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Short Communication

Orexin-A levels in reproductive age group women and its association with body mass index

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ABSTRACT

Objectives: Orexins are hypothalamic neuropeptides, which are involved in feeding behaviour, sleep-wakefulness, and neuroendocrine homeostasis in the body. The study was conducted with the aim to estimate the serum orexin levels in reproductive age group (RAG) women and to determine the association of serum orexin levels with body mass index (BMI) in females of RAG.

Materials and Methods: One hundred and forty apparently healthy women of RAG (20–40 years) were randomly selected. Fasting serum orexin levels were measured using ELISA and BMI was calculated in women based on their height and weight.

Results: Serum orexin levels were significantly higher in women with BMI ≥ 25 kg/m^2 ($P = 0.035$) as compared to women with BMI < 25 kg/m^2.

Conclusion: In the present study, BMI correlated significantly with mean serum orexin levels. However, serum orexin levels did not correlate with the age of women.

Keywords: Orexin, Reproductive age group, Women, Body mass index, Serum orexin levels

INTRODUCTION

Orexin/hypocretin was first described in 1998 by De Lecea *et al.*[1] The name orexin was derived from the word 'orexis' which means appetite. Orexins A and B are newly discovered hypothalamic neuropeptides, which are involved in feeding behaviour, sleep-wakefulness, and neuroendocrine homeostasis in the body. Orexins promote alertness during waking and feeding. They are neuroexcitatory peptides produced in approximately 6700 neurons in rats confined to the feeding centre in the brain located in lateral hypothalamus.[2,3] Orexin neurons in hypothalamus have widespread projections throughout the brain.[4] The orexin receptors are also present in peripheral structures in vagal nerve, in testes, thyroid, adrenals, kidneys, placenta as well as in the gut enteric nervous system, pancreatic plexus, islets acini and endocrine cells in stomach and small intestine.[5-8] It has also been postulated that orexin-A, but not orexin-B, permeates the blood–brain barrier.[9] Orexins have been detected in blood, yet not much about the source and the physiological role of circulating orexin-A is known.[10] Muroya *et al.*[11] demonstrated that orexins are involved in the regulation of neuropeptide-Y, pro-opiomelanocortin, and glucose-responsive neurons in the arcuate and ventromedial hypothalamus, therefore explaining the

orexigenic action of orexins. Orexin-A could be considered not only as a neurotransmitter and/or neuromodulator but also as a hormone due to the secretion of this peptide directly into circulating blood.[12] The peripheral levels of orexin-A in fertile females will help to establish a new vision toward its functions. In a longitudinal study done by Hillemeier *et al*.[13] on reproductive age group (RAG) women, the younger women are more likely than older women for the transition from normal weight to overweight. Hormonal factors in women play a role in appetite regulation.[14] Moreover, the role of orexin neurons is more significant in the regulation of energy expenditure than food intake, and an imbalance of energy homeostasis may ultimately lead to metabolic complications.[15]

According to a study done by Mengesha Kassie *et al*.[16] on non-pregnant RAG women, unlike men, raised body mass index (BMI), overweight and obesity in women are more prevalent. The activity of orexin neurons is regulated by energy balance.[17] Kastin *et al.*[9] showed that because orexin-A rapidly crosses the blood-brain barrier and is found in peripheral tissues, it might contribute to appetite control and energy expenditure in humans by acting peripherally in addition to its central role. The study of orexin action in humans has been and still is opening many new insights into human physiology and unfolding the development of unfamiliar scientific approaches.

Aims of study

The study was conducted with the aim to estimate the serum orexin levels in RAG women and to determine the association of serum orexin levels with BMI in females of RAG.

MATERIALS AND METHODS

The study was conducted in the campus of King George Medical University, Lucknow, Uttar Pradesh. The previous review of the literature gave an idea that the correlation coefficient between BMI and orexin level is −0.43. Considering this correlation coefficient in the population with 80% power and 95% confidence, 140 samples are included in this study. The sample size was calculated using Sample Software n-Master and ethical clearance was taken.

The inclusion criteria of the study comprised 140 apparently healthy women of RAG that is, 20–40 years of age, recruited from women employees, nursing staff, and students at this university with no previous or current history of any significant disease. Informed consent was taken from the participants before initiating the study.

Women who had any kind of systemic disease, any gynaecological/obstetrical problem, or pregnancy were excluded from the study.

