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Effect of Short-Term Practice of Bhramari Pranayama on Sleep Quality and Perceived Stress in School Students

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Abstract

Background: In today's highly-competitive era of modern education, students are constantly exposed to 'high' academic stress. Stress, in turn, affects sleep quality. Deterioration in sleep quality adversely affects overall health. Yogic breathing exercise i.e., 'Pranayama' practice is an easy yet effective way to maintain sound physical and mental health. Traditional yogic literatures particularly recommend 'Bhramari' Pranayama (the 'Humming Bee' breath) for effectively reducing stress and improving quality of sleep. Due to lack of specific scientific evidence to support these benefits from Bhramari Pranayama, this study was undertaken to evaluate the effect of Bhramari Pranayama practice on sleep quality and perceived stress in school students.

Objectives: To evaluate the effect of short-term (6 weeks) practice of Bhramari Pranayama on Sleep Quality and Perceived Stress in school students.

Methodology: After obtaining Ethical clearance, 60 school students of class X were randomly selected for the study. Assent from participants and written informed consent from their parents were obtained. After history-taking and general physical examination, 'baseline' data including assessment of Sleep quality and Perceived stress were obtained using the PSQI (Pittsburgh Sleep Quality Index) and PSS (Perceived Stress Scale) questionnaires respectively. Thereafter, Bhramari Pranayama was practiced by the students for 6 weeks. Finally, at the end of 6 weeks sleep quality and perceived stress were re-assessed using the above questionnaires. Pre- and post- Bhramari pranayama data were compared and analysed using descriptive statistics and Student's t-test; p-value <0.05 was considered as statistically significant.

Results: Post Bhramari Pranayama practice, there was significant improvement in Sleep quality & a significant reduction in Perceived stress (p-value<0.05).

Conclusion: Hence, just a few weeks practice of Bhramari Pranayama significantly improves sleep quality and reduces perceived stress.

Keywords: *Academic stress, Bhramari Pranayama, Perceived Stress, Sleep Quality*

Introduction

Today, while India gropes with the achievement of a target ''Education for All'', another set of problems concerning the educationalists in the country today are issues related to the ever-increasing burden of high 'academic stress' and their adverse effects on students.[1] Various studies carried out after the year 2000 revealed a significantly high prevalence of academic stress among Indian students. One of the studies by Deb et al. in the year 2015 revealed that nearly two-thirds (63.5%) of the Indian students reported stress due to high academic pressure.[2]

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Chronic high-academic stress adversely affects student's learning process and overall health.[3] Apart from having a plethora of ill-effects on almost all the major physiological systems of the body, prolonged stress also affects the quality of sleep adversely. Again, the deterioration in sleep quality, in turn affects the overall health.[4]

'Pranayama', a form of Yogic-breathing exercise, has proved to be an easy yet effective way to maintain a sound physical and mental health.[5] The Sanskrit word 'Pranayama' has been derived from two root words namely- 'Prana' (meaning Vital force) &, 'Yama' (meaning Regulation). Hence, 'Pranayama' literally means- a yogic act regulating flow of the vital energy that governs all the physiological processes in the body.[6] While there are different forms of Pranayama, the 'Bhramari' Pranayama (also known as 'the Humming-Bee' breath) is well-known for its multiple health-benefits.[7]

Also, some of its special features which make this Pranayama notifiable are- its simplicity of slow breathing, complemented with the 'Humming' sound (to be produced during expiration) which makes it more interesting to perform, & finally the fact that it can be easily practiced by everyone, irrespective of age & gender.[6] Along with its numerous other health benefits, Bhramari Pranayama is recommended by the traditional yogic-literatures particularly for: effectively reducing stress and improving the quality of sleep.[8] However, there is no modern scientific evidence to support these specific benefits from Bhramari Pranayama.

Hence this study was undertaken, to evaluate the effect of Bhramari Pranayama practice on sleep quality and perceived stress in school students.

Objectives:

To evaluate the effect of short-term (6 weeks) practice of Bhramari Pranayama on Sleep Quality and Perceived Stress in school students.

Methodology

After obtaining ethical clearance from the Institutional Ethics Committee of BMC&RI, Bengaluru, as well as obtaining a written permission from the head of the school, students were randomly selected from class X of a private school in South Bengaluru for this 'Experimental study' which was conducted during December 2019 to January 2020. Subjects were recruited based on the following Eligibility criteria:

Inclusion criteria: -

1. Age-group: 15-17 years.
2. Apparently healthy students.
3. Subjects who voluntarily gave an Assent to participate in the study and, who also provided a written-informed consent from their parents.

Exclusion criteria: -

1. Subjects with sleep, anxiety/psychiatric disorders.
2. Subjects with ear, respiratory tract infections.
3. Recent history of surgery of ear/ vocal apparatus.
4. History of any other acute/chronic illness.
5. Subjects on regular medication, especially on CNS drugs.
6. Those practicing any form of Pranayama, Yoga, Meditation or other relaxation techniques for past one year.

After explaining about the study in detail and procuring a relevant history and General physical examination, finally 60 school students of class X of both genders were enrolled for the study. At first the 'baseline' data, including assessment of Sleep quality and Perceived Stress, were obtained using the PSQI (Pittsburgh Sleep Quality Index) and the PSS-10 (Perceived Stress Scale) questionnaires respectively, before the actual training and practice started.

The Pittsburgh Sleep Quality Index (PSQI)

The Pittsburgh Sleep Quality Index (PSQI) is a standardized, self-rated questionnaire which was designed to measure sleep quality and sleep disturbances in clinical population. The PSQI questionnaire asks subjects to rate their sleep quality and disturbances over the last month preceding test administration. This 19-item questionnaire generates seven component scores, with

subscale scores 0 to 3, for the following 7 components- Subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and Daytime dysfunction. Adding up of scores from these 7 components yields a 'Global PSQI score' of Sleep quality. The global score ranges from 0 to 21; a score measuring <5 indicates 'Good' sleep quality, whereas a score of ≥5 is indicative of a 'Poor' sleep quality. The sensitivity of the tool is 89.6% and specificity is 86.5% in distinguishing good and poor sleepers. PSQI has good reliability with high internal consistency ($\alpha = 0.83$) and a good test-retest reliability ($r= 0.85$).[9]

Perceived Stress Scale (PSS-10)

The Perceived Stress Scale is a classic stress assessment tool which remains the most widely used psychological instrument for measuring the 'perception of stress'. It is a measure of the degree to which situations in one's life are appraised as 'stressful'. The questions in this scale ask about the feelings and thoughts of the participants during the last month. The questions are of a general nature and hence are relatively free of content specific to any subpopulation group. The PSS-10 questionnaire consists of 10 items, with each item rated on a 5-point Likert scale ranging from 'never' (0) to 'very often' (4). Positively worded items are 'reverse' scored, and then the ratings are summed across all 10 items, with 'higher' scores indicating 'more' perceived stress. Total score ranges from 0 to 40. Score of 0-13 is considered low stress, 14-26 is moderate stress & 27-40 is severe stress.[10]

After obtaining 'baseline' data including assessment of Sleep quality and Perceived stress at the baseline, subjects were trained by a certified Yoga-instructor for 1 session to perform Bhramari pranayama as per the standard method,[11] with following instructions: "sit in a comfortable posture with the eyes closed, close the ears with thumbs, place the index fingers on the forehead right above eyebrows & the other 3 fingers by the side of nose, slowly inhale through the nose, keeping the mouth closed, slowly & deeply exhale by making a 'humming' sound (like a bumble-bee)". The rate at which the participants were asked to perform the Pranayama was: 3-4 Bhramari breaths/minute, for 5 minutes, followed by 2 minutes of rest. This was considered '1 cycle'. 5 cycles were performed in a 45 minutes session per day, for 6 days a week, for 6 continuous weeks.

At the end of 6 weeks, Sleep quality and Perceived stress were reassessed using the above questionnaires, and their scores of Pre- and Post- Bhramari Pranayama practice were compared and statistically analysed.

Statistical Analysis

Statistical analysis was performed using SPSS software (version 25.0, IBM). Data were presented as 'mean ± standard deviation'. Student's t-test (two tailed) was used to compare the groups. p-value < 0.05 was considered as statistically significant.

Results

A total of 60 subjects including 30 males and 30 females were included in the study. Mean age of the participants was 15.77 ± 0.11 yrs.

Table 1 shows 'Baseline-data' for the study participants.

Table 1: 'Baseline' Demographic, Sleep quality (PSQI score) & Perceived stress (PSS score) Data-

VARIABLES	MALE	FEMALE	TOTAL	p-value
Number	30	30	60	-
Age (years)	15.82 ± 0.13	15.72 ± 0.09	15.77 ± 0.11	0.202
BMI (Kg/m2)	20.33 ± 0.76	20.52 ± 0.44	20.43 ± 0.6	0.486
PSQI score	5.29 ± 0.51	6.1 ± 1.09	5.7 ± 0.57	0.143
PSS score	19.1 ± 2.06	20.2 ± 1.87	19.65 ± 1.28	0.385

Table 2 shows the **effect of short-term practice of Bhramari Pranayama** on sleep quality and perceived stress in the study participants.

Table 2: Comparison of Sleep quality (PSQI score) & Perceived stress (PSS score) before & after 6 weeks practice of Bhramari pranayama-

VARIABLES	Pre-Pranayama	Post-Pranayama	p-value
PSQI score	5.7 ± 0.57	3.82 ± 0.33	**<0.0001***
PSS score	19.65 ± 1.28	12.2 ± 0.86	**<0.0001***

(*p-value<0.05)

PSQI: Pittsburgh Sleep Quality Index

PSS: Perceived Stress Scale

Bhramari Pranayama practice even for a relatively short duration of 6 weeks led to a significant ($p<0.05$) decrement in scores of both PSQI and PSS, indicative of a significant improvement in Sleep quality and significant reduction in Perceived stress.

Discussion

The present study revealed that practicing Bhramari pranayama even for a relatively short duration of six weeks significantly improves sleep quality and decreases perceived stress.

Pranayama practice is believed to have multiple health benefits and many studies have been conducted in the past experimenting these benefits, still there is very little documentation on benefits of 'specific' pranayama individually. The Bhramari pranayama is one such technique that has got numerous health benefits but, on the contrary, has very little scientific evidence showing its specific health effects. Most of the literatures available are the 'shared effects' of Bhramari pranayama practice along with other Pranayamas together, and very less effort has been put in the past to decipher the various health benefits of Bhramari pranayama individually[6]. As the per the knowledge of the authors, this study is the first scientific attempt to verify the claims made by traditional yogic-texts that Bhramari pranayama practice is one of the most effective ways to treat sleep related disorders by improving the overall quality of sleep, and to effectively reduce stress levels[8]. Following are the findings of some of the studies done previously to investigate the benefits from Bhramari pranayama practice.

In a study done in the year 2010 by Pramanik et al. to find the Immediate effect of Bhramari pranayama practice, they concluded that slow Bhramari breathing just for five minutes balances the autonomic nervous system through enhanced activation of the parasympathetic system and can be practiced for mental relaxation and reduction of stress in daily life[6]. In another study titled 'EEG paroxysmal gamma waves during Bhramari Pranayama: A yoga breathing technique' done by Vialatte et al. in 2008, they found that Bhramari pranayama practice has a significant influence on the brain activity and induces a feeling of 'blissfulness'[12]. In their study titled 'Role of self-induced sound therapy: Bhramari Pranayama in Tinnitus', Pandey et al. concluded that Bhramari pranayama practice promotes parasympathetic predominance and it significantly reduces the irritability, depression and anxiety associated with tinnitus[13].

Although none of the previous studies have clearly elucidated the 'exact' mechanisms behind how Bhramari Pranayama practice brings about the desired effects, here the improvement in sleep quality and reduction in stress could be due to the following reasons- Bhramari pranayama practice ramps up the production of Nitric oxide (NO), which apart from having several other key health benefits, also improves the quality of sleep. It is estimated that 'humming' during the exhalation phase of Bhramari pranayama increases the endogenous generation of nitric oxide levels by 15-fold as compared to quite exhalation. This in turn helps to dilate the arteries, improve blood circulation and the tissue oxygenation[14]. The 'Acoustic vibration' produced by the humming sound acts as a beneficial stimulus

for the brain tissues, helps to soothe the brain and the nerves and thus has a significant impact in producing the desired effects[8]. Also, the 'self-induced humming sound' in this practice resembles mantra-meditation technique, and induces subjective feelings of mind refreshment and blissfulness[6]. All the previous studies directly or indirectly have found the effect of Bhramari Pranayama practice leading to 'Parasympathetic dominance', thus causing reduction in stress levels and a more calm state of mind, and hence an improved quality of sleep[6]. Further, the neural respiratory elements may be responsible for a mechanism that brings about the above effects as Bhramari Pranayama practice modifies the normal breathing rhythm, with prolonged exhalation & short inhalation, and thus produces significant impact in the physiological system through neural respiratory elements[15].

This study demonstrated that Bhramari Pranayama can prove to be an effective modality to reduce stress and improve the quality of sleep when practiced even for a shorter duration of time. If future studies conducted on a larger population, using more advanced scientific tools for assessment, are able to reproduce similar results, the implications of these findings can be huge. Bhramari Pranayama, then can be prescribed as a scientifically approved modality to address health issues related to stress and diminished quality of sleep, and alongside it will also provide a myriad of other added health benefits.

Conclusion

Bhramari Pranayama when practised regularly even for a short-term period of few weeks can significantly improve sleep quality and reduce perceived stress.

Clinical Implications:

During a time when academic stress and its related adverse effects on health are on the rise alarmingly, measures like the practice of Bhramari Pranayama can prove to be an inexpensive, safe, fast and effective way to reduce stress levels and improve overall quality of sleep, along with providing a multitude of other health benefits.

Limitations:

Findings in the present study were obtained with a relatively small sample size. Future studies should be carried out on a larger and more diverse population to generalize the findings obtained here. Also, here the Sleep quality and Stress levels were assessed using 'self-rating' by the subjects. In order to further validate the above findings, a more precise measurement for these parameters should be done in future studies using better tools like Polysomnography and serum markers of stress.

Conflict of Interest: None

Source of Funding: Self

References

1. Verma S, Sharma D, Larson RW. School stress in India: Effects on time and daily emotions. Int J Behav Dev. 2002;26(6):500-508.
2. Deb S, Strodl E, Sun J. Academic stress, parental pressure, anxiety and mental health among Indian high school students. Int J Psychol Behav Sci. 2015;5:26-34.
3. Rentala S, Nayak RB, Patil SD, Hegde GS, Aladakatti R. Academic stress among Indian adolescent girls. J Educ Health Promot. 2019;8:158.
4. Rebello CR, Kallingappa PB, Hegde PG. Assessment of perceived stress and association with sleep quality and attributed stressors among 1st-year medical students: A cross-sectional study from Karwar, Karnataka, India. Tzu Chi Med J. 2018;30(4):221-226.
5. Jain R, Tonpay PS. Effect of pranayama on cognitive functions of medical students. Indian J Basic Appl Med Res. 2016;6(1):471-476.
6. Kuppusamy M, Kamaldeen D, Pitani R, Amaldas J, Shanmugam P. Effects of Bhramari pranayama on health - A systematic review. J Tradit Complement Med. 2018;8(1):11-16.
7. Manjunatha U, Bhat JS, Radish KB, Bajaj G, Shruthi P, Nayak PS et al. Effect of Bhramari Pranayama on the Acoustic and Aerodynamic Parameters of Voice in Normophonic Females. Evid Based Complement Alternat Med. 2018;2018:4176803.
8. Saraswati SS. Asana Pranayama Mudra Bandha. Reprint Edition. Munger, Bihar: Yoga Publications Trust; 2009. p.401.
9. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh sleep quality index:

A new instrument for psychiatric practice and research. Psychiatry Res.1989; 28(2):193-213.

10. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. J Health Soc Behav. 1983;24:386-396.
11. Kuppusamy M, Kamaldeen D, Pitani R, Amaldas J. Immediate Effects of Bhramari Pranayama on Resting Cardiovascular Parameters in Healthy Adolescents. J Clin Diagn Res. 2016;10(5):CC17-CC19.
12. Vialatte FB, Bakardjian H, Prasad R, Cichocki A. EEG paroxysmal gamma waves during Bhramari pranayama: A yoga breathing technique. Conscious Cogn. 2009;18:977-988.
13. Pandey S, Mahato NK, Navale R. Role of self-induced sound therapy: Bhramari Pranayama in Tinnitus. Audiol Med. 2010;8(3):137-141.
14. Taneja M K. Nitric oxide, Bhramari Pranayama and deafness. Indian J Otol. 2016;22(1):1-3.
15. Sathe S, Thodge K, Rajandekar T, Agrawal A. To Find Out Immediate Effect of Bhramari Pranayama on Blood Pressure, Heart Rate and Oxygen Saturation in Hypertensive Patients. Int J Cur Res Rev. 2020;12(19):193-197.

