase also elevated significantly.

Broadly, the aging process may be divided into two groups: aging associated with damage accumulation and developmentally programmed aging. However, an emerging hypothesis insists over the free radical theory that is damage accumulation theory of aging (Peterson et al, 1998) . In this study we pointedly specified in our data that yoga and meditation might reduce the level of oxidative DNA damage accumulation biomarker (8OHdG) up to normal (Kiecolt-Glaser et al, 2002). Some reports explain that telomere shortening and activity of telomerase might be one of the best biomarker for the overall stress response of an organism to various pathogenic conditions (Mohan et al, 2011). Furthermore, shortened telomere length and reduced telomerase activity are correlated with early mortality as well as a health risks which might be controlled partially by psychological stress (Ornish et al, 2008). Also, there are possibilities that telomere shortening might be slowed down or reversed by yoga and meditation interventions, could provide an opportunity for translating novel preventative and therapeutic approaches.

Also, the data regarding the efficacy of lifestyle intervention in this study lasting less than 6 months confirm that yoga/meditation can reduce oxidative stress both by reduction of free radical levels and up regulation of total anti oxidant capacity. Keeping this in view and simple-to-follow yoga and meditation based lifestyle intervention can significantly reduce oxidative stress and inflammation, up regulation of telomerase may aid in telomere length maintenance and prevent accelerated telomere shortening and thus aids in maintenance of chromosomal stability and maintain genomic.

6. Conclusion

In the recent years, life has become immensely stressful. Adoption of simple healthy habits and lifestyle can profoundly impact health. Our data in this study supports that yoga/meditation based lifestyle intervention reduced the markers of oxidative stress and cellular aging. The results of this case study suggests yoga based lifestyle intervention can be used as an effective complementary and alternative medicine therapy in obesity, and may be therapeutic for oxidative DNA damage and lifestyle diseases. Further studies for longer duration are warranted to study sustained benefits of this practice.

References

[1] Bernadotte, A., Mikhelson, V.M., Spivak, I.M., 2016. Markers of cellular senescence. Telomere shortening as a marker of cellular senescence. Aging 8, 3–11. https://doi.org/10.18632/aging.100871

[2] Cathcart, M.K., 2004. Regulation of superoxide anion production by NADPH oxidase in monocytes/macrophages: contributions to atherosclerosis. Arterioscler. Thromb. Vasc. Biol. 24, 23–28. https://doi.org/10.1161/01.ATV.0000097769.47306.12

[3] Cawthon M R. Telomere measurement by quantitative PCR. Nucleic Acids Research. 2002 ;30: No. 10 e47.

[4] Chen, J.-H., Hales, C.N., Ozanne, S.E., 2007. DNA damage, cellular senescence and organismal ageing: causal or correlative? Nucleic Acids Res. 35, 7417–7428. https://doi.org/10.1093/nar/gkm681

[5] Harman E, Akcay S, Buke Y, Niacin EH. Does it affect 8-hydroxy-2-deoxyguanosine levels in patient with low HDL cholesterol?. Medicine Science. 2013;2(2):618-23 .

[6] Kiecolt-Glaser JK, McGuire L, Robles TF, Glaser R. Emotions, morbidity, and mortality: New perspectives from psychoneuroimmunology. Annu Rev Psychol. 2002;53:83–107.

[7] Madanmohan, null, Udupa, K., Bhavanani, A.B., Krishnamurthy, N., Pal, G.K., 2002. Modulation of cold pressor-induced stress by shavasan in normal adult volunteers. Indian J. Physiol. Pharmacol. 46, 307–312.

[8] McTiernan, A., 2008. Mechanisms linking physical activity with cancer. Nat. Rev. Cancer 8, 205–211. https://doi.org/10.1038/nrc2325.

[9] Mohan A, Sharma R, Bijlani RL. Effect of meditation on stress-induced changes in cognitive functions. J Altern Complement Med. 2011;17:207–212.

[10] Ornish D, Magbanua MJ, Weidner G, Weinberg V, Kemp C, Green C, Mattie MD, Marlin R, Simko J, Shinohara K, Haqq CM, Carroll PR. Changes in prostate gene expression in men undergoing an intensive nutrition and lifestyle intervention. Proc Natl Acad Sci U S A. 2008;105(24):8369-8374.

[11] Parks, C.G., Miller, D.B., McCanlies, E.C., Cawthon, R.M., Andrew, M.E., DeRoo, L.A., Sandler, D.P., 2009. Telomere length, current perceived stress, and urinary stress hormones in women. Cancer Epidemiol. Biomark. Prev. Publ. Am. Assoc. Cancer Res. Cosponsored Am. Soc. Prev. Oncol. 18, 551–560. https://doi.org/10.1158/1055-9965.EPI-08-0614.

[12] Petersen S, Saretzki G, von Zglinicki T. Preferential accumulation of single-stranded regions in telomeres of human fibroblasts. Exp Cell Res.1998; 239: 152-160.

[13] Pubmeddev, al, Q.S., et, n.d. Rapid gene expression changes in peripheral blood lymphocytes upon practice of a comprehensive yoga program. - PubMed - NCBI [WWW Document]. URL https://www.ncbi.nlm.nih.gov/pubmed/23613970 (accessed 1.30.20).

[14] Puterman, E., Lin, J., Blackburn, E., O'Donovan, A., Adler, N., Epel, E., 2010. The power of exercise: buffering the effect of chronic stress on telomere length. PloS One 5, e10837. https://doi.org/10.1371/journal.pone.0010837.

[15] Richards, J.B., Valdes, A.M., Gardner, J.P., Paximadas, D., Kimura, M., Nessa, A., Lu, X., Surdulescu, G.L., Swaminathan, R., Spector, T.D., Aviv, A., 2007. Higher serum vitamin D concentrations are associated with longer leukocyte telomere length in women. Am. J. Clin. Nutr. 86, 1420–1425. https://doi.org/10.1093/ajcn/86.5.1420.

[16] Shammas, M.A., 2011. Telomeres, lifestyle, cancer, and aging. Curr. Opin. Clin. Nutr. Metab. Care 14, 28–34. https://doi.org/10.1097/MCO.0b013e32834121b1.
[17] Sun, Q., Shi, L., Prescott, J., Chiuve, S.E., Hu, F.B., De Vivo, I., Stampfer, M.J., Franks, P.W., Manson, J.E., Rexrode, K.M., 2012. Healthy lifestyle and leukocyte telomere length in U.S. women. PloS One 7, e38374. https://doi.org/10.1371/journal.pone.0038374.
[18] Tolahunase, M., Sagar, R., Dada, R., 2017. Impact of Yoga and Meditation on Cellular Aging in Apparently Healthy Individuals: A Prospective, Open-Label Single-Arm Exploratory Study [WWW Document]. Oxid. Med. Cell. Longev. https://doi.org/10.1155/2017/7928981.
[19] Yadav, R.K., Ray, R.B., Vempati, R., Bijlani, R.L., 2005. Effect of a comprehensive yoga-based lifestyle modification program on lipid peroxidation. Indian J. Physiol. Pharmacol. 49, 358–362.