IS NITRIC OXIDE RELATED TO BMI IN POST-MENOPAUSAL FEMALES?

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Abstract:
Introduction: Menopause is cessation of menstrual flow and is defined as one year without menses. The age at which menopause occurs is genetically defined and is around 51 years on an average. The ovaries start to lose their estrogen producing capacity in the late thirties which is completed by mid-fifties. This phenomenon is known as the menopausal transition. There is progressive loss of estrogen, which is responsible for vasomotor disturbances as well as weight problems among postmenopausal women. The BMI in postmenopausal females is considered as a factor of diminishing reproductive hormones. So, a correlation of BMI and serum nitric oxide in north Indian post-menopausal hypothyroid females may provide us with a probable link between BMI and nitric oxide levels in determining the causes of deterioration of cardiovascular health in postmenopausal women.
Methods: This study was conducted in the Department of Biochemistry in collaboration with Department of Medicine and Department of Obstetrics and Gynecology, Pt. B. D. Sharma. A total of 30 apparently healthy postmenopausal women were enrolled. Nitric oxide was estimated by griess reagent and for routine biochemistry we used Randox Suzuka autoanalyzer.
Results: The mean BMI of post-menopausal women was found be on higher side with a mean of 29.03±3.56. The mean NO levels were 33.67±5.17. We observed a positive correlation between BMI and serum NO levels.
Conclusion: The study found that there is a link between the body fat and the synthesis of nitric oxide which may be a compensatory mechanism for the obese people. Clinicians while observing nitric oxide levels should keep in mind the BMI status of the patient.

IndexTerms **- Nitric oxide, Menopause, Estrogen, BMI**

INTRODUCTION

The ovaries progressively lose their estrogen producing capacity with age. This process begins in the late thirties and near-complete loss of estrogen production occurs by mid-fifties. The transition from normal ovarian function to ovarian failure is described as the menopausal transition. The late phase of post-menopause is defined as 5 years after the onset of menopause until death.[1] This is a natural process of aging which tends to occur over a period of time. This terminal phase of reproductive aging is preceded by many hormonal changes and it affects tissue regeneration, collagen homeostasis in skin, bone and generative tracts.[2] The natural menopause has been defined as twelve consecutive months of amenorrhea according to some major studies.[3-5] This study included recently menopausal women with duration of menopause of more than one year but less than two years in order to minimize the age related effects. Premenopausal women have a lower risk of coronary heart disease than age-matched men, whereas after menopause there is decline in male-female ratio of coronary heart disease deaths.[6,7] Young women with bilateral oophorectomy also have an increased risk of coronary heart disease unless they are treated with estrogens.[7] These observations, together with the favorable effect of hormonal replacement therapy on cardiovascular morbidity and mortality in postmenopausal women, have led to the assumption that ovarian hormones, especially estrogens, may protect women from coronary heart disease in the midlife and that their relative absence after menopause may contribute to accelerated progression of coronary artery disease.[8] Nitric Oxide (NO) is a diatomic hydrophobic gas that transmits signals in organisms. It is produced from one cell, penetrates through membranes and regulates the function of another cell; this represents an entirely new principle for signaling in biological systems.[9] It is also a free radical as it possesses an unpaired electron. Such a free radical prefers to steal electrons from the lipid membrane of the cell, initiating a free radical attack on cell known as peroxidation. There are at least two known physiological pathways in which NO synthesis occurs ie NO synthase (NOS) dependent and NOS independent.[10] The amino acid L-Arginine is responsible for the synthesis of nitric oxide, as it is oxidized to nitric oxide by the action of the NOS enzymes.[11] L-Citrulline has been indicated to be a secondary NO donor in the NOS dependent pathway, and the reason for this is that it can be converted to L-Arginine.[11] There are three different forms of nitric oxide which are synthesized by three deferent enzymes i.e. Neuronal nitric oxide synthase (nNOS), Endothelial nitric oxide synthase (eNOS) and inducible nitric oxide synthase (iNOS)

Nitric oxide is the most potent vasodilator which is abundantly produced in healthy endothelial cells91 and theoretically the increased release of nitric oxide could account for vasomotor symptoms. Nitric oxide is rapidly oxidized to nitrite/nitrate metabolites (NOx), which diffuse to the plasma flushing endothelial cells.[11]
In this study, we sought to characterize the relation of NO with body mass index in postmenopausal apparently healthy females.

MATERIAL AND METHODS

The present study was conducted in the Department of Biochemistry in collaboration with Department of Medicine and Department of Obstetrics and Gynecology, Pt. B. D. Sharma Post Graduate Institute of Medical Sciences, Rohtak. For this, 30 postmenopausal apparently healthy females were enrolled.

Inclusion criteria: postmenopausal women with more than 1 year but less than two years of menopause were assessed on the basis of history, clinical examination and routine biochemistry and were included in the study group.

Exclusion criteria: Patients with any kind of malignancy, hormonal disorders and other major illnesses involving liver, kidney and cardiovascular system or taking any hormonal preparations, drugs or antioxidant supplements which affect levels of nitric oxide were excluded.

Six mL of fasting venous blood was collected under all aseptic conditions in a plain vacutainer from all the subjects. Estimation of routine biochemical investigations along with NO was done. Weight and height were also noted.