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Effect of Acute Warm Water Swim Stress on Antioxidant Levels in Swiss Albino Rats

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Abstract

Background: Heat stress affects both physical and mental tasks. Imbalance in maintenance of temperature leads to oxidative stress and damage to the body systems. **Aim:** To evaluate the effect of acute warm water swim stress on antioxidant status changes in albino rats. **Materials and Methods:** The present study was conducted in the Department of Physiology, Meenakshi medical College& Research Institute, Chennai. Twenty male albino rats were randomly divided in to two groups, control group and experimental group. Experimental group of rats were exposed to warm water swim stress at 40ºc for duration of 15min of continuous single exposure. The antioxidant status namely enzyme activity (LPO,CAT, SOD & GPx) and non-enzyme activity (Vitamin C & Vitamin E) were estimated as per standard procedures. **Results:** There was a significant (P<0.001) increase in Lipid peroxidation and was significantly (P<0.001) decrease in enzyme activity (SOD, CAT, & GPx) and non- enzyme activity (Vitamin C & Vitamin E) when compared with their normal controls. **Conclusion:** The changes in antioxidant estimation helps in developing a new approach in understanding the changes in the body under acute exposure to heat water swim stress which is mainly responsible for pathophysiological changes and to know the thermoregulatory activities of the mammals.

Key words: *Antioxidant, stress, warm water*

Introduction

Stress is a universal phenomenon and induces physiological and behavioral changes in an organism to maintain the homeostasis[1]. Acute stress exposure has detrimental effect on several cell functions. Swimming is not always a simple exercise stress, because emotional factors are difficult to be eliminated[2]. Swimming in small laboratory animals has been widely used for studying the physiological changes and the capacity of the organism in response to stress[3]. Maintenance of water temperature is another important factor contributing to swim stress. By varying the water temperature and found that rats could survive as long as 80 hours in lukewarm water[4]. Increasing or decreasing the water temperature above or below this point influences the overall behavior of the animal and changes the involvement of glucocorticoids[5]. Free radicals may be either oxygen derived (ROS, reactive oxygen species) or nitrogen derived (RNS, reactive nitrogen species). Antioxidant act as radical scavengers, and convert the radicals to less reactive species. The antioxidative system includes both enzymatic and non-enzymatic systems[6,7]. We intend to explore the physiological changes that can happen during heat stress and biomarker involved in this type of specific stress. The present study was undertaken to evaluate the effect of acute heat water swim stress on antioxidant status changes in albino rats.

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Materials and Methods

Twenty Adult male albino rats weighing about 150-180grams were used for the study. The study was conducted in Department of Physiology, Meenakshi

medical College& Research Institute, Chennai. The experimental rats were housed in polypropylene cages and maintained under standard conditions. Standard pelletized feed and tap water were provided *ad libitum*. The rats were randomly divided in to two groups, Group-I (Control) and experimental group. The experimental group rats were exposed to heat water swim stress at 40ºC for duration of 15min between 09.00AM to11.00AM for one day. Blood samples are collected from jugular vein after heat water swim stress for antioxidant estimation[8]. The Lipid peroxidation (LPO), enzymatic antioxidant estimation like Superoxide dismutase (SOD), Glutathione peroxidase (GPx), and non-enzymatic antioxidants like Vitamin C, Vitamin E are estimated. The Institutional Animal Ethical Committee approved the study.

Results

There was a significant increase in lipid peroxidation (Table-1) with decrease in antioxidant enzymes like superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT) in heat water swim stress when compared to control group animals (Table-2). The non-enzymatic antioxidants vitamin C and E are significantly decreased in heat water swim stress group when compared to control group (Table-3). All the parameters were recorded and analyzed by using student's t- test and considered P< 0.05 as statistically significant.

Table 1: Lipid peroxidation (LPO)

LPO (nmoles of MDA/min/mg/ptn)	Mean+Sd	P-value
Controls	84.98+3.25	<0.05*
Hot water swim stress	111.66+7.08	

Table 2: Enzymatic Antioxidants: SOD, CAT and GPX

Enzymatic	Mean+Sd	P-value
SOD(min/mg/ptn) Control	5.68+0.22	<0.05*
Heat water swim stress	2.60+0.75	<0.05*
CAT (min/mg/ptn) Control	3.71+0.21	<0.05*
Heat water swim stress	2.34+0.36	<0.05*
GPx (min/mg/ptn) Controls	6.40+0.28	<0.05*
Heat water swim stress	4.56+0.62	<0.05*

Table 3: Non-Enzymatic Antioxidants: VIT C and VIT E

Non-Enzymatic	Mean + Sd	P-value
VIT C (µ/mg ptn) Controls	2.33+0.28	<0.05*
Hot water swim stress	1.25+0.62	
VIT E µ/mg ptn Controls	2.41+0.05	<0.05*
Hot water swim stress	1.24+0.62	

Discussion

There has been limited research on the effects of acute heat water swim stress. The effect of acute exposure to heat water swim stress on antioxidant status in rats has been intensively investigated. The present study indicates that the acute exposure to heat water swim stress for 15 min at 38ºC in a single day showed significant increase in lipid peroxidation. The increased level of lipid peroxidation is the evidence most frequently cited in support of the involvement of oxidative stress in tissues. It is a molecular mechanism of cell injury leading yield a wide range of cytotoxic products, most of which are aldehydes, malondialdehyde[9]. The data suggest that there is the activation of free radical precursors in all investigated tissues. Antioxidants both enzymatic (superoxide dismutase, glutathione peroxidase & catalase) and nonenzymatic (vitamins C and E) provide necessary defense against oxidative stress generated due to high ambient temperature[10]. The concentration of free radicals during normal oxygen metabolism is controlled by various antioxidants and a balance exists between pro-oxidant and antioxidant processes. Free radicals damage biomembranes, reflected by increased lipid peroxidation, thereby compromising cell integrity and function due to reduced antioxidants. Superoxide dismutase (SOD) in conjugation with catalase and glutathione peroxidase (GPx) scavenges both intracellular and extracellular superoxide radicals and prevents lipid peroxidation[11].Reduced glutathione, glutathione peroxidase and superoxide dismutase form a part of the antioxidant defense systems produced by the body to protect the cellular constituents from the damages caused by ROS. Ascorbic acid is an important antioxidant in plasma and acts in tissues, involving ROS in aqueous phase[12]. It is a major antioxidant since, mice lack of L- gulunolactose oxidase, a gene responsible for synthesis of ascorbic acid leads to decreased plasma antioxidant capability, suggesting that these animals may be susceptible to increased level of oxidative stress in the brain. In the brain, ascorbic acid has a dual effect– at low concentrations it promotes lipid peroxidation and at higher concentrations it acts as an antioxidant[13].It is also an anti-stress factor [13,14]. Our study also concurs with similar anti-stress effect of ascorbic acid. Vitamin E is the primary lipid soluble antioxidant, and plays an important role in scavenging of free oxygen radicals and stabilizes the cell membranes in maintaining its permeability[15].It is bound to the protein complexes in the inner mitochondrial membranes and may affect oxidative changes which occur in organelle[16]. In our study, vitamin E has definite role in counteracting stressful situations in animals and it concurs with our study. Alpha-Tocopherol has a peripheral anti-inflammatory effect and this could be related to inhibition of scavenging of free radicals developed due to stress. Vitamin E increases the level of prostaglandins which was decreased during stress which may enhance the exploratory and loco motor activity[8]. Apha-Tocopherol inhibits the activity of nitric oxide .This action was done by inhibiting the gene responsible for activation of the transcription factor NF – κ KB by nitric oxide[17]. Vitamin C and E cause the inhibition of peroxidation, mopping up of free radicals and disorganization and breakage of peroxidation chain reactions by an inhibition of glutathione peroxidase and proteinkinase, resulting in blockade of oxidative mechanism[18]. To conclude, antioxidants like vitamin E and ascorbic acid act synergically, preventing lipid peroxidation and cell destruction.

Conclusion

The exposures to heat water swim stress leading to oxidative damage and generation of free radicals. The human antioxidant protection system involves a variety of components both endogenous and exogenous functions interactively and synergistically to neutralize free radicals caused by reactive oxygen species. These studies support accumulating evidence for brain activity to be dynamically regulated by immune system factors.

References

1. Nayanatara A K, Nagaraja H S, and Anupama B K. The effect of repeated swimming stress on organ weights and lipid peroxidation in rats. Thai journal of physiological sciences.2005; 18:3-9.
2. Kramer K, Dijkstra H, and Bast A. Control of physical exercise of rats in a swimming basin. Physiol Behav.1993; 53: 271-276.
3. Greenen D, Buttrick P, and Scheuer J. Cardiovascular and hormonal responses to swimming and running in the rat. J Appl Physio.1988; 65: 116-123.
4. Tan N, Morimoto K, Sugiura T, Morimoto A, and Murakami N. Effects of running training on the

blood glucose and lactate in rats during rest and swimming. Physiol Behav.1992; 51: 927-931.

5. Richter C P. On the phenomenon of sudden death in animals and man. Psychosom Med.1957; 9: 191-198.
6. Ames B.N, Shigenega M.K, Hagen T.M. Oxidants and the degenerative diseases of ageing" Proc Nati Acad Sci.1993; 90: 7915-22.
7. Shenoy R, Shirwaikar A, "Anti-inflammatory and free radical scavenging studies of Hyptis suaveolens (labiatae). Indian drugs.2002; 39: 574 –577.
8. Ige SF, Akhigbe RE, Omobowale GK, Azeez OM, Ajao FO, Saka WA and Oyekunle OS: Immunomodulatory effect of warm water swim stress in adult female Sprague Dawley rats. Research Journal of Immunology 2011; 4(1): 25-30.
9. Gutteridge JMC. Lipid peroxidation and antioxidants as biomarkers of tissue damage. Clin Chem.1995; 41(12):1819-28.
10. Astrand,P.O. and Rodahl,K.(1970) Text book of work physiology ,McGraw-Hill Book company,New York,USA.
11. Halliwell B, Gutteridge JMC. Oxygen radicals and the nervous system. Trends Neurosci. 1985;8:22-6.
12. Frei B, England L, Ames BN. Ascorbate is an outstanding antioxidant in human blood plasma. Proc Natl Acad Sci.1989;86:6377-81.
13. Chinoy NJ, Sharma M, Michael M. Beneficial effects of ascorbic acid and calcium on reversal of fluoride toxicity in male rats. Fluoride 1993;26:45-56.
14. Chinoy NJ. Metabolic significances of ascorbic acid in animal and human tissues.J Animal Morphol Physiol.1978:68-75.
15. Shaikh Z.A., Vu T.T. and Zaman K. Oxidative Stress as a Mechanism of Chronic Cadmium-Induced Hepatotoxicity and Renal Toxicity and Protection by Antioxidants, Toxicol. Appl. Pharmacol.1999; 154: 256-263.
16. Ernster L., Fosmark P. and Nordenbrand K. The mode of action of lipid-soluble antioxidants in biological membranes. Relationship between the effects of ubiquinol and vitamin E as inhibitors of lipid peroxidation in submitochondrial particles, J. Nutr. Sci. Vitaminol. Spec.1992: 548-551.
17. Frei B, England L, Ames BN. Ascorbate is an outstanding antioxidant in human blood plasma. Proc Natl Acad Sci.1989;86:6377-81.
18. Murray,K.M. Granner,D.K.Mayer,P.A. and Rodwell,V.W. Text book of Harpers biochemistry 25th edition. 2000;8 : 83-85,130-136.

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Hypothyroid Patients with Positive Thyroid Antibodies and Relation to Nerve Conduction Study Findings

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Abstract

Neuropathies are common manifestations of more than half the patients attending medical out patient departments . These neuropathies could be due to many causes. Some of the patients are not diabetics or alcoholics and thyroid profile revealed hypothyroidism . Most of the patients were not on thyroid supplementation and some are on irregular treatment. Primary symptoms are vague not pointing to either thyroid deficiency or diabetes mellitus complained of lethargy , pain in the fingers stabbing in nature ,wight gain, dryskin ,constipation . Nerve conduction studies on median and ulnar nerves in these patients without diabetes and other deficiency disorders point to miss hypothyroid state in these patients, as stress is put on diagnosing more common conditions like diabetes mellitus. If these conditions are excluded it is not difficult to diagnose hypothyroid conditions.

Key words : *Anti-thyroid antibodies, nerve conduction studies, TPO, thyroid peroxidise antibodies, thyroid-autoimmunity.*

Introduction

Hashimoto's thyroiditis (HT), the most frequent autoimmune thyroid disorders (AITDs), is the leading cause of hypothyroidism in the iodine-sufficient areas of the world. About 20–30% of patients suffer from HT, whose cause is thought to be a combination of genetic susceptibility and environmental factors that causes the loss of immunological tolerance, with a consequent autoimmune attack to the thyroid tissue and appearance of the disease.

The pathologic features of lymphocytic infiltration, especially of T cells, and follicular destruction are the histological hallmark of autoimmune thyroiditis (AIT), that lead to gradual atrophy and fibrosis. An important role in the immune-pathogenesis of AITDs is due to chemokines and cytokines.

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Inflammatory cytokines and in particular IL6 and TNFα, released during local or systemic inflammation are the main molecular candidates in driving TH(thyroid hormone) tissue alterations[1]. Thus tissue concentrations of THs and their molecular mediators possibly more effectively reflects the functional state of the thyroid system (TS) at target than circulating hormones[2].

Major concepts of Hashimoto's neuropathy are vasculitis theory, hormone dysregulation theory explaining the disease via direct action of the autoantibodies against various thyroid (thyroperoxidase, thyroglobulin, and TSH-receptor) and several extrathyroid antigens (alpha-enolase and other enzymes, gangliosides and MOG-protein, onconeuronal antigens) all of them expressed in the brain[3].

A thyroid antibodies test is used to help diagnose autoimmune disorder of the thyroid. Thyroid peroxidise antibodies (TPO) ,Thyroglobulin antibodies (Tg) , presence is a sign of Hashimoto disease.

Auto antibodies (proteins of the immune system that aberrantly react against the body's own cells) that bind to fibroblasts to produce and release chemical

signals and biologic materials that lead to swelling and congestion of the tissues affected. These auto antibodies can be measured in the blood to help monitor disease activity and severity does not always correlate with thyroid hormone levels[4].

Thyroid peroxidise antibodies should be measured if the TSH is borderline high on two occasions and there are no overt symptoms of hypothyroidism as this will guide the frequency of future monitoring[5]. This test is commonly used to confirm or exclude Hasimoto's thyroiditis as the reason for hypothyroidism.

Thyroid peroxidase is the major antigen in human Hashimoto's disease, and anti-TPO antibodies induce complement-dependent cytotoxicity. Furthermore, antibodies against complement (anti-C1q) are detected in patients with Hashimoto's disease. These antibodies can damage the thyroid follicular cells directly by activating the complement cascade.They are correlated with thyroid-stimulating hormone (TSH) levels[6]. Modelling of thyroid peroxidase reveals insights into its enzyme function and autoantigenicity[7] .

TPO is oxidized by H_2O_2 and then only TPO can oxidize iodide ions. Oxidized iodide ions bind to tyrosyl residues of thyroglobulin (TG). Formation of T4 and T3 iodothyronines is an effect of oxidation and coupling of hormonogenic iodotyrosines.

As the TPO enzyme is a heme peroxidase, it cannot oxidize the substrate without having been oxidized. To oxidize TPO, the H_2O_2 molecule is necessary. The H_2O_2 molecule is generated only at the apical surface of thyrocytes, and the TPO molecules that are present at this surface are activated.

Intracellular Content and TH Genomic Effects In the brain , T4 is taken up by astrocytes, probably by OATP1C1 (organic anion transporter 1 C1) transporter.

Intracellularly the enzyme type-2 iodothyronine deiodinase (D2) generates T3 by catalyzing the removal of ring iodine atoms in the cytosol, from which T3 easily reaches the nucleus. In other cell types, such as neurons, D3 catalyzes the removal of the outer- or inner-ring iodine atoms to produce T2 or the inactive form rT3, respectively[8]. T3-target cells also include neurons, oligodendrocytes, and many other cell types in the nervous tissue.

This is linked to the extremely complex metabolism of THs in the CNS, and particularly to the interplay between TH membrane transporters and deiodinase activity. The THs actually cross the BBB partially via gaps among the cells that compose the blood–brain barrier, but mainly using transporters, thus through a saturable process[9]. Thus, tissue hypothyroidism during inflammation could impact on cellular processes, requiring an appropriate TH drive, including OPC differentiation into myelinating OL[10]. These results and considerations form the basis of preclinical studies attempting to correct myelination and remyelination failure in experimental conditions characterized by intense tissue inflammation and TS signaling dysregulation, starting from the fact that the block of TH-dependent OPC differentiation has been described in both perinatal and adult animal and human samples[11].