Estimation of serum nitric oxide

Nitric oxide was estimated in serum by Greiss reaction. Nitric oxide was measured as nitrite (NO2-) which is a stable and non-volatile breakdown product of NO. Nitrite reacted with Greiss Reagent to form a purple coloured complex, the absorbance of which was measured at 546 nm using colorimeter.[12]

Samples were analyzed for routine biochemistry on auto-analyzer (Randox Suzuka, United Kingdom, model no. 6L7WD5J) using kits provided by Randox laboratories

The results were analyzed by standard statistical methods using SPSS. Coefficient of correlation was calculated using pearson's correlation between Body mass index (BMI) and NO.

RESULTS

The range of age of postmenopausal females in our study group was from 46 to 57 years. The mean age was found to be 52.8±2.38 years. The age wise distribution is given in Figure 1. Anthropometric evaluation with BMI is given in Table 1. The mean serum NO levels in postmenopausal women were observed to be 33.67±5.17 µmol/L. There was positive correlation between BMI and serum nitric oxide levels with a 'r' value of 0.10 and 'p' value of 0.5 as shown in Figure 2.

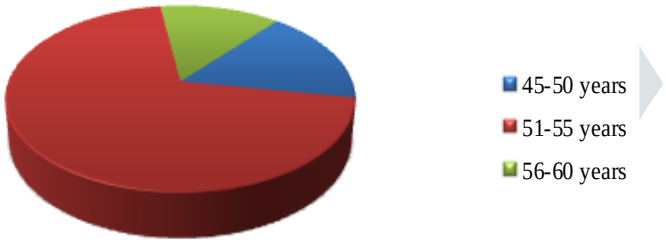

Figure 1: Age-wise distribution of postmenopausal females

Table1: Anthropometric evaluation

Parameter			**Mean value with range**
Weight (kg)			66.1±7.6 (58-84)
Height (m)			1.53±0.03 (1.46-1.58)
Body mass index (kg/m2)			29.03±3.56
Distribution of females according to BMI	**BMI**		**No. of PM females**
	< 18.5		Nil
	18.5 to 24.9		3
	25 to 29.9		17
	> 30	30-34.9	8
		35-39.9	2
		> 40	Nil

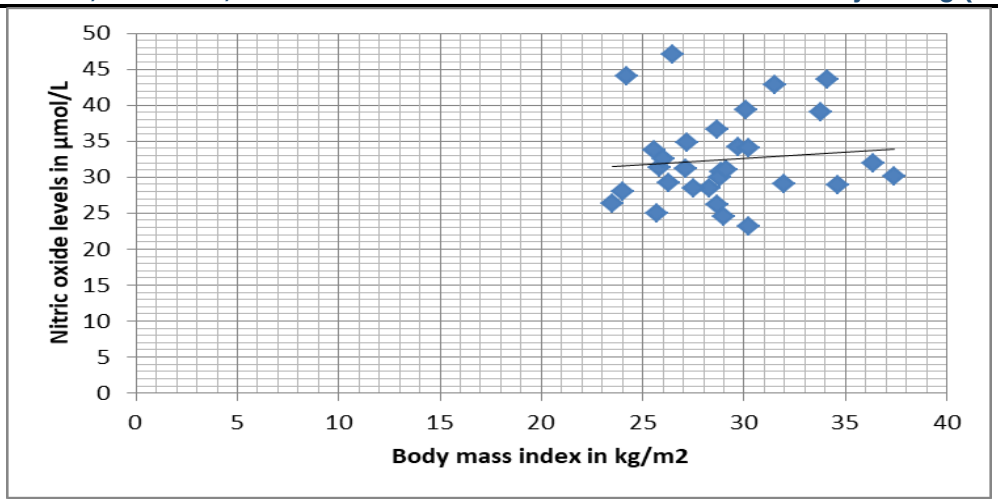

Figure2: Correlation between NO and BMI

DISCUSSION

According to WHO, out of total postmenopausal females, 10% were within normal range, 50% were observed to be preobese and 12% were in obese category. The mean age of PM women in our study group was 52.8 years, it can be stated that BMI is a positive function of age .[13] Postmenopausal women have higher BMI than premenopausal women because of action of estrogen.[14,15] Estrogen maintains fat distribution by increasing the use of lipids as energy source, which promotes reduction in abdominal fat. This effect occurs via the facilitation of fat oxidation in the muscle by the inhibition of lipogenesis in the liver and muscle through the regulation of peroxisome proliferator activated receptor γ (PPARγ) and an increase in LPL expression. The peroxisome proliferator activated receptors (PPARs) are the members of steroid hormone receptor superfamily of ligand activated transcription factors.[16] Estrogen can modulate PPARα function via estrogen receptors.[16]

We observed a statistically non-significant positive correlation between BMI and NO of postmenopausal females. Fujita, et al. reported a higher level of serum NO among obese subjects, which may be due to NO production by the visceral fat.[17] Increased NO metabolites have been reported in overweight and obese adolescents.[18] Previously nitrite and nitrate have been considered as products of NO but it has been shown that they can act as reservoirs of NO.[19] NO requires transportation in order to act on distant organs, for this i t uses the nitrite form and provide protection against ischemic injury.[20] Overweight subjects may utilize high levels of blood nitrates as compensatory mechanism against obesity-related changes.

It has been shown that NO synthase enzyme is present in subcutaneous tissue of humans[21] and that inhibition of this NOS led to increased lipolysis.[22] There are no extensive studies on how NOs and weight are related.

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