Oligodendrocyte progenitor cell (OPC) also responsible for myelin repair during adulthood as remyelination is the only true regenerative capability of the CNS[12]. OPCs are present in the mature CNS, where they represent a major proliferating cell population, constituting 5% of the total cell population[13]. In response to myelin loss or increased demand, "adult" OPCs have the capacity to differentiate into mature myelinating OL [14] to guarantee an appropriate white matter turnover. This significant capability, demonstrated in physiological conditions, led to the so-called recapitulation hypothesis for myelin repair which suggested that remyelination after myelin damage follows several myelination steps and molecular mechanisms occurring during developmental myelination[15]. Several studies have confirmed the impact of TH on myelin development, homeostasis, and repair focusing on the regulation of TH tissue signaling under physiological and pathological conditions affecting myelination and/or myelin repair during early postnatal age and during adulthood.

"Tissue hypothyroidism in the CNS" [16] In a recent paper, it was suggested a direct link between cytokines, D3 expression, and OPC differentiation failure[17] .

Experiments have demonstrated that under cytokine exposure a dramatic rise in the number of D3-positive cells was observed in OPC derived from neural

precursors. Using the deiodinase blocker iopanocic acid (IOP) in order to decrease D3 activity and then increase T3 intracellular availability. This treatment was able to restore the capability of the OPC culture to express differentiation markers (CNPase and MBP), also restoring OL mature morphology. It may thus be concluded that IOP inhibits D3, thereby restoring an appropriate T3 content in OPCs that overcome the cytokine-induced OPC differentiation block. This effect could explain the positive results obtained by in vivo TH supplementation in experimental models of inflammatory demyelination. Indeed, these studies indicated that TH supplementation restores the expression on a number of TH-dependent genes which are key determinants for OPC maturation the activation of which is necessary to promote remyelination[18].

The remyelination failure in neurological conditions characterized by intense inflammation is likely due not only to a loss of OL, but also to OPC differentiation block. The intense inflammation also causes a complex dysregulation of TH signaling in the CNS, characterized by D3 upregulation and TR downregulation, possibly leading to tissue hypothyroidism. Since T3 is a critical player for OPC differentiation, the decreased availability of the active T3 in the tissue, particularly in OPC during inflammation, might contribute to OPC differentiation failure. Thus, the possibility of including TH as adjuvant therapy in diseases and injuries during the acute inflammatory phase might well be considered. It was demonstrated that pulsed TH treatment increases the MBP content, restores myelin sheath thickness, normalizes neurofilament immunoreactivity[19].

A complex dysregulation of the TH tissue signaling is reported in experimental model of inflammatory/demyelinating diseases. A downregulation of all TRs, including TRα, which is responsible for oligodendroglial lineage induction from neural stem cell as well as TRβ, which is responsible for OPC maturation into oligodendrocytes was found[20]. A 30-fold upregulation was found in theT3-inactivating enzyme D3 mRNA,and the ectopic expression of D3 observed also in astrocytes, NG2-IR (nerve glial antigen 2 immunoreactive) OPCs was found. D3 protein strongly upregulates in vitro in astrocytes exposed to proinflammatory cytokines. Alterations in TR and D expression correlate with the rise of inflammatory cytokines released[21]. The overall scenario emerging from in vivo data collected in animal models of inflammatory diseases like that from human patients, namely, D3 overexpression and TR downregulation, supports the hypothesis that inflammation leads to a substantial tissue hypothyroidism. Inflammatory cytokines and HIF (hypoxia inducible factor) are regarded as potential candidates for mediating at least the D regulation in many experimental models.

Method and Materials

Patients presenting with neurological manifestations to medical outpatient department evaluated first by detailed general, physical, systemic, and neurological examination. T3 (FT3), T4 (FT4), and (TSH) levels evaluated.

A normal range of TPO-Ab(+) was defined as below 16IU/mL.

Hypothyroid patients between 35-45 yrs age are subjected to the study after taking written informed consent . They are explained in detail about the test .

50 hypothyroid patients negative for thyroid antibodies as controls.

50 hypothyroid patients positive for thyroid antibodies as cases

After biochemical investigations, electrophysiological studies were done.

Materials :A computer system ; Chart software ; Power Lab (with built-in Bio Amp or Power Lab and Bio Amp front-end); Five-lead Shielded Bio Amp Cable & snap-connect Shielded Lead Wires; Disposable ECG recording electrodes; Stimulus Bar Electrode ; Electrode gel ; Alcohol swabs; Dry earth.

Watch, jewelry, etc. removed from the wrists. The five-lead Bio Amp cable connected to the bio amp. Dry earth lead connected to earth connection of bio amp cable. Skin cleaned with alcohol , 2 disposable ECG electrodes are attached to the skin overlying the abductor pollicis brevis muscle 2–3 cm apart after applying small drop of electrode gel. Four shielded lead wires connected to bio amp cable ports for positive and negative, 1 and 2 channels . Stimulus electrode connected to stimulator output of the Power Lab positive to positive and negative

to negative. Stimulus electrode placed over the median nerve at the wrist along the axis of the arm, with the negative lead towards wrist. The nerve stimulated by a mild and brief single electrical shock from the stimulating electrode and same strength is used for all subjects. The resulting electrical activity is recorded by recording electrodes. Distance between the electrodes and the time taken by electrical impulses to travel between electrodes are used to measure conduction velocities. Amplitudes and latencies are also calculated from the chart. Nerve action potentials were amplified in the conventional way and displayed on power lab monitor. All tests were carried out in a warm room with the subject lying on a couch in relaxed position as records are affected by muscular contraction.

The system is adjusted in such a way that the stimulus takes place after 5 ms of pressing start button and record is taken for 70 ms. Recording shows two tracings one is stimulus tracing which shows the point of stimulus and with tracing of action potential below it marked by the digital system of the power lab.

Inclusion criteria:

Subjects attending medical OP with symptoms of peripheral neuropathy without diabetes or any other deficiency disorders like VitB12 ,alcoholism and thyroid profile showing hypothyroidism and with thyroid antibody test results both positive and negative .

Exclusion criteria:

Subjects already diagnosed and being treated as diabetes mellitus , alcoholics , people suffering with nutritional deficiencies like Vit B12.

Observational ,cross-sectional study was performed in the Department of Physiology in collaboration with Department of Medicine at Shadan Institute of Medical Sciences Hyderabad .

The protocol of the study was approved by the Institutional Ethics Committee.

Informed consent is obtained from all the patients subjected to the test.

Results

Correlation was observed in antibodies presence and the results. Patients with positive antibodies showed nerve conduction disturbances of increased latency,decreased amplitude and conduction velocity. These findings are in concordance with the well known nerve damage and other laboratory findings in hypothyroidism more commonly in patients diagnosed with autoimmune type of hypothyroidism damage to thyroid gland.

Table 1. Amplitudes, latencies, conduction velocities of motor nerves compared in hypothyroid patients with negative and positive antibodies.

Parameters	Hypothyroid with Negative antibodies mean (SD)	Hypothyroid with Positive antibodies mean (SD)	t - test	p - value
Amplitude(mV)				
Median Nerve	4.50 (0.48)	4.02 (0.35)	7.92	<0.001
Ulnar Nerve	6.68 (0.92)	6.95 (1.39)	1.77	0.07
Conduction Velocities (m/s)				
Median Nerve	59.23 (4.67)	53.91 (4.45)	9.03	<0.001
Ulnar Nerve	54.86 (5.21)	53.32 (5.90)	2.14	0.03
Latency (ms)				
Median Nerve	2.91 (0.63)	3.54 (1.05)	5.63	<0.001
Ulnar Nerve	2.76 (0.52)	3.03 (1.13)	2.37	0.01

Table 2. Amplitudes, latencies, conduction velocities of sensory nerves compared in hypothyroid patients with negative and positive antibodies.

Parameters	Hypothyroid with negative antibodies mean(SD)	Hypothyroid with positive antibodies mean(SD)	t-test	p-value
Amplitude (mV)				
Median Nerve	24.72 (11.90)	18.35 (8.41)	4.78	<0.001
Ulnar Nerve	20.52 (6.30)	18.15 (5.71)	3.05	<0.01
Conduction Velocities (m/s)				
Median Nerve	54.47 (6.34)	49.25 (5.21)	6.96	<0.001
Ulnar Nerve	50.29 (7.45)	44.52 (5.00)	7.04	<0.001
Latency (ms)				
Median Nerve	2.29 (0.42)	2.70 (0.21)	9.56	<0.001
Ulnar Nerve	3.37 (0.51)	4.01 (1.23)	5.26	<0.001

Discussion

Primary hypothyroidism is a chronic and insidious disease caused by failure of thyroid hormone production mostly due to inflammation, thyroidectomy, use of ^{131}I, and anti-hyperthyroid drugs. A wide variety of systems may be affected, such as renal, digestive, cardiac, circulatory and nervous. The nervous system may be damaged centrally or peripherally. Dysfunction of the peripheral nerve system (PNS) is not infrequent and should prompt correct diagnosis and treatment of this endocrinopathy when present. Early treatment provides overall clinical amelioration. The so called myxoedematous myopathy represents to 10% of acquired myopathies. This myopathy, in its full expression, is unusual but by that time, frequent are complaints as weakness, cramps, and stiffness. Slowness of relaxation time of deep reflexes is found in 80% of the case. Thus, it should be considered that the real incidence of muscle dysfunction may be underestimated. Hypoesthesia, pain and paraesthesias, deep reflexes hyporeflexia, atrophy, and disautonomy may be present in hypothyroidism. The electrophysiological diagnosis of peripheral neuropathy reaches 72% of cases. The real prevalence of hypothyroidism neuropathy and/or myopathy depends on the diagnostic criteria used, either clinical, electrophysiological, laboratorial, structural or combined. In addition, most available data published are case reports[22].

Peripheral neuropathy has a variety of systemic, metabolic, and toxic causes. The most common treatable causes include diabetes mellitus, hypothyroidism, and nutritional deficiencies. The diagnosis, thus, requires careful clinical assessment, judicious laboratory testing, and electrodiagnostic studies or nerve biopsy. Peripheral neuropathy can involve different nerve types including motor, sensory, and autonomic nerves. Peripheral neuropathy can also be categorized by the size of the nerve fibers involved, large or small.

Thyroid hormones exert multiple effects on neural development and function[22]. Overt hypothyroidism is associated with significant alterations both in the neuromuscular system and brain functions. The neurological manifestations of clinical hypothyroidism in adults are varied and include peripheral neuropathy, entrapment neuropathy, mental dysfunction, hearing loss, seizures, possibly cerebellar ataxia, and myxedema coma. In some patients with clinical hypothyroidism, peripheral nerves dysfunction may be the main and presenting manifestation. Peripheral neuropathy may be caused by severe, long-term, untreated hypothyroidism. Although the association between hypothyroidism and

peripheral neuropathy is not fully understood, it is known that hypothyroidism can cause fluid retention resulting in swollen tissues that exert pressure on peripheral nerves.

There are many reports on electroneuromyography (ENMG) changes in hypothyroidism. The objectives of the present study were to relate the signs and symptoms of PNS dysfunction; and compare mean values of nerve conduction studies in patients with neurological abnormalities in hypothyroidism and correlate them with neurological signs and symptoms and thyroid antibody levels; and to compare latency, amplitude and nerve conduction velocity from selected nerves. 100 patients suffering from primary hypothyroidism were submitted to nerve conduction studies. Abnormalities were found in patients positive for thyroid antibodies. Clinical, laboratorial and nerve studies correlation was observed in patients with hypothyroidism and thyroid antibodies. The patients with positive thyroid antibodies showed a significant tendency of nerve conduction slowness as compared without antibodies. The findings are in concordance with the well-known nerve and muscle damage in hypothyroidism.

Conclusion

Association between Hashimoto's hypothyroidism and peripheral neuropathy is not fully understood and exact role of antithyroid antibodies in the pathogenesis of neuropathy is not precisely clear.

Absence of antecedent infections, fever, diabetes, vitamin deficiencies, hypothyroid profile with antithyroid antibody seropositivity suggests Hashimoto's neuropathy as a possible cause of abnormal nerve conduction studies. Anti-thyroid antibodies might have pathogenic significance and early detection and correction of thyroid deficiency and other treatments for autoimmunity,may help to prevent major complications .

Ethical Clearance: Institutional clearance is obtained.

Conflict of Interest: None.

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References

1. Calza, L., Fernandez, M., Giuliani, A., D'Intino, G., Pirondi, S., Sivilia, S., et al. Thyroid hormone and remyelination in adult central nervous system: A lesson from an inflammatory-demyelinating disease. Brain Research Reviews, 48, 339–346,2005.

2. Little, A. G. A review of the peripheral levels of regulation by thyroid hormone. Journal of Comparative Physiology B, 186, 677–688,2016.

3. Nielsen CH, Brix TH, Leslie RG, et al. A role for autoantibodies in enhancement of pro-inflammatory cytokine responses to a self-antigen, thyroid peroxidase. Clin Immunol ;133:21827,2009.

4. Rc Mcleod DS, Caturegli P, Cooper DS, Motos PG, Hutfless S. Variation in rates of autoimmune thyroid disease by race/ethnicity in US military personnel. JAMA ;311:1563-5,2014. [PMID 24737370].

5. Carlê A, Laurberg P, Knudsen N, et al. Thyroid peroxidase and thyroglobulin auto-antibodies in patients with newly diagnosed overt hypothyroidism. Autoimmunity,39:497503,2006.

6. Lee, J. Y., & Petratos, S.;Thyroid hormone signaling in oligodendrocytes: From extracellular transport to intracellular signal. Molecular Neurobiology, 53, 6568–6583,2016.

7. PLoS ONE ;10:e0142615. doi:10.1371/journal.pone.0142615,2015. [PMC free article] [PubMed] [CrossRef] [Google Scholar)

8 &10. Calza, L., Fernandez, M., & Giardino, L.; Role of the thyroid system in myelination and neural connectivity; Comprehensive Physiology, 5, 1405–1421, 2015.

9. Bernal, J., Guadan ˜o-Ferraz, A., & Morte, B; Thyroid hormone transporters Functions and clinical implications. Nature Reviews Endocrinology, 11, 406–417,2015.

11. Buser, J. R., Maire, J., Riddle, A., Gong, X., Nguyen, T., Nelson, K., et al. Arrested preoligodendrocyte maturation contributes to myelination failure in premature infants. Annals of Neurology, 71, 93 –109,2012.

12&13. Crawford, A. H., Chambers, C., & Franklin, R. J. Remyelination: The true regeneration of the central nervous system. Journal of Comparative Pathology, 149, 242–254,2013.

14. Crawford, A. H., Tripathi, R. B., Richardson, W.

D., & Franklin, R. J. Developmental origin of oligodendrocyte lineage cells determines response to demyelination and susceptibility to age-associated functional decline. Cell Reports, 761–773. http://dx.doi. org/10.1016/j.celrep.2016.03.069, 2016.

15. Franklin, R. J., & Ffrench-Constant, C. ; Remyelination in the CNS: From biology to therapy. Nature Reviews Neuroscience, 9, 839–855, 2008.

16&17. D'Intino, G., Lorenzini, L., Fernandez, M., Taglioni, A., Perretta, G., Del Vecchio, G., et al.; T3 administration ameliorates the demyelination/remyelination ratio by correcting tissue hypothyroidism. Journal of Neuroendocrinology, 23, 778–790,2011.

18. Zhang, M., Ma, Z., Qin, H., Yao, Z. Thyroid hormone potentially benefits via facilitating remyelination. Molecular Neurobiology, 53, 4406–4416,2015.

19,20&21. Fernandez, M., Giuliani, A., Pirondi, S., D'Intino, G., Giardino, L., Aloe, L., et al., Thyroid hormone administration enhances remyelination in chronic demyelinating inflammatory disease. Proceedings of the National Academy of Sciences of the United States of America, 101, 16363–16368,2004.

22. Boyages SC. The neuromuscular system and brain in hypothyroidism. In: Braverman LE, Utiger RD, editors.Werner and Ingbar′s the Thyroid: A Fundamental andClinicalText.8 th ed. Philadelphia: Lippincott Williams & Wilkins; p. 803-10,2000.

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A Study on Prevalence of Colour Vision Defects and Correlation with Sex, Visual Acuity and Blood Groups of the Study Group

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Abstract

Inherited color blindness is a lifelong challenge. While it may limit prospects for certain jobs, most people find ways to adapt to the condition. Colour vision defect is usually for red-green colour and it is X-linked recessive trait. It is mainly homozygous that develop colour vision defects. Female heterozygous usually have normal vision. Colour vision defects also have a strong genetic component , especially if both parents have colour vision defects , and people with a particular blood group , and very myopic or hypermetropic , there is a good chance their child will be same. Color blindness is often apparent at a young age when children are learning their colours and goes undetected because as they grow they learn to associate specific colours with certain objects.For example, they come to know that grass is green, so they call the colour they see green. If symptoms are very mild, a person may not realize that they don't see certain colours.

Key Words: *Partial colour blindness, Mutations in OPN1LW, OPN1MW,Deuteranopia , Protanopia, Photopigment of Reti*na.

Introduction

John Dalton described his own color blindness in 1794. In common with his brother, he confused scarlet with green and pink with blue. Dalton supposed that his vitreous humor was tinted blue, selectively absorbing longer wavelengths. He instructed that his eyes should be examined after his death, but the examination revealed that the humors were perfectly clear. Experiments on DNA extracted from his preserved eye tissue showed that Dalton was a deuteranope, lacking the middlewave photopigment of the retina. This diagnosis is shown to be compatible with the historical record of his phenotype, although it contradicts Thomas Young's belief that Dalton was a protanope[1].

Seeing colors is subjective. It is impossible to know how people with colour vision defects (CVD) see reds, greens, and other colors the same way as people with perfect vision. It is important for children to be tested before they start school because many early childhood educational materials involve identifying colors. However, there's no cure for inherited color blindness. When detected eye specialist may prescribe tinted glasses or contact lenses that can assist in distinguishing colors.

Processing of visual information under photopic conditions is initiated by three types of photoreceptor S, M, and Lsensitive cone and subsequently mediated by a luminance and two opponent chromatic mechanisms, the red/green (or L/M) and yellow/blue (or [L+M]/S) channels. Each cone type is sensitive to a broad range of wavelengths, but has its own peak sensitivity (e.g., 440, 543, and 566 nm for the S, M, and L-cones, respectively[2]. Signals of the M- and L-cones are additively fed into the luminance channel and compared in the L/M chromatic opponent channel. The (L+M)/S chromatic opponent channel compares the responses from the S-cone and the summed responses from the L- and M-cones[3].

Colour vision is mediated by three types of cones and two chromatic opponent mechanisms. Absence or alteration of any cone type causes color vision deficiency (CVD) and lead to dichromatic or anomalous trichromatic color vision[4,5,6,7]. The most common CVD is X-chromosome-linked red-green colour blindness which

occurs mostly in males[8] and has two subtypes: protan and deutan. The protan subtype is further subdivided into protanopia, characterized by missing L-cones, and protanomaly, characterized by defective L-cones with a shift in peak sensitivity toward that of M-cones. The deutan subtype can be subdivided into deuteranopia, characterized by missing M-cones, and deuteranomaly, characterized by defective M-cones with a shift in peak sensitivity toward that of L-cones[8]. The luminance response for protan subjects is dominated by normal M-cones, whereas L-cones dominate the response for deutan subjects. Thus, relative to normal colour vision (CN), with which luminance sensitivity is determined by a combination of both normal L- and M-cones, protan subjects are more sensitive to shorter wavelengths, whereas deutan subjects are more sensitive to longer wavelengths. If luminance sensitivity and cone contrast are important factors controlling emmetropization and myopia development, as suggested by Rucker and Kruger[9], refraction measurements for eyes with CVD and eyes with CN should be different.

Objectives: To study the prevalence of colour vision defects in students joining our medical college.

Materials & Methods

The presence of CVD is determined using the Ishihara pseudoisochromatic plates, and repeating the test for the second time to avoid false positives. Tests were performed binocularly with spectacle correction under artificial daylight illumination. It is appreciated that this technique is of practical value in investigating colour vision defects. All 1000 students were also tested for errors of refraction. 96 students were myopic and are wearing glasses and they are instructed to read Ishihara charts without removing glasses. The refractive status of all 1000 students is tested by using Snellen charts.Blood group testing is done for all the participants by glass slide method using anti-A,anti-B antisera. As a diagnostic procedure, Ishihara / pseudoisochromatic charts are of advantage and provides information about the colour vision function which is a subjective test and in our study group students being from medical college cooperation from the subjects does not require any special skill or preparation. For students who are unable to understand the test at all, explaining them the physiological aspects of the test made them easy undergo the tests. The main difficulty is to make the subjects able to tell what exactly they are seeing in the Ishihara charts.

In this study we have subjected one thousand students who routinely undergo vision screening tests at the time of admission into medical college for visual acuity and colour vision by Snellen and Ishihara charts.Testing is done by using special images called pseudoisochromatic plates. These images are made of colored dots that have numbers or symbols embedded within them. Only people with normal vision can see these numbers and symbols. If color blind, subject may not see the number or may see a different number. We made students to understand the test and tell what exactly they see. If the student is wearing glasses or contact lenses ,he should continue to wear them during the exam.This test has no associated risks, and no special preparation is necessary.

Inclusion criteria: Medical students of Shadan Institute of Medical Sciences, after taking written informed consent.

Exclusion criteria: Students diagnosed with eye diseases such as squint or cataracts were excluded from the study.

Results

Of the 1000 participated in the color vision screening, 572 (57.2%) males and 428 (42.8%) females, aged 18 to 21 years. Of these, 78 students were having abnormal color vision with red-green CVD that could not be classified by the two color tests. All 78 students with suspected color vision defects by first test are examined for the second time after sometime and confirmed to avoid false positives.Out of 1000 students subjected to the tests ,78 colour vision defect cases were identified and all of them are males and have red – green type of colour vision defect which is significant number and correlation with blood group shows almost equal prevalence in ‘O’ & ‘B’ +ve blood groups as 35% and 33% respectively, followed by ‘A’ 22% and ‘AB’ 8%.None of the female students detected with colour vision defect. Out of 572 males and 428 females 52 males and 44 females are having myopia respectively and none of them have colour vision defects

Table 1. Different blood group types in the study group and visual acuity findings.

Total No.of Subjects	Gender	Type of Blood Group								Visual acuity			Type of color vision defect	
		A		B		AB		O						
1000	M/F	Rh +ve	Rh -ve	Rh +ve	Rh -ve	Rh +ve	Rh -ve	Rh +ve	Rh -ve	Normal	Myopia		Red-Green	Others
											< 4	>4		
Male	572	118	10	214	04	48	0	164	14	520	38	14	78	-------
Female	428	89	08	138	04	34	0	134	21	384	34	10	nil	nil

Table 2. Percentage Distribution of Blood Groups among subjects with normal and deficient colour vision

Blood group type	Normal Subjects				Subjects with colour vision defects			
	Number		Percentage %		Number		Percentage %	
	Male	Female	Male	Female	Male	Female	Male	Female
A	128	97	22	23	25	-	32	-
B	218	142	38	33	21	-	27	-
AB	48	35	8	8	8	-	10	-
O	178	154	32	36	24	-	31	-
Total	572	428	100	100	78		100	

Discussion

OPN1LW produces red-sensitive opsin, OPN1MW and OPN1SW, produce green-sensitive and blue-sensitive opsin respectively[10]. OPN1LW and OPN1MW are on the X chromosome at position Xq28[11]. Genetic changes of the OPN1LW and/or OPN1MW genes can cause red-green colourblindness[12]. These genetic changes involve recombination events between the highly similar genes of OPN1LW and OPN1MW, which can result in deletion of one or both of these genes[13].

Protanopia is caused by defective or total loss of the OPN1LW gene function, causing vision that is entirely dependent on OPN1MW and OPN1SW[14]. Affected individuals have dichromatic vision, with the inability to fully differentiate between green, yellow, and red colour.

During eye development, early visual experience plays a critical role in controlling eye growth, with a predictable change in axial length to match the position of the image focal plane with the retinal plane[14]. Shifting the image focal plane to a position in front of or behind the retina, leads to a shorter or longer axial length and consequently a hyperopic or myopic eye[15]. The process by which the eye grows to match its retina with the image focal plane is called emmetropization, responsible for elimination of refractive errors in neonates during early eye development. The optical system is not free of

chromatic aberration. Longitudinal chromatic aberration (LCA), caused by the dispersion of the ocular media, causes a single object to form multiple chromatic images within the eye, located at different distances from the retina for different color images. A distant object could produce a red (long-wavelength [L]) image behind the retina, a blue (short-wavelength [S]) image in front of the retina, and green and yellow (middle-wavelength [M]) images near or at the retina. In the human eye, the long-wavelength (700 nm) and short-wavelength (450 nm) images are separated by approximately 1.7 to 2.0 D, with very small individual variations[16].

As Blood group types and CVDs are inherited as genetic traits from parents, several studies are conducted to find the influence of blood type on CVDs. For CVD and blood type phenotype –genotype correspondence reflects a shared genetic influence. No significant differences in the distribution of both these genetic traits is found. No significant correlation in blood type and CVDs are evident. Some studies have shown prevalence of CVDs in males with blood type "B+Ve".

Conclusion

Screening test for congenital colour vision deficiencies should be made mandatory for children as there is injury risk. Experimental study by Reiss and colleagues suggested that CVDs impaired recognition of blood in body fluids may contribute to missing certain diseases like haematuria ,as recognition of blood may contribute to seeking prompt medical consultations and accelerate the diagnosis.

People who are colorblind often consciously apply certain techniques or use specific tools to make life easier. For example, memorizing the order of the lights from top to bottom on a traffic light removes the need to distinguish its colors.Labeling clothing can assist in matching colors properly. Some software applications (apps developed by CVD patients themselves) transform computer colors into those that colorblind people can see. Inherited color blindness is a lifelong challenge. While it may limit prospects for certain jobs, such as working as an electrician who must tell the difference between color-coded wires, most people find ways to adapt to the condition. With the use of software and /or glasses that may help in identifying colours early diagnosis will help to improve vision, if not in total as there is no cure for colour blindness and help them cope with the defect by applying certain techniques or use specific tools to make life easier and safe.

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References

1. D M Hunt, K S Dulai, J K Bowmaker, J D Mollon. et al. The chemistry of John Dalton's color blindness; 1995, doi:10.1126/science.267(5200)984-8.
2. Smith VC, Pokorny J. Spectral sensitivity of the foveal cone photopigments between 400 and 500 nm. Vision Res;1975, 15:161– 171.
3. Derrington AM, Krauskopf J, Lennie P. et al.Chromatic mechanisms in lateral geniculate nucleus of macaque. J Physiol, 1984, 357:241–265.
4. Pokorny J, Moreland JD, Smith VC. et al. Photopigments in anomalous trichromats. J Opt Soc Am, 1975, 65:1522–1524.
5. Alpern M, Moeller J. The red and green cone visual pigments of deuteranomalous trichromacy. J Physiol.1977, 266:647–675.
6. He JC, Shevell SK. Variation in color matching and discrimination among deuteranomalous trichromats: theoretical implications of small differences in photopigments. Vision Res. 1995,n35:2579– 2588.
7. Smith VC, Pokorny J. Color matching and discrimination. In: Shevell SK, ed. The Science of Color. 2nd ed. Oxford, UK: Elsevier. 2003:103–148.
8. DeMarco P, Pokorny J, Smith VC. et al. Full-spectrum cone sensitivity functions for X-chromosome-linked anomalous trichromats. J Opt Soc Am A.9: 1992, 1465–1472.
9. Rucker FJ, Kruger PB. Cone contributions to signals for accommodation and the relationship to refractive error. Vision Res; 2006,46:3079–3089.
10. Hofmann l, Palczewski K. "Advances in understanding the molecular basis of the first steps

in colour vision". Progress in Retinal and Eye Research. 2015,49:46-66.

11. Merbs SL, Nathans J. "Absorption spectra of human cone pigments".Nature.1992, (6368):433-5.
12. Neitz J, Neitz M. "The genetics of normal amd defective color vision".Vision Research. 2010,51(7)633-51.
13. Deeb SS "Genetics of variation in human colour vision and the retinal cone mosaic". Current Opinion in Genetics and Development. 2006 16(3): 301-7.
14. Wald G, Griffin DR. The change in refractive power of the human eye in dim and bright light. J Opt Soc Am; 1947, 37:321–336.
15. Bedford RE, Wyszecki G. Axial chromatic aberration of the human eye. J Opt Soc Am:1957,47:564-565.
16. Howarth PA, Bradley A. The longitudinal chromatic aberration of the human eye and its correction. Vision Res; 1986, 26:361– 366.

Mechanism of Biological Aging-A Review

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Abstract

Aging is a universal, inherent, natural phenomenon that occurs in all organism. Aging involves morphological and functional changes in cellular and extracellular components leading to progressive decline in most biological functions. It causes reduction in strength, basal metabolism, sexual activity and the body's defenses.

Aging is the progressive decline in the maintenance of homeostasis, which leads to decreased response of the body against internal and external stress. It involves imbalance between free radicals and the antioxidant mechanism lead to damaged cells, tissues, and organs resulting in age related changes.

With age there is modifications in energy metabolism, insulin sensitivity, neuroendocrine function and induction of hormesis response. Telomere shortening, mitochondrial dysfunction, increase of oxidative stress, alteration of insulin-like growth factor and growth hormone signaling are considered to be important contributors of aging process.

Recently many genes and changes in gene expression have been found associated with aging which affects many biological processes and are associated with senescence and oxidative stress.

This review focuses on the underlying mechanism of biological aging. With an increase in the number of elderly population and the patients of age-related diseases, it is becoming increasingly important to consider these in the field of research. We have attempted to discuss the different aging mechanism along with the newer concepts, which can give a direction for the future research studies.

Keywords: *Hormesis, Senescence, Epigenetic, Endocrine dysfunction, IGF1 regulation.*

Introduction

Aging is a time-sequential deterioration of body function that occurs in most animals and considered as an inevitable fact of life. It is a complex multifactorial process characterized by progressive functional decline at the molecular, cellular, tissue, and organismal levels.

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Adaptations with evolutionary changes occurs in most complex organisms that involves biological mechanisms that purposely limit their internally determined lifespans beyond a certain species-specific age. Senescence results in programmed aging and it is an unavoidable side effect of a beneficial property. Evolutionary theories of aging explain why mortality rises with age as health and function decline. According to this as individuals age, mutation and natural selection causes mortality because less of lifetime fertility remains.[1]

Different natural aging mechanisms together result in progressive deterioration of body function and failure of metabolic processes. This review discusses different

mechanism responsible for biological aging mechanisms.

For this review, we conducted a literature search on PubMed and google scholar ranging from February 1, 1993 to May 30, 2020, querying the following terms and related synonyms: "senescence and aging", "telomerase activity and lifespan", "epigenetic regulation of aging", "metabolic changes with aging", "endocrine and metabolic changes in stress", "oxidative stress in aging", "inflammatory changes with aging". Search also included individual key terms like "Hormesis", "IGF regulation", "Klotho gene", "Nrf/CNC protein". We restricted our search to articles published in English.

Hormesis and Aging

Breakdown of self-organizing systems, homeostasis and reduced ability to adapt to the environment results in aging. According to the concept of evolution aging occurs due to the absence of natural selection after reproductive stage of life. Fitness can be defined as the ability of an individual to leave copies of its genes to future generations.[2]

Hormesis is viewed as an evolutionary-based adaptive responses. Hormesis is the adaptive responses to stress and environmental challenges with beneficial effects of biological systems. It helps in improving cellular functions and its tolerance to more severe stress. Hormesis can be explained as an evolutionary adaptation that acts to maintain fitness in a changing external environment. [2,3]

Cells and organisms evolved to survive exposures to toxic agents and further to use those toxic agents to their advantage. Low concentrations of toxic metals activate stress defense mechanisms and through this induce hormetic effects. Spinoso-Castillo et.al. through their study proved that low concentrations of toxic metal silver nanoparticles induce hormetic effects through activating plant stress defense mechanisms.[4]

Hormesis is characterized by stimulation of many independent cellular functions such as enhancements of DNA repair, antioxidant defenses and autophagy. Recent findings have demonstrated that hormesis can occur when a challenge is imposed after acute injury. Preconditioning and the adaptive response causes postinjury metabolic challenges and faster recovery.[5] One of the ways dietary restriction improves cellular functioning is by enhancing endogenous cellular stress responses and energy metabolism. Prophylactic intermittent fasting (e.g., every-other-day fasting [EODF]) can protect neurons against injury by dampening oxygen free radical formation and inflammation, and activating cell survival pathways. It causes increase in the growth factor expression and axonal plasticity. Jeong M et.al. studied the effect of dietary restriction, in the form of every-other-day fasting (EODF), prior to (pre-EODF) and after (post-EODF) an incomplete cervical SCI in rats. Both the prophylactic pre-EODF and therapeutic post-injury-initiated EODF resulted in improved functional recovery.[6]

Senescence Association with Aging

Senescence is cellular program that induces a stable growth arrest and limits the proliferation of aged or damaged cells. It is a stress response triggered by insults associated with aging. Mitotic cells divide a finite number of times before they cease replication and senescence starts. Genomic instability and telomere attrition are associated with triggering senescence and are considered primary aging hallmarks. A stable growth arrest ensures that the damaged or transformed cells do not transfer their genomes. [7,8]

Aging is considered to be associated with decline in mitochondrial function contributing to specific aspects of the aging process like cellular senescence, chronic inflammation and the age-dependent decline in stem cell activity. [9]

Telomerase activity and telomere length are found to be associated with stressful conditions. At the cellular level, stress can promote earlier onset of age-related effects. In a study on 58 healthy premenopausal women the perceived stress and chronicity of stress was found significantly correlated with higher oxidative stress, lower telomerase activity, and shorter telomere length. The high-stress group had significantly shorter telomeres (raw mean T/S ratio = 1.13 ± 0.17), than the low-stress group (raw mean T/S ratio = 1.33 ± 0.15). There was 550-bp telomere length shortening in the high-stress group compared with the low-stress group which indicates that their lymphocytes had aged the equivalent of 9–17 additional years.[10]

Recent studies are focusing on methods for improving telomerase activity and telomere length. Tolahunase M. et. al. studied the effect of Yoga and Meditation based lifestyle intervention (YMLI) on cellular aging in healthy individuals. They found significant increase in the telomerase activity, total antioxidant capacity β-endorphin, BDNF, and sirtuin-1 after 12 weeks of YMLI.[11]

TA-65 is a small molecule telomerase activator used as dietary supplement discovered from a traditional Chinese medicine. In a study conducted in Barcelona, Spain subjects taking the low dose of TA-65 (250 U) had significantly increased telomere length over the 12 months period.[12]

Lin P.C. et. Al. did a double-blind placebo-controlled trial to evaluate the antiaging effects of a food supplement containing placental extract. Samples were evaluated for $CD34^+$ cells, insulin-like growth factor 1 (IGF1), and telomerase activity, which are all markers related to aging. Telomerase activity differed significantly between the control and food supplement groups. The average telomerase activity was found to increase by 30%. [13]

Epigenetic Regulation

Gene expression is central to the cellular function and its fate. Maintenance of the fundamental structure of chromatin is key to slowing down the aging process. Transcription factors, histone proteins, DNA methylation, and nucleosome positioning, are related to control of gene expression. Also, non-coding RNAs have been found to play a crucial role in regulating chromatin states and gene expression.[14]

Increased genomic instability and inappropriate transcription are associated with increased aging. The packaging of the eukaryotic genome into nucleosome wrapped around histones plays a critical role in regulating the activities of the genome. Histone post-translational modifications have been shown to affect aging. Sen P. et. al. showed in their study the critical role of H3K36 methylation in restoring chromatin structure and prevents spurious cryptic transcription. The study found that the Loss of H3K36me3 in aged yeast cells results in the production of intragenic short transcripts and a shorter life span.[15]

Oxidative stress contributes to various age-related degenerative diseases and the process of aging. Past studies have found transcription regulators which function in stress responses and functions continuously to maintain homeostasis of these various processes in th body. One of them is the SKN-1 protein in the C. elegans and Nrf/CNC protein in the mammals. They are considered importance in aging and longevity. Nrf/CNC proteins are associated with cellular protective and maintenance function. Nrf2 act as a regulator of antioxidant and xenobiotic defense, proteostasis and metabolic regulator. [16]

p53 is a transcription factors well known to be associated with senescence, thus to the aging process. Long non-coding (lnc)RNA molecules, are a vast class of regulators of gene expression affecting both transcriptional processes and post-transcriptional events. Senescence-associated lnc RNAs (SAL-RNAs) shows lower abundance in senescent cells. Reduced *SAL-RNA1* levels causes enlarged morphology, positive β-galactosidase activity, and heightened p53 levels. By these mechanisms it delays senescence and aging. [17]

Disruption in the DNA methylation patterns are found associated with aging. Heyn et. al. performed whole-genome bisulfite sequencing (WGBS) of newborn and centenarian genomes. They observed that the centenarian DNA had 494,595 less methylated cytosine—phosphate—guanine dinucleotides (mCpGs) than did the newborn DNA. More hypomethylated CpGs were observed in the centenarian DNA compared with the neonate and it covered all genomic compartments, such as promoters, exonic, intronic, and intergenic regions. [18]

Gentilini et. al. studied human population for the role of epigenetics in the modulation of longevity. Global DNA methylation and Alu elements methylation were higher in centenarian's offspring than in offspring of non-long-lived parents. In all old subjects they identified a pattern of 709 CpG loci, exclusively located within CpG islands, with hypermethylation. They confirmed that genome-wide levels of methylation decrease with age, there is a tendency for DNA methylation to increase mainly in CpG islands localized in the promoter regions.[19]

Another gene related with aging is klotho. It is an aging-suppressor gene., which partially explains why a mutation to the *Klotho* gene causes extensive aging phenotypes. Circulating Klotho also has direct effects on tissues and cells that do not express Klotho. It is positively correlated with the expression of IGF-1 and IGF binding protein-3. Increases resistance to oxidative stress. *β*Klotho contributes to the regulation of energy metabolism and α-Klotho have been associated with ovarian tumors.[20]

Arking et.al. performed DNA sequencing to screen for mutations in *KLOTHO* that could influence human aging and identified an allele, termed KL-VS, containing six sequence variants in complete linkage disequilibrium, two of which result in amino acid substitutions F352V and C370S. They demonstrated that heterozygosity for KL-VS contributed to improved longevity. [21]

Endocrine Dysfunction and Aging

Aging results in subtle changes both in ACTH and cortisol secretion. According to neuroendocrine theory, decreased sensitivity of hypothalamus and peripheral receptors would cause energy misbalance, inadaptability, and weakening of immune and reproductive ability. The loss of hypothalamic sensitivity leads to progressive loss of homeostasis, alterations in hormone concentrations, and reduction of neurotransmitters and signaling molecules. [22]

Glucocorticoid excess is associated with age-related changes, including loss of muscle mass, hypertension, osteopenia, visceral obesity, and diabetes, among others.[23]

High levels of cortisol in humans is observed to have neurodegenerative effects. Reduction of corticosterone level reduces learning and memory deficits and attenuates loss of neuronal viability and plasticity. In a study done on rats the effect of calorie restriction along with adrenalectomy was found to be neuroprotective with an elevated level of levels of brain-derived neurotrophic factor (BDNF), transcriptions factors (pCREB). Both are considered the markers of neurotrophic activity. Hippocampal complex governs the age-related cognitive decline. More protection of the pyramidal neurons in the CA2/3 region of the Hippocampal complex was observed in the group with combination of calorie restriction along with adrenalectomy.[24]

Secretion of growth hormone declines with aging. With age Genetic mutations causes disruption of growth hormone signaling, the production of growth hormone-releasing hormone, and the growth hormone receptor function. In a study intended to explores the effects of caloric restriction and genetic disruption of growth hormone signaling on murine aging, it was found that the mice subjected to both caloric restriction and disruption of growth hormone signaling survived longer.[25]

Banks et.al. studied the effects of treatment with the GH-releasing hormone (GHRH) receptor antagonist MZ-5-156 on SAMP8 mice, a strain that develops with aging cognitive deficits and has a shortened life expectancy. Mice treated for 4 months with MZ-5-156 showed increased telomerase activity, improvement in oxidative stress in brain and muscle strength. IGF-I measured 2 h after single injection of MZ-5-156 showed a significant decrease of about 12%. Also mean life expectancy increased by 8 weeks with no increase in maximal life span, and tumor incidence decreased from 10 to 1.7%. [26]

Metabolism and Aging

Aging is considered as a progressive failure of metabolic processes. Studies have shown that carbohydrate intolerance develops as part of the aging process. The peripheral insulin resistance causes carbohydrate intolerance. It is considered to be caused by a post-receptor defect in target tissue. The development of insulin resistance may be more closely related to abdominal adiposity commonly seen in aged individuals. [27,28]

Skeletal muscle loss is a major unfavorable phenotypic change observed with aging. Sarcopenia is suggested to be due to a reduced basal rate of muscle protein synthesis. Muscle proteins are resistant to the anabolic action of insulin in the elderly. Rasmussen et.al. in their study found that muscle protein synthesis increased only in the young individuals during hyperinsulinemia. Changes in muscle protein synthesis were correlated with changes in leg amino acid delivery and blood flow. [29]

IGF1 pathway plays a key role in regulating longevity and studies indicates that common genetic mechanisms may exist for regulating IGF1 levels and lifespan. Yuan et.al. studied the median lifespans, and circulating IGF1 levels at 6, 12 and 18 months for 32 female and 32 male mice. Plasma IGF1 levels showed a significant inverse correlation with median lifespan at 6 months. Also, for the longer-lived mice strains, the negative correlation of IGF1 and lifespan became stronger and more significant. [30]

Genetic factors attribute to the variation in IGF-1 level and longevity. Leduc et.al. identified a major genetic determinant of IGF-1 level variation on Chr 10 that was associated with longevity. Their analysis confirmed a relationship between a locus regulating IGF-1 level (*Igf1q4* and *Igf1q8*) and longevity. The haplotype associated with lower IGF-1 was also associated with an increase in median lifespan and a lower mortality rate. [31]

Inflammation and Aging

Multiple mediators of cell maintenance are known to decline in aging. Recent evidence suggests that dysregulation of molecular inflammatory process plays a key role in the aging process. Chronic up-regulation of pro-inflammatory mediators occurs during the aging process due to an age-related redox imbalance that activates many pro-inflammatory signaling pathways. NF-κB is considered to be the major culprit responsible for the systemic inflammatory process seen during aging as it regulates the transcription of pro-inflammatory molecules. NF-κB is a transcription factor activated by oxidative stimuli and have shown increased activity with aging in a variety of tissues, including heart, liver, kidney, and brain tissues. [32,33]

Bruunsgaard et. al. explored the effects of TNF-α and IL-6 on survival in healthy 80-year-old people after the adjustment for known risk factors and co-morbidity. In the follow-up period of 6 years TNF-α was found associated with mortality in men, but not in women, whereas low-grade elevations in IL-6 were found associated strongly with mortality in both sexes. [34]

Inflammation observed in aging also relates to increased heat shock proteins, increased ROS and oxidized lipoproteins which activate the Toll-like-receptors (TLRs) pathway, initiating an inflammatory response whose key mediators are IL-1, IL6 and TNFα. [35]

Evidence suggests that antioxidants and anti-inflammatories can reduce the pace of shortening of telomere length during aging.[36] Shin C et. at. suggested that with low-grade inflammation along with moderately elevated serum homocysteine (HCY) levels may influence the attrition of leukocyte telomere length (LTL) in older adults. They found a significant inverse association between HCY levels and LTL in participants with serum hs-CRP levels of ≥ 2 mg/L ($p < 0.05$).[37]

In summary, aging is a gradual accumulation of molecular damage due to failure of maintenance of biological functions and defense against stress. Genes are associated with aging in form of lifespan regulator, effector, involving mitochondrial function, energy metabolism and cellular senescence. Aging is a progressive failure of metabolic processes and it is characterized metabolically by insulin resistance, changes in body composition, and declines in growth hormone (GH), insulin-like growth factor-1 (IGF-1) functioning.

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References

1. Goldsmith TC. Evolution of aging theories: Why modern programmed aging concepts are transforming medical research. Biochemistry (Moscow). 2016 Dec 1;81(12):1406-12.
2. Forbes VE. Is hormesis an evolutionary expectation?. Functional Ecology. 2000 Feb;14(1):12-24
3. Calabrese EJ, Mattson MP. How does hormesis impact biology, toxicology, and medicine? NPJ Aging Mech Dis. 2017 Sep 15;3:13
4. Spinoso-Castillo JL, Chavez-Santoscoy RA, Bogdanchikova N, Pérez-Sato JA, Morales-Ramos V, Bello-Bello JJ. Antimicrobial and hormetic effects of silver nanoparticles on in vitro regeneration of vanilla (Vanilla planifolia Jacks. ex Andrews) using a temporary immersion system.

Plant Cell, Tissue and Organ Culture (PCTOC). 2017 May 1;129(2):195-207.

5. Zhang L, Liu H, Xu K, Ling Z, Huang Y, Hu Q, et.al. Hypoxia preconditioned renal tubular epithelial cell-derived extracellular vesicles alleviate renal ischaemia-reperfusion injury mediated by the HIF-1α/Rab22 pathway and potentially affected by microRNAs. Int J Biol Sci. 2019 May 7;15(6):1161-1176.
6. Jeong MA, Plunet W, Streijger F, Lee JH, Plemel JR, Park S et.al. Intermittent fasting improves functional recovery after rat thoracic contusion spinal cord injury. J Neurotrauma. 2011 Mar;28(3):479-92.
7. McHugh D, Gil J. Senescence and aging: Causes, consequences, and therapeutic avenues. Journal of Cell Biology. 2018 Jan 2;217(1):65-77.
8. Bernadotte A, Mikhelson VM, Spivak IM. Markers of cellular senescence. Telomere shortening as a marker of cellular senescence. Aging (Albany NY). 2016;8(1):3-11.
9. Sun N, Youle RJ, Finkel T. The Mitochondrial Basis of Aging. Mol Cell. 2016 Mar 3;61(5):654-666.
10. Epel ES, Blackburn EH, Lin J, Dhabhar FS, Adler NE, Morrow JD, Cawthon RM. Accelerated telomere shortening in response to life stress. Proceedings of the National Academy of Sciences. 2004 Dec 7;101(49):17312-5.
11. Tolahunase M, Sagar R, Dada R. Impact of Yoga and Meditation on Cellular Aging in Apparently Healthy Individuals: A Prospective, Open-Label Single-Arm Exploratory Study. Oxid Med Cell Longev. 2017;2017:2784153.
12. Salvador L, Singaravelu G, Harley CB, Flom P, Suram A, Raffaele JM. A natural product telomerase activator lengthens telomeres in humans: a randomized, double blind, and placebo controlled study. Rejuvenation research. 2016 Dec 1;19(6):478-84.
13. Lin PC, Chiou TW, Liu PY, Chen SP, Wang HI, Huang PC et.al. Food supplement 20070721-GX may increase CD34+ stem cells and telomerase activity. J Biomed Biotechnol. 2012;2012:498051.
14. Booth LN, Brunet A. The aging epigenome. Molecular cell. 2016 Jun 2;62(5):728-44.
15. Sen P, Dang W, Donahue G, Dai J, Dorsey J, Cao X et.al. H3K36 methylation promotes longevity by enhancing transcriptional fidelity. Genes & development. 2015 Jul 1;29(13):1362-76.
16. Blackwell TK, Steinbaugh MJ, Hourihan JM, Ewald CY, Isik M. SKN-1/Nrf, stress responses, and aging in Caenorhabditis elegans. Free Radical Biology and Medicine. 2015 Nov 1;88:290-301.
17. Abdelmohsen K, Panda A, Kang MJ, Xu J, Selimyan R, Yoon JH et.al. Senescence-associated l nc RNA s: senescence-associated long noncoding RNA s. Aging cell. 2013 Oct;12(5):890-900.
18. Heyn H, Li N, Ferreira HJ, Moran S, Pisano DG, Gomez A, et al. Distinct DNA methylomes of newborns and centenarians. Proc Natl Acad Sci U S A. 2012 Jun 26;109(26):10522-7.
19. Gentilini D, Mari D, Castaldi D, Remondini D, Ogliari G, Ostan R et al. Role of epigenetics in human aging and longevity: genome-wide DNA methylation profile in centenarians and centenarians' offspring. Age (Dordr). 2013 Oct;35(5):1961-73.
20. Kim JH, Hwang KH, Park KS, Kong ID, Cha SK. Biological Role of Anti-aging Protein Klotho. J Lifestyle Med. 2015 Mar;5(1):1-6.
21. Arking DE, Krebsova A, Macek M Sr, Macek M Jr, Arking A, Mian IS et. al. Association of human aging with a functional variant of klotho. Proc Natl Acad Sci U S A. 2002 Jan 22;99(2):856-61.
22. Zjačić-Rotkvić V, Kavur L, Cigrovski-Berković M. Hormones and aging. Acta Clinica Croatica. 2010 Jan 1;49(4):549-54.
23. Yiallouris A, Tsioutis C, Agapidaki E, Zafeiri M, Agouridis AP, Ntourakis D et.al. Adrenal Aging and Its Implications on Stress Responsiveness in Humans. Front Endocrinol (Lausanne). 2019 Feb 7;10:54.
24. Qiu G, Spangler EL, Wan R, Miller M, Mattson MP, So KF et.al. Neuroprotection provided by dietary restriction in rats is further enhanced by reducing glucocortocoids. Neurobiol Aging. 2012 Oct;33(10):2398-410.
25. Koopman JJ, van Heemst D, van Bodegom D, Bonkowski MS, Sun LY, Bartke A. Measuring

aging rates of mice subjected to caloric restriction and genetic disruption of growth hormone signaling. Aging (Albany NY). 2016 Mar;8(3):539-46.

26. Banks WA, Morley JE, Farr SA, Price TO, Ercal N, Vidaurre I et. al. Effects of a growth hormone-releasing hormone antagonist on telomerase activity, oxidative stress, longevity, and aging in mice. Proc Natl Acad Sci U S A. 2010 Dec 21;107(51):22272-7.
27. Ross R, Després JP. Abdominal obesity, insulin resistance, and the metabolic syndrome: contribution of physical activity/exercise. Obesity. 2009 Dec;17(S3):S1-2.
28. Kohrt WM, Kirwan JP, Staten MA, Bourey RE, King DS, Holloszy JO. Insulin resistance in aging is related to abdominal obesity. Diabetes. 1993 Feb 1;42(2):273-81.
29. Rasmussen BB, Fujita S, Wolfe RR, Mittendorfer B, Roy M, Rowe VL et.al. Insulin resistance of muscle protein metabolism in aging. The FASEB journal. 2006 Apr;20(6):768-9.
30. Yuan R, Tsaih SW, Petkova SB, Marin de Evsikova C, Xing S, Marion MA et.al. Aging in inbred strains of mice: study design and interim report on median lifespans and circulating IGF1 levels. Aging Cell. 2009 Jun;8(3):277-87.
31. Leduc MS, Hageman RS, Meng Q, Verdugo RA, Tsaih SW, Churchill GA et.al. Identification of genetic determinants of IGF-1 levels and longevity among mouse inbred strains. Aging Cell. 2010 Oct;9(5):823-36.
32. Chung HY, Cesari M, Anton S, Marzetti E, Giovannini S, Seo AY et.al. Molecular inflammation: underpinnings of aging and age-related diseases. Ageing Res Rev. 2009 Jan;8(1):18-30.
33. Chung HY, Lee E K, Choi YJ, Kim JM, Kim DH, Zou Y et al. Molecular inflammation as an underlying mechanism of the aging process and age-related diseases. J Dent Res. 2011;90(7):830-840.
34. Bruunsgaard H, Ladelund S, Pedersen AN, Schroll M, Jørgensen T, Pedersen BK. Predicting death from tumour necrosis factor-alpha and interleukin-6 in 80-year-old people. Clin Exp Immunol. 2003 Apr;132(1):24-31.
35. Cannizzo ES, Clement CC, Sahu R, Follo C, Santambrogio L. Oxidative stress, inflamm-aging and immunosenescence. J Proteomics. 2011;74(11):2313-2323.
36. Prasad KN, Wu M, Bondy SC. Telomere shortening during aging: Attenuation by antioxidants and anti-inflammatory agents. Mechanisms of ageing and development. 2017 Jun 1;164:61-6.
37. Shin C, Baik I. Leukocyte Telomere Length is Associated With Serum Vitamin B12 and Homocysteine Levels in Older Adults With the Presence of Systemic Inflammation. Clin Nutr Res. 2016 Jan;5(1):7-14.

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Major Depression Induced Endocrine Modulation is a Risk Factor for Low bone Mineral Density in Premenopausal Women

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Abstract

Background: The significant physiological effects of psychological depression are beginning to be recognized as exacerbating common diseases, including osteoporosis. This review discusses the current evidence for psychological depression-associated mental health disorders as risk factors for osteoporosis, the mechanisms that may link these conditions, and potential implications for treatment

Osteoporosis is a major public health threat and depression is second most important cause of disability worldwide in 2020. Several studies have reported an association between depression and low bone mineral density, but a causal link between these two conditions is disputed.We propose that depression induces early bone loss in premenopausal women, primarily via specific endocrine mechanisms associated poor lifestyle habits contributory.

Aim and Objectives: To find the clinical correlation between depression, serum cortisol, vitamin D, hypothyroidism and BMD in Premenopausal Women.

To find out a new risk factor of secondary osteoporosis in premenopausal women.

Methods: The study group consisted of 80 osteoporotic female patient's age range between 30-60years.The state of depression was analyzed by using Ham D scale. BMD and endocrine parameters was measured by DEXA and chemiluminisence,ELISA. Statistical correlation analyzed by SPSS22software.

Results: A highly significant ($P < 0.00001$) correlation was observedbetween HAM-D score and serum cortisol. The correlation between HAM-D and BMD was also significant ($P < 0.05$).No significant correlation was found between BMD and serum cortisol ($P > 0.05$).The correlation of serum vitamin D with BMD was far more significant ($P < 0.00001$) compared to the association with TSH ($P < 0.0001$).

Discussion & Conclusion: A high score of depression associated with low vitamin D level or high serum cortisol and TSH level which is a risk factor for low BMD in premenopausal women to develop secondary osteoporosis

It can be concluded that Irrespective of the specific causes, subjects with depression should be considered for screening for bone mineral density and, vice versa, subjects with low BMD should be considered for screening for depression in early stage of life and supplementation of vitamin D with regular physical activity in premenopausal women for prevention of secondary osteoporosis.

Keywords: *BMD, Cortisol, Depression, Premenopausal women, Vitamin D, secondary osteoporosis.*

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Introduction or background

Emerging evidence points to the potential pathological impact of mental health on disease. It has

long been held that depression has negative impacts on health and disease risk, but the specific mechanisms, by which this occurs, as well as implications for treatments and clinical recommendations, have not been examined in-depth. In this review, we first highlight mechanisms that impact both bone health and mental health toward identification of potentially overlapping signaling pathways. We then review current literature regarding the impact of common life style modification for treatment of osteoporosis -+and mental health disorders to promote recognition of the potential interaction of these therapeutic agents in patients with concurrent mental health disorders and osteoporosis to encourage a broad view of disease management toward improved patient health. Finally, we provide a perspective outlook on the potentially Provisional beneficial effects of alternative treatments, such as exercise and nutritional supplementation, on both osteoporosis and depression.

***Rationale*:**

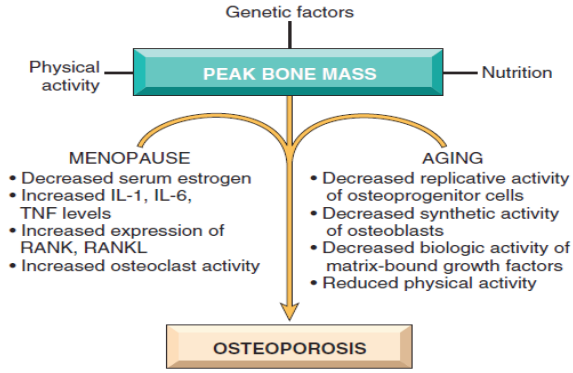
- Prognosis for osteoporosis treatment is poor.

- The rationale of this study is to ascertain the mode of action of depression in lowering the BMD in premenopausal women and whether life style modification can be a prophylactic measure.

Osteoporosis is the most common form of metabolic bone disease and is characterized by low bone mass and micro-architectural bone deterioration. The World Health Organization defines osteoporosis as a bone mineral density (BMD) that is ≤2.5 standard deviations below peak bone mass, which is typically achieved around age 30. In the United States alone, osteoporosis accounts for over 1.5 million fractures per year [1]. By 2025, treatment costs are estimated to exceed $25 billion [2]. Osteoporosis is characterized by an imbalance of skeletal remodeling, resulting in increased osteoclast activity and/or decreased numbers of osteoblasts, which can lead to decreased bone strength and mass, as well as increased susceptibility to fracture.

Osteoporosis is an umbrella term for a group of distinct pathological conditions and has been traditionally classified into primary and secondary types based on mechanism of disease [3]. There are two main types of primary osteoporosis: type I osteoporosis and type II osteoporosis. The theoretical framework in figure 2 depicts the type I osteoporosis occurs most frequently in postmenopausal women and primarily results from estrogen deficiency. Type II osteoporosis is associated with aging and is commonly observed in men and women after the age of 60. Secondary osteoporosis is characterized by bone loss resulting from an underlying etiology, such as Cushing's syndrome, or prolonged treatment with glucocorticoids.

In glucocorticoid-induced osteoporosis, bone loss occurs within several months of glucocorticoid treatment. Excess glucocorticoids exert an inhibitory effect on osteoblast differentiation [4]. Glucocorticoid-induced osteoporosis is the most common form of secondary osteoporosis and is the most common form of osteoporosis among young people (reviewed in [5]. Secondary osteoporosis can also be caused by disuse.



In acute psychological and physical stress, stress signaling is initiated through the hypothalamic-pituitary-adrenal (HPA) axis and the sympathomedullary (SAM) pathway via secretion of stress hormones, which include glucocorticoids (cortisol) and catecholamines (epinephrine, norepinephrine).

Psychological stress can have lasting impact on risk for development of comorbid disease, as well as significant impact on pre-existing diseases. In regard to osteoporosis, U.S. military veterans diagnosed with PTSD have a higher risk of developing osteoporosis [6].

Material and Methods:

- An Observational - cross sectional study was conducted on 80 osteoporotic patient's age range 30-60 years in department of Physiology in collaboration with Orthopaedic OPD in KPCMCH, Kolkata.

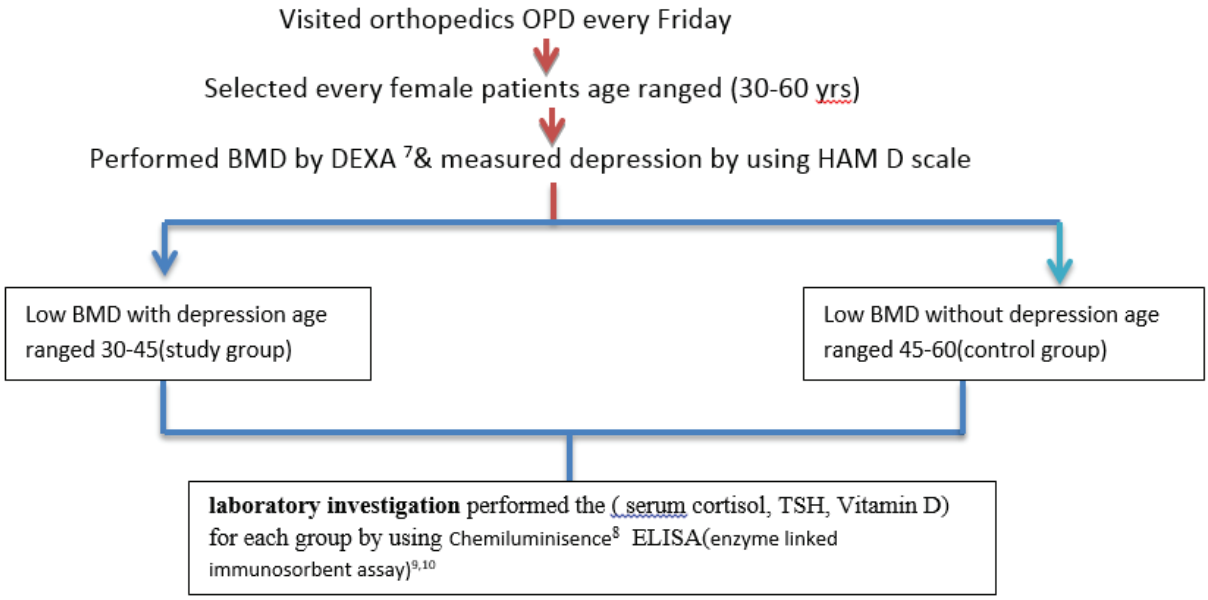
- Institutional ethical clearance was obtained and

inclusion, exclusion criteria decided.

Visited orthopedics OPD every Friday

Selected every female patients age ranged (30-60 yrs)

Performed BMD by DEXA [7]& measured depression by using HAM D scale



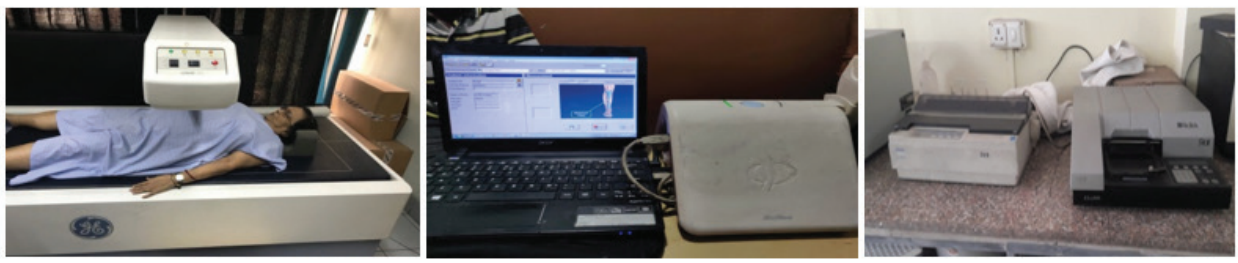


Figure: DEXA(dual energy X-ray absorptiometry ,Ultrasound & ELISA (enzyme linked immunosorbent assay)

Statistical Analysis: The results were expressed as mean ± SD. P <0.05 was considered as significant. One way ANOVAand correlation analysis was applied. Statistical analysis done by using the software GRAPHPAD PRISM Version 5.00 March 7, 2007

Findings

Scatter diagram 1- 5 showing correlation coefficient between these different endocrine variables with depression and bone mineral density in premenopausal women.

Scatter diagram 1- 4 showing correlation coefficient between these different endocrine variables with depression and bone mineral density in postmenopausal women.

Discussion

Scatter diagram 1- 5 showing correlation coefficient between these different endocrine variables with depression and bone mineral density in premenopausal women.

- In scattered diagram no 1 showed the

correlation between HAM-D and BMD showed R=-0.257(moderately negative correlation) and statistically also significant (P <0.05).

- A highly significant (P <0.00001) correlation was observed between HAM-D score and serum cortisol which showed a moderately positive correlation with R value of 0.57 in scattered plot no 2.

- No significant correlation was found between serum cortisol and BMD (P> 0.05) which showed R= -0.16 in scattered plot no 3.

- Last scattered plot no 4 & 5 showed the correlation of serum vitamin D with BMD was far more significant (P<0.00001) compared to the association with TSH (P<0.0001) although vitamin D is negatively correlate (R= 0.23) whereas TSH is moderately positive correlation(R= 0.51) with BMD.

Scatter diagram 1- 4 showing correlation coefficient between these different endocrine variables with depression and bone mineral density in postmenopausal women.

- BMD is reduced consequently due to aging leading to primary osteoporosis in postmenopausal women.

- As the correlation between HAM-D and BMD showed R=-0.15 which is a negligible correlation in scatter plot no2 as well as no such relation also not find out between Cortisol

with BMD in postmenopausal women in scattered plot no 3.

- Scattered plot 4 & 5 showed the correlation of serum TSH with BMD was far more significant (P<0.00001) compared to the association with vitamin D (P<0.0001) although vitamin D is negatively correlate (R= 0.24) whereas TSH is positive correlation(R= 0.62) with BMD in postmenopausal women.

Conclusion

In the present study it was found that premenopausal women suffering secondary osteoporosis with reduced BMD due to depression induced necrosis of osteoblast and inhibits differentiation and bone mineralization associated with altering different endocrine parameters specially vitamin D.

On the other hands primary type 1 osteoporosis occurs most frequently in post menopausal women were sufferings due to estrogen deficiency which may affects both bone resorption and bone formation not altering endocrine parameters as such in our present study.

It can be concluded that Irrespective of the specific causes, subjects with depression should be considered for screening for bone mineral density and, vice versa, subjects with low BMD should be considered for screening for depression in early stage of life and supplementation of vitamin D with regular physical activity in premenopausal women for prevention of secondary osteoporosis.

Conflict of Interest: The authors declare no conflict of interest.

Source of Finding: Self

Ethical Clearance: Certificate taken.

References

1. Kanis JA. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis: synopsis of a WHO report. WHO Study Group. Osteoporos Int J Establ Result Coop Eur Found Osteoporos Natl Osteoporos Found USA. 1994 No v;4(6):368–81.
2. America's Bone Health: The State of Osteoporosis and Low Bone Mass in Our Nation. The Foundation; 2002. 110 p.
3. Simpson AH, Murray IR. Main differences in osteoporotic fracture models: which should I use? Injury. 2016 Jan;47 Suppl 1:S15-20.
4. Compston J. Glucocorticoid-induced osteoporosis: an update. Endocrine. 2018;61(1):7–16.
5. Briot K, Roux C. Glucocorticoid-induced osteoporosis. RMD Open. 2015 Apr 1;1(1):e000014.
6. El-Gabalawy R, Blaney C, Tsai J, Sumner JA, Pietrzak RH. Physical health conditions associated 976 with full and subthreshold PTSD in U.S. military veterans: Results from the National Health and Resilience in Veterans Study. J Affect Disord. 2018 Feb;227:849–53. 9

7. Gordon CM, Bachrach LK, Carpenter TO, Crabtree N, Fuleihan GE, Kutilek S, Lorenc RS, Tosi LL, Ward KA, Ward LM, Kalkwarf HJ. Dual energy X-ray absorptiometry interpretation and reporting in children and adolescents: the 2007 ISCD Pediatric Official Positions. Journal of Clinical Densitometry. 2008 Jan 1;11(1):43-58.

8. Torres MS, Ramirez L, Simkin PH, Braverman LE, Emerson CH. Effect of various doses of recombinant human thyrotropin on the thyroid radioactive iodine uptake and serum levels of thyroid hormones and thyroglobulin in normal subjects. The Journal of Clinical Endocrinology & Metabolism. 2001 Apr 1;86(4):1660-4.

9. Lewis JG, Elder PA. An enzyme-linked immunosorbent assay (ELISA) for plasma cortisol. Journal of steroid biochemistry. 1985 May 1;22(5):673-6.

10. Zerwekh JE. Blood biomarkers of vitamin D status. The American journal of clinical nutrition. 2008 Apr 1;87(4):1087S-91S.

Original Research Article

Prevalence of High Risk Pregnancy: in A Tertiary Care Centre of Sagar Division of M.P.

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Abstract

Background: High risk pregnancy is broadly defined as one in which mother, fetus or newborn is or will be at increased risk for morbidity or mortality before or after delivery. According to WHO, globally about 830 women die from pregnancy or childbirth-related complications every day. About 20-30% of all pregnancies belong to high-risk category, which is responsible for 70–80% of perinatal mortality and morbidity.

Hence, the current study was done to determine the prevalence of high-risk pregnancies and associated high risk factors among antenatal women in a tertiary care centre of central India.

Aims & Objectives: To know the prevalence of high-risk pregnancies and associated high risk factors.

Materials and methods: Ethics approval to conduct the study was obtained from the Institutional Ethics Committee. It is a record-based retrospective longitudinal study done among 3898 antenatal women who have attended/ referred to our tertiary care institute, Bundelkhand Medical College, Sagar, M.P. during February 2020 to May 2020.

High-risk pregnancy was classified based on the guidelines from the Pradhan Mantri Surakshit Matritva Abhiyan.

Results: Among 3898 antenatal case record reviewed. Results of this study show that the prevalence of high-risk pregnancy among study participants was 16.54%.

Most of the pregnant women were in age group of 20-35 years that is 94.72%.

Most of the pregnant women were multigravida 57.20% by gestation.

Regarding obstetric and neonatal outcomes, majority had normal vaginal delivery (60.6%). The most common high risk factors were history of previous cesarean section 31.94 %, Hypertension in Pregnancy 22.17% & Abnormal Presentation were 13.95%.

Conclusion: The current study found that almost one-sixth (16.54%) of the pregnant women have high-risk pregnancy. Hence, early detection of high-risk pregnancy needs to be done to improve the maternal, obstetric, and neonatal outcomes.

Keywords: *Prevalence, High-risk pregnancy, Cesarean section, Hypertension in Pregnancy.*

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Introduction

Pregnancy (gestation) is the physiological process of a developing fetus within the maternal body.

High risk pregnancy is defined as one where pregnancy is complicated by factor or factors that

adversely affects the outcome- maternal or perinatal or both.[1] All pregnancies and deliveries are potentially at risk. However, there are certain categories of pregnancies where the mother, the fetus or the neonate is in a state of increased jeopardy.

According to WHO, globally about 830 women die from pregnancy or childbirth-related complications every day. About 20-30% of all pregnancies belong to high- which is responsible for 70–80% of perinatal mortality and morbidity.[2]

Women with high-risk pregnancies should receive care from a special team of health care providers to ensure the best possible outcomes.

High risk pregnancy may result because of various conditions which are there either before getting pregnant such as diabetes or high blood pressure, and complications from a previous pregnancy, or conditions during pregnancy or delivery.

In India about 20-30% pregnancies belong to high risk category, which is responsible for 75% of perinatal morbidity and mortality. Early detection and effective management of high risk pregnancy can contribute substantially in reduction of maternal and foetal adverse outcomes. Published by : NHP (National Health Portal of India) in Oct 14, 2019.[3]

Pradhan Mantri Surakshit Matriva Abhiyan is an initiative of Ministry of Health and Family Welfare Government of India to identify high risk pregnancies early and follow them so that they can be referred to health care centers with proper facilities so that women with high risk pregnancies may have healthy pregnancies and deliveries without complications.

Identification of high-risk pregnancy, causes, and its complications through quality antenatal care helps in achieving favorable maternal, obstetric, and neonatal outcome.[4,5]. In addition, women identified to be at high risk need to be followed up at regular intervals through routine care by the health workers at health facility and home visits to prevent the development of any maternal or fetal complications.

Apart from follow-up care, appropriate laboratory investigations and referral services also required to improve the outcome of pregnancy. Prognosis of the outcome also depends on the type of high-risk pregnancy among pregnant mothers.[6] Hence, identification of type of high-risk pregnancy at earliest stage will be useful in directing the appropriate intervention measures for pregnant women.

Material and Methods

Ethics approval to conduct the study was obtained from the Institutional Ethics Committee.

This is a record-based retrospective longitudinal study conducted among 3898 antenatal women who have attended/ referred our tertiary care hospital during February 2020 to May 2020 in the Department of Obstetrics and Gynaecology, Bundelkhand Medical College and associated hospitals Sagar M.P. which is a tertiary care hospital in the Bundelkhand region of Sagar division of M.P. India, in which a review of all pregnancy data, which occurred over a four months period was done.

The hospital Maternal and Child Health register was used to collect a list of all pregnancy that occurred during the study period. Medical records of all high risk pregnancy were reviewed. Information of all the cases was extracted from the patient's case notes and Maternal and Child Health register records.

The confidentiality of the patient's personal information was protected.

High-risk pregnancy was classified based on the guidelines provided by Pradhan Mantri Surakshit Matritva Abhiyan (PMSMA) for identification of high-risk pregnancy by health-care workers.

The parameters considered for diagnosis of high-risk pregnancy were also defined as per the guidelines provided by PMSMA. Antenatal women with the following conditions were categorized under high-risk pregnancy:

a. Severe anemia with hemoglobin level <7 g/dl

b. Hypertensive disorder in pregnancy (blood pressure >140/90 mmHg)

c. Pregnant women positive for HIV/Syphilis

d. Hypothyroidism (thyroid-stimulating hormone

values – first trimester: 0.1–2.5 mIU/L, second trimester: 0.2–3 mIU/L, and third trimester: 0.3–3 mIU/L)

e. Gestational diabetes mellitus (glucose challenge test ≥140 mg/dl)

f. Twin pregnancy or multiple pregnancy

g. Previous history of lower segment cesarean section

h. Younger primi (age <20 years) or elderly gravida (age >35 years)

i. Malpresentation

j. Bad obstetric history (history of congenital malformation, stillbirth, abortion, premature birth, and obstructed labor)

k. Rh incompatibility

l. Low-lying placenta or placenta previa.

m. Patient with History of any current systemic illnesses)/past illness.

Outcome of pregnancy was categorized based on the following domains:

Obstetric outcome

i. Type of delivery – preterm (<37 weeks of pregnancy), term (37–42 weeks of pregnancy), and postterm delivery (>42 weeks of pregnancy)

ii. Mode of delivery – spontaneous vaginal delivery, assisted vaginal delivery, and lower segment cesarean section.

Neonatal outcome:

i. Birth weight of child – low-birth weight baby (birth weight <2.5 kg), normal baby (birth weight ≥2.5 kg)

ii. Status of birth – live birth, stillbirth, and abortion.

The data collected included maternal age, gestation age, referring facility, date of admission, high risk factors etc. Data was captured and analyzed using Microsoft Excel, and Descriptive statistics was used to analyses data. Categorical variables are displayed as percentages.

Results

Total 3898 antenatal case record reviewed. Results of this study show that the prevalence of high-risk pregnancy among study participants was 16.54% (n-645).

Most of the pregnant women were in age group of 20-35 years that is 94.72% and 2.32% of pregnant women were less than 20 years old, and 2.79% percent were more than 35 years of age.

And 2.80 % of pregnant women were multigravida by gestation.

Regarding obstetric and neonatal outcomes, majority had normal vaginal delivery (60.6%).

The most common high risk factors were history of previous cesarean section 31.94%, Hypertension in Pregnancy 22.17% & Abnormal Presentation were 13.95%.

Table.1 Prevalence of high risk pregnancy (%)

S.NO.	PREGNANCY	NUMBER	PERCENTAGE
1	High Risk Pregnancy	645	16.54 %
2	Low Risk Pregnancy	3253	83.46 %
3	Total Pregnancy	3898	100 %

The prevalence of high-risk pregnancy among study participants was 16.54%.

Table.2 Age wise distribution of prevalence of high risk pregnancy

S.NO.	AGE IN YEARS	NUMBERS	PERCENTAGE
1	<20	15	2.32 %
2	20-35	611	94.72 %
3	>35	18	2.79 %
4	Total	645	100 %

Most of the high risk pregnant women are in age group of 20-35 years that is 94.72%.

Table.3 Distribution of high risk pregnancy according to the Gravidity

S. NO.	GRAVIDITY	NUMBERS	PERCENTAGE
1	Primigravida	258	40 %
2	Multigravida	369	57.20 %
3	Grand multigravida	18	2.80 %
4	Total	645	100 %

Most of the high risk pregnant women were multigravida 57.20% by gestation.

Table.4 Distribution of high risk pregnancy according to the mode of delivery

S.NO.	MODE OF DELIVERY	NUMBERS	PERCENTAGE
1	Normal Vaginal Delivery	391	60.62 %
2	Cesarean Delivery	254	39.38 %
3	Total Delivery	645	100 %

Majority had normal vaginal delivery (60.6%).

Table.5 Distribution of high risk pregnancy according to the high risk factors.

S.NO.	TYPE OF RISK FACTOR	NUMBERS	PERCENTAGE
1	H/O Previous cesarean section	206	31.94 %
2	Hypertension in pregnancy	143	22.17 %
3	Abnormal presentation	90	13.95 %
4	Anemia in present pregnancy	82	12.71 %
5	Ante partum hemorrhage	23	3.56 %
6	Grand multipara	18	2.79 %
7	Twin pregnancy	14	2.17 %
8	Post term pregnancy	13	2.01 %

Cont... **Table.5 Distribution of high risk pregnancy according to the high risk factors.**

9	Medical disorders	8	1.21 %
10	Elderly primi	6	0.93 %
11	Obstructed labour	5	0.77 %
12	Ectopic pregnancy	4	0.62 %
13	Short stature	4	0.62 %
14	Total	645	100 %

The most common high risk factors were history of previous caesarean section 31.94%, Hypertension in Pregnancy 22.17%, Abnormal Presentation were 13.95%, Anemia in present pregnancy13.95% and Ante partum hemorrhage 3.56%.

Discussion

The prevalence of high-risk pregnancy in my study was found to be 16.5%.

A study done in Puducherry, South India by Marie Gilbert Majella, Gokul Sarveswaran et al also reported the prevalence of high-risk pregnancy were 18.3%.[7]

Other studies in India have reported higher proportion of high-risk pregnancy in contrast to current study findings. Studies done in Nagpur, Haryana, Karnataka and Dharwad have reported that almost one-third of antenatal women had high-risk pregnancy when compared to the current study finding of 16.5%. [8,9,10,11]

Variable prevalence is contributed to difference in regions, populations, methodologies, and diagnostic criteria, level of health care centre etc.

In the present study 94.72% were in the age group between 20 to 35 years, followed by >35 years (2.79%) and least (2.32%) were <20 years.

In a study by Jaideep KC, Prashant D, et al. 88% were in the age group between 20 to 29 years, followed by <19 years (7%) and least (5%) were >30 years. [10]

A study conducted by Fereshteh Farajnezhad, Faramarz Shaahmadi et al. Show that 4.4 percent of women were less than 18y/o and %7.4 were more than 35y/o and the most age abundance was in age group of 18-35y/o that was 88.2 percent. [12]

Prevalence of high risk pregnancy was higher i.e.57.20% in multigravida as compared to primigravida (40 %).

In a study by Jaideep KC, Prashant D, et al. Prevalence of high risk pregnancy was higher i.e. 77% in multigravida compared to primigravida (23%).[10]

Another study done in Rohtak, Haryana showed that prevalence of high risk pregnancy was 13.7% in multigravida.[9]

In my Present study majority had normal vaginal delivery (60.6%), and 39.4% had caesarean delivery.

The most common high risk factors in my study were history of previous caesarean section 31.94%, Hypertension in Pregnancy 22.17%, Abnormal Presentation were 13.95%, Anemia in present pregnancy12.71%, Ante partum hemorrhage 3.56%, Grand multipara 2.79% and Twin pregnancy2.17%.

A. Jadho et al (2017) in their study among pregnant mothers of rural area of Nagpur district found that previous caesarean section was the most common risk factor (14.49%) followed by malpresentation (7.94%).[8]

In A study, by Mehta B, Vijay K, et al. showed that in high risk pregnancies the most common risk factors were as follows: History of abortion (27.4%), followed by height less than 145 cm (24.7%), hypertension in pregnancy (22%),history of chronic medical disorder,

parity more than 4 (13.7%), history of preterm birth (11.6%), history of stillbirth (9.9%), history of cesarian section (8.2%), and history of birth with congenital anomalies (3.8%).[9]

J.Chaubey et al (2017) in their cross-sectional study in Karnataka found that bad obstetric history (59.8%) was the common risk factor among the high-risk mothers.[10]

M. Kumar et al (2015) in their study in Dharwad found that most common risk factor seen was height < 140 cm 15(40.5%), followed by history of ≥ 2 abortion 11(29.7%) hypertension in pregnancy 4(10.8%), history of chronic medical disorders 4(10.8%), Parity ≥ 2 (5.4%), history of pre-term birth 5(13.5%), history of still birth 3(8.1%), history of caesarean section 5(13.5%).[11]

A study conducted by Fereshteh Farajnezhad, Faramarz Shaahmadi et al. Show that the most risk factor in the scene of previous pregnancies was previous cesarean section (%17.1).[12]

In a study by Omima A. Muhammeda, Nora A. Khalilb,et al. In the high risk group, the most prevalent risk factors were as follows: History of previous cesarean section (55%), history of abortion (35.4%), history of delayed pregnancy (16%), early pregnancy bleeding less than 20 weeks of gestation (12.5%), edema (10.4%), anemia (9.4%), [13]

H. Akhtar et al (2009) in their study among the high-risk mothers in Bangladesh found that among the high-risk pregnancies, preeclampsia and PIH were the most common risk factors (30.97% each) followed by primigravid (17.69%).[14]

Conclusion

In the current study we found that almost one-sixth (16.54%) of the pregnant women have high-risk pregnancies. History of previous caesarean section 31.94% and Hypertension in Pregnancy 22.17% were found to be significantly associated with the prevalence of high risk Pregnancy.

Hence, early detection of high-risk pregnancy needs to be done to improve the maternal, obstetric, and neonatal outcomes.

Pradhan Mantri Surakshit Matriva Abhiyan is an initiative of Ministry of Health and Family Welfare Government of India to identify high risk pregnancies early and follow them so that they can be referred to health care centers with proper facilities so that women with high risk pregnancies may have healthy pregnancies and deliveries without complications.[15]

Ethical Clearance: Yes

Financial Interest: None

Conflict of Interest: None

References

1. Dutta D C. Special Topics in Obstetrics. D C Datta's Text book of Obstetrics. 8th edi. JAYPEE The health science publisher New Delhi 2015, 716.
2. Mufti S and Mufti S. Identification of High Risk Pregnancy by a Scoring System and its Correlation with Perinatal Outcome. Indian Journal for the Practising Doctor. 2008; 5(1): 1-7.
3. NHP (National Health Portal of India) in Oct 14, 2019.
4. Backett EM, Davis AM, Petroz-Barzavian A. Geneva: World Health Organization; 1984. The Risk Approach in Health Care with Special Reference to Natural and Child Health; World Health Organization Public Health Papers. No. 76; p. 113.
5. Nasah BT, Leke RJ, Doh AS, Moyo JK, Fomulu J, Njikam OM, et al. The risk approach for reducing maternal mortality: The yaounde experience. Int J Gynaecol Obstet. 1991;36:195–201.
6. Singh R, Chauhan R, Nandan D, Singh H, Gupta SC, Bhatnagar M. Morbidity profile of women during pregnancy: A hospital record based study in western UP. Indian J Community Health. 2012;24:342–6.
7. Marie Gilbert Majella, Gokul Sarveswaran, Yuvaraj Krishnamoorthy, K. Sivaranjini, Kalaiselvy Arikrishnan, and S. Ganesh Kumar A longitudinal study on high risk pregnancy and its outcome among antenatal women attending rural primary health centre in Puducherry, South India. J Educ Health Promot. 2019; 8: 12.
8. Jadhao AR, Gawade MD, Ughade SN. Outcome of pregnancy among high risk pregnancies in rural area of Nagpur, Maharashtra, Central India. Int J

Community Med Public Health. 2017;4:628–33.

9. Mehta B, Vijay K, Amandeep K, Sumit C, Manisha M. Prevalence and correlates of high risk pregnancy in rural Haryana: A community based study. Int J Basic A Med Sci. 2013;3:212–7.
10. Jaideep KC, Prashant D, Girija A. Prevalence of high risk among pregnant women attending antenatal clinic in rural field practice area of Jawaharlal Nehru medical college, Belgavi, Karnataka, India. Int J Community Med Public Health. 2017;4:1257–9.
11. Kumar MP, Gnanadeep NV, Dixit UR, Patil PS. Prevalence of high risk pregnancy in rural Dharwad. J Dent Med Sci. 2015;14:29–32.
12. Fereshteh Farajnezhad, Faramarz Shaahmadi, Zahra Fashi, Laila Daaylar Prevalence of high risk pregnancy and some relevant factors in referred women to health centers. Journal Of Scientific Achievements Volume 2, Issue 12, December 2017, Page: 4-7
13. Mohammed A. Omarac, Mona A. Khattab Risky pregnancy among women attending a rural, family healthcare unit. Menoufia Medical Journal, Volume 30 | Number 4 | October-December2017.1093-1097.
14. Akthar H, Sultana S and Siddique A (2009). Neonatal Out Come in High Risk Pregnancy. *The Journal of Teachers Association RMC, Rajshahi* 22(1) 26-29.
15. Ministry of Health and Family Welfare. Pradhan Mantri Surakshit Matritva Abhiyan. Ministry of Health and Family Welfare. 2016 .

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Changes in the Polysomnographic Measures in Patients of Chronic Insomnia on Drug Therapy Vs Mindful Awareness

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Abstract

Background:- Modern day 24*7 lifestyle is witnessing an increase in people with insomnia like never before. The deep and restoring sleep like a baby seems to have vanished from our hectic lifestyles ,and sleep disorders like insomnia have crept in involving people across all ages and sections of society. In the given scenario it remains a matter of concern that most primary physicians are not trained in the various modalities which could be used for the treatment of insomnia. In the absence of required knowledge in insomnia management hypnotic medication remain the preferred treatment for insomnia . The present study was undertaken with a view to study the effectiveness of mindfulness based relaxation therapy vs hypnotic medication for the treatment of insomnia.

Methods :- A cross sectional study was conducted on 100 patients suffering from insomnia in two groups, pharmacotherapy (PCT) group and Mindfulness based stress reduction (MBSR) group. MBSR a program of mindfulness meditation training consisting of one hour long class daily which includes training in progressive muscular exercises, breathing exercises, standing, sitting and walking meditations. Home practice expectations were 30 minutes of medication per day and following an attitude of mindfulness through out the day during the four week follow.

Result :- The study showed comparable results on all sleep parameters for both groups. There was a significant increase in total sleep time in both groups, the increase was more with drug group compare to the MBSR group.

Conclusion :- While the time commitment associated with participating in and practicing a behavioral intervention such as MBSR is more than with medication, our results suggest that this is not a deterrent to most of our participants. Given patient preferences, the side effects of pharmacotherapy, evidence of the efficacy of MBSR and the potential positive benefits of meditation that go beyond management of insomnia symptoms.

Keywords:- *Insomnia, Pharmacotherapy, Relaxation Therapy, Mindful awareness.*

Introduction

Sleep and Insomnia

Sleep has been defined behaviorally as a reversible state of perceptual disengagement from and unresponsiveness to the environment. Sleep is a complex state in which changes occur in physiologic and behavioral processes just like with wakefulness. Sleep is physiologic, necessary, temporary, reversible, and cyclic. To sustain optimal alertness throughout the day, the requirement varies across individuals, with the mean being 7 to 8 hours for adult humans.

The term *insomnia* refers to a condition characterized by difficulties initiating and/or maintaining sleep,

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accompanied by clinically significant daytime sleepiness or distress related to the ongoing sleep difficulties Given this observation, it is best to use the term *comorbid insomnia* when prominent, clinically significant insomnia symptoms are observed concurrent to another medical, psychiatric, or sleep disorder .

The modern era of hypnotic pharmacology began in the 1960s with the introduction of the benzodiazepines ,or diazepam-like compounds, which dominated until the development of the newer, nonbenzodiazepine agents in the 1990s All of the current FDA-approved agents—with the exception of ramelteon and doxepin—act by modulating the function of the γ-amino butyric acid (GABA)[1].

Mindfullness based stress reduction

The Mindfullness based stress reduction ,MBSR facilitates adaptation to the stresses of living[2]. The MBSR program teaches participants to learn how to focus their attention through a variety of meditative techniques. Participants are trained to perceive their immediate emotional and physical state, including pain or discomfort, and to let thoughts come and go in awareness with no attempt to change, suppress or elaborate on thoughts. Through mindfulness training, participants learn to view their thoughts as mental events and not facts. In this way, participants become exposed to the positive and negative content of their thoughts, and do not get absorbed in thought, caught up in planning for the future or worrying about the past. By "breaking up" cycles of rumination and worry, mindfulness is hypothesized to reduce "verbal over-regulation" and facilitate the dis-engagement necessary to fall asleep[3].

Aims & Objective

The aim of this study was to compare the effectiveness of mindfullness based stress relaxation therapy MBSR vs commonly taken medicine zolpidem in altering the sleep parameters in whole night polysomnographic studies in patients of chronic insomnia

Inclusion Criteria

Patients were recruited between July, 2012 and September 2012, by clinician referral. Age 18 to 65 Ability to read and speak hindi,

Diagnosis of primary chronic insomnia. Chronic insomnia was defined as difficulty initiating or maintaining sleep despite adequate opportunity for sleep, with related daytime dysfunction on 3 or more nights a week for the past 6 months or)longer, consistent with the DSM-IV-TR and International Classification of Sleep Disorders (ICSD-3)[4].

Exclusion Criteria:

Persons with medical conditions, mental disorders, or different sleep disorders suspected of being directly related to the insomnia ,those taking medications affecting sleep were excluded.

Material and Method

MBSR, a program of mindfulness meditation training consisting of one hour long class daily for 5 days which included training in progressive muscular exercises , breathing exercises, standing, sitting and walking meditations, Home practice expectations were 30 minutes of meditation per day and following an attitude of mindfulness throughout the day during the 4 week follow-up; Our pharmacotherapy group was modeled on clinical practice. It is standard and common practice to prescribe on a nightly basis for a number of months during the initial management of chronic primary insomnia.

The PCT treatment consisted of .5 mg of zolpidem nightly for 4 weeks. Patients initially met in a small group with the sleep physician who gave instructions for properly taking medication and explained potential side effect . A 10-minute sleep hygiene presentation was included in both interventions . Both groups were asked to practice sleep restriction and not indulge in afternoon nap, no caffeinated drink after 3:pm The study was conducted on 100 patients suffering from insomnia who presented to the OPD of M L B Medical College, Jhansi , with the chief complain of insomnia. They were divided into two groups one group was given 5 mg zolpidem every night , inetial polysomnographic studies were conducted followed by PSG every week for 4 weeks to monitor the changes in sleep parameters.). Screening protocol applied for diagnostic criteria for primary insomnia included a structured psychiatric interview (SCID-IV), completion of a screening sleep diary, and a history and physical examination conducted

by a physician with training in sleep medicine group.

Observation

Table 1 Shows- Result of drug versus mindfullnress on sleep study parameters

Paired Samples Statistics					
TOTAL SLEEP TIME		**Mean**	**N**	**Std. Deviation**	**Std. Error Mean**
Pair 1	bd	315.10	30	10.842	1.979
	ad	345.60	30	10.301	1.881
Pair 2	bt	301.13	30	36.757	6.711
	at	322.03	30	41.018	7.489
SLEEP LATENCY					
Pair 1	Bd	49.93	30	1.982	.362
	Ad	29.30	30	2.756	.503
Pair 2	Bt	50.30	30	2.037	.372
	At	25.43	30	1.695	.310
SLEEP EFFICIENCY					
Pair 1	Bd	77.70	30	3.395	.620
	Ad	85.73	30	3.503	.640
Pair 2	Bt	78.57	30	2.661	.486
	At	89.43	30	2.176	.397
REM LATENCY					
Pair 1	bd	106.97	30	3.978	.726
	ad	135.70	30	4.027	.735
Pair 2	bt	105.33	30	3.536	.646
	at	130.10	30	3.689	.674
WAKE AFTER SLEEP ONSET					
Pair 1	bd	45.83	30	3.455	.631
	ad	62.33	30	3.294	.601
Pair 2	bt	46.67	30	4.302	.785
	at	62.27	30	3.084	.563
TIME IN REM SLEEP					
Pair 1	bd	49.43	30	3.137	.573
	ad	48.00	30	2.971	.542
Pair 2	bt	50.57	30	3.126	.571
	at	48.80	30	3.134	.572
AROUSAL					
Pair 1	bd	8.00	30	.830	.152
	ad	6.63	30	.718	.131
Pair 2	bt	8.00	30	.871	.159
	at	4.17	30	.699	.128

bd-before starting drug therapy, ad- after starting the drug therapy , bt-before the mindfulness therapy, at- after mindfulness therapy

Table-2 shows a significant difference in all parameters(pvalue<.05) both after drug and mindfulness therapy

Paired Samples Test									
TOTAL SLEEP TIME		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	bd - ad	-30.500	3.589	.655	-31.840	-29.160	-46.549	29	.000
Pair 2	bt - at	-20.900	18.159	3.315	-27.681	-14.119	-6.304	29	.000
SLEEP LATENCY									
Pair 1	bd - ad	20.633	1.938	.354	19.910	21.357	58.302	29	.000
Pair 2	bt– at	24.867	1.042	.190	24.478	25.256	130.753	29	.000
SLEEP EFFICIENCY									
Pair 1	bd - ad	-8.033	.890	.162	-8.366	-7.701	-49.443	29	.000
Pair 2	bt - at	-10.867	1.502	.274	-11.428	-10.306	-39.614	29	.000
REM LATENCY									
Pair 1	bd - ad	-28.733	1.363	.249	-29.242	-28.224	-115.474	29	.000
Pair 2	bt - at	-24.767	1.775	.324	-25.429	-24.104	-76.425	29	.000
WAKE AFTER SLEEP ONSET									
Pair 1	bd - ad	-16.500	3.330	.608	-17.743	-15.257	-27.143	29	.000
Pair 2	bt - at	-15.600	2.711	.495	-16.612	-14.588	-31.513	29	.000
TIME IN REM SLEEP									
Pair 1	bd - ad	1.433	.728	.133	1.162	1.705	10.785	29	.000
Pair 2	bt - at	1.767	.679	.124	1.513	2.020	14.253	29	.000
AROUSAL									
Pair 1	bd - ad	1.367	.490	.089	1.184	1.550	15.272	29	.000
Pair 2	bt - at	3.833	.648	.118	3.591	4.075	32.415	29	.000

bd-before starting drug therapy, ad- after starting the drug therapy , bt-before the mindfulness therapy, at-after mindfulness therapy

Observation

The study showed comparable results on all sleep parameters for the two groups .There was a significant increase in total sleep time in both groups, the increase was more with the drug group compared to the MBSR group. The decrease in sleep latency was almost equal in both groups being only marginally more in the drug group (20.63 min vs 24.8 min).The improvement in sleep effciency was almost similar in both groups ,it was increased slightly more in the MBSR group 89.73 vs 85.43.The increase in REM latency was more in the drug group 28.73 min vs 24.76 min .The changes in wake aGer sleep onset time was almost equal in both groups 16.3 vs 15.5 min. Time in REM was decreased to a similar extent in both groups 1.43 min vs 1.76 min. The number of arousals decreased more with MBSR compared to drug 3.83 vs 1.36 min.

Discussion

This study provides initial evidence for the efficacy of a complementary and alternative treatment modality, MBSR, as a viable treatment for chronic insomnia as measured by changes in polysomnographic parameters Our results suggest that MBSR, when combined with a brief sleep hygiene presentation, is able to achieve reductions in improvements in sleep quality comparable to regular use of an FDA-approved sedative hypnotic..

Patients who completed 5 or more MBSR classes reported sleep changes that were large and clinically meaningful – total sleep time increased by over 30 minutes, sleep onset latency reduced by over 20 minutes and sleep efficiency increased to 88.5%. Moreover the patients randomized to MBSR met stringent criteria for recovery from insomnia at the end of the study, and average treatment satisfaction scores were high. Whereas patients in the PCT arm obtained similar benefits to sleep outcomes, their treatment satisfactions scores were not high,

Impacts found following MBSR compare favorably to outcomes reported from trials of cognitive-behavioral therapy (CBT) for patients with chronic or persistent insomnia. Morin et al.[5] recently reported the results of a trial of where adults with persistent insomnia were randomized to 6 weeks of group CBT. These patients improved from an average ISI score of 17.26 at baseline to an average of 8.11 at 6 month follow-up; sleep efficiency measured by diary improved from 69% to 82.4%, and large improvements in sleep onset latency and time awake after sleep onset were also found. Our finding of durable improvements to sleep outcomes from MBSR is consistent with results reported by Edinger et al.[6]from their seminal trial of CBT in primary insomnia.

Our findings build upon positive results from several longitudinal studies of mindfulness-based treatment approaches with insomnia patients. Three uncontrolled studies with a total of 56 patients and one waitlist-controlled trial with 52 patients reported reductions in insomnia symptoms and improvements on other sleep outcomes in patients with mood and/or anxiety disorders following a MBCT. Ree and Craigie included the ISI in a study of MBCT for psychiatric outpatients with insomnia[7]., and reported significant improvement (ISI, d =.84) for 23 patients following the program, and benefits maintained at 3 month follow-up. Heidenrich et al.[8] reported that 14 patients with refractory chronic insomnia co-morbid with other mental disorders showed pre- to post-MBCT improvements in total sleep time and sleep latency measured by sleep diary, and a decline in dysfunctional thoughts about insomnia. Yook et al.[9] reported PSQI scores were significantly decreased among 19 patients with anxiety disorders and insomnia after an 8-week MBCT program. Britton et al.[10] studied the sleep outcomes of 7 women with insomnia following an abbreviated MBSR program and found that WASO measured by sleep diary was reduced. In a subsequent waitlist-controlled trial, Britton et al.5 enrolled adults with insomnia co-morbid with depression, and randomized them to an 8-week MBCT program or a waitlist. Compared to controls (n=17), MBCT participants' sleep diary reports (n=25) indicated significantly shorter WASO, and trends for decreased SOL and decreased awakenings, adjusted for use of antidepressants. These studies, all of which found reductions in one or more measures of mood or cognition (depression, anxiety, worry or rumination) as well as sleep improvements, complement the growing literature on the health benefits of mindfulness training with MBSR These findings, in conjunction with the results of the present study, suggest that mindfulness training has potentially broad application for improving insomnia and closely associated problems that may perpetuate insomnia - symptoms of anxiety and depression.

Strengths of our study include a rigorous screening process to eliminate individuals likely to have insomnia due to another underlying disorder. We tried to stick with MBSR along with training in basic sleep hygine so that the findings could be tested in future studies and be generalised.. Limitations included lack of additional control groups, such as a medication placebo and a behavioral attention control, to exclude the possibility that non-specific factors such as expectancy, attention, or regression to the mean might account for the positive effects found. Other limitations include the homogeneity of participants in terms of belonging to same geographical area and race. Another limitation was a lack of follow up which would help us know if the changes in sleep parameters were sustained after few months of inetiating therapy .Our study focused on changes in polygraphic measures only, a more comprehensive study including changes in patient sleep diaries, actigraphy and daytime impairment due to insomnia.

Conclusion

While the time commitment associated with participating in and practicing a behavioral intervention such as MBSR is more than with medication, our results suggest that this is not a deterrent to most of our participants. Given patient preferences, the side effects of pharmacotherapy, evidence of the efficacy of MBSR and the potential positive benefits of meditation that go beyond management of insomnia symptoms, it is important that health care providers be aware of the range of non-pharmacologic therapy approaches and that clinicians offer patients options that include MBSR. Future studies of MBSR for insomnia should employ larger sample sizes, and longer follow up to assess the durability of treatment interventions, and include design features that could reveal mechanisms of action and deduce the most effective components of this intervention.

Ethical Clearance: Present study was approved by institutional and review committee. MLB Medical College Jhansi, UP India.

Conflict of Interest – Nil

Source of Funding- Self

References

1. Janette D. Lie, PharmD, BCACP; Kristie N. Tu, PharmD, BCPS, CGP; Diana D. Shen, PharmD Candidate; and Bonnie M. Wong, PharmD Candidate Pharmacological Treatment of Insomnia pharmacy and therapeutics 2015 Nov; 40(11): 759-768, 771.

2. Morin CM, LeBlanc M, Daley M, Gregoire JP, Merette C. Epidemiology of insomnia: prevalence, self-help treatments, consultations, and determinants of help-seeking behaviors. Sleep Medicine. 2006;7:123–30.

3. Winbush NY, Gross CR, Kreitzer MJ. The e□ects of mindfulness-based stress reduction on sleep disturbance: A systematic review. EXPLORE: The Journal of Science & Healing. 2007;3:585–91.

4. American Academy of Sleep Medicine . International Classification of Sleep Disorders: 2nd Ed Diagnostic and Coding Manual: American Academy of Sleep Medicine. 2005.

5. Morin CM, LeBlanc M, Daley M, Gregoire JP, Merette C. Epidemiology of insomnia: prevalence, self-help treatments, consultations, and determinants of help-seeking behaviors. Sleep Medicine. 2006;7:123–30.

6. Edinger JD, Wohlgemuth WK, Radtke RA, Marsh GR, Quillan RE. Cognitive behavioral therapy for treatment of chronic primary insomnia: A randomized controlled trial. JAMA. 2001;285:1856–64.

7. Bastien CH, Vallieres A, Morin CM. Validation of the Insomnia Severity Index as an outcome measure for insomnia research. Sleep Medicine. 2001;2:297–307

8. Heidenreich T, Tuin I, Pflug B, Michal M, Michalak J. Letter to the editor: Mindfulness-based cognitive therapy for persistent insomnia: A pilot study Psychother Psychosom. Vol. 75 2006.

9. Yook K, Lee SH, Ryu M, et al. Usefulness of mindfulness-based cognitive therapy for treating insomnia in patients with anxiety disorders. A pilot

study The Journal of Nervous and Mental Disease. 2008;196:501–3.]

10. Grossman P, Niemann L, Schmidt S, Walach H. Mindfulness-based stress reduction and health benefits. A meta-analysis. J Psychosom Res. 2004;57:35–43.]

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