Complete information about medical history and other medical complications were taken in a structured pro forma. All the participants underwent a standardised interview using a questionnaire inquiring about the menstrual history, obstetrical history, and medical history.

In all subjects, the anthropometric measurements were taken, by one investigator using standard techniques with the subject standing upright, relaxed, and face directed toward the examiner. Weight was measured by calibrated balance scale to within 100 g without heavy clothing. Height measured by rigid stadiometer to the nearest centimetre while barefoot. BMI was calculated as the weight in kg divided by metre square of height. Fasting blood samples were collected in all subjects at 8 am in the morning on day 10 of their menstrual cycle to avoid diurnal and cyclic variation. The serum was separated by centrifugation at 3000 rpm.

Fasting serum orexin levels were measured by orexin-A/hypocretin-enzyme immunoassay kit (human, rat, mouse, and bovine, Phoenix Pharmaceuticals Inc., Catalog – EK-003-30).

The statistical analysis was done using Statistical Package for the Social Sciences Version 15.0 statistical analysis software. The values of continuous data were represented in number (%), mean and standard deviation. To test the significance of two means, the Student's '*t*'-test was used. For comparing means in more than 2 groups, we have used ANOVA to check the significant difference. $P < 0.05$ was considered statistically significant. Pearson's correlation was performed to calculate the correlation of orexin-A with continuous variables.

RESULTS

Out of 140 females, the majority of them were aged between 20 and 25 years (51.42%). A total of 31 (22.14%) women were aged between 26 and 30 years, 21 (15%) were aged between 31 and 35 years, and the remaining 16 (11.42%) were aged above 35 years. Mean serum orexin levels (pgm/ml) among different age groups ranged from 46.88 ± 15.92 (>35 years) to 50.84 ± 14.53 (26–30 years). However, comparison among different groups did not reveal a statistically significant intergroup difference ($P = 0.819$).

The relation between the weight of women with serum orexin levels (r = 0.176, $P = 0.31$) as well as BMI of women with serum orexin levels (r = 0.165, $P = 0.044$) shows a positively correlation which is statistically significant.

Age-wise distribution of women with their respective serum orexin levels is shown in [Table 1]:

Eighty-nine women of the total 140 women were having BMI < 25 and 51 women were having BMI ≥ 25. Serum orexin level was higher in subjects with BMI ≥ 25 kg/m^2 ($P = 0.035$) as compared to women with BMI < 25 kg/m^2 which is statistically significant.

[Table 2] shows the distribution of women in different BMI categories and their respective mean S. orexin.

DISCUSSION

In our study comprising 140 women aged between 20 and 40 years, it was observed that serum orexin levels were independent of age, although with increasing age the mean serum orexin levels showed a decreasing trend. In a longitudinal study done by Hillemeier *et al*.[13] on RAG women, transitioning from normal weight to overweight and from overweight to obesity in a short time period was seen which emphasises the need to identify the behavioural and hormonal factors that increase the risk of younger aged women progressing to raise BMI. Williamson *et al*.[18] observed that absolute gain in BMI declined with increasing age and the incidence of major weight gain was greatest in women and men 25–34 years of age. In a study done by Gupta *et al*. on premenopausal women, there was no correlation of serum orexin-A levels with age which corroborated with our findings. In another study done by Kawada *et al*.[19] on obese children, orexin-A was not correlated with the age of the subjects. According to the study done by Matsumura *et al*.[20] on subjects, whose ages ranged from 23 to 79 years, the plasma orexin-A level was higher in the elderly adults than in the younger ones. However, further studies are needed to assess whether plasma concentrations of orexin-A level are dependent on the ages of the subjects.

Orexin has been detected in the circulation and its levels respond to changes in the metabolic state. Orexin neurons are present in the dorsal and lateral hypothalamus.[1] However, the source of plasma orexin-A in peripheral circulation has not been elucidated. Orexin neurons in the hypothalamus and enteric nervous system are activated in response to fasting.

Table 1: Age and serum orexin levels.

S. No.	Age group (years)	Number of women	% of total women	Serum orexin levels (pgm/ml) Mean±SD
1.	20–25	72	51.42	50.00±13.70
2.	26–30	31	22.14	50.84±14.53
3.	31–35	21	15.00	50.43±12.30
4.	>35	16	11.42	46.88±15.92

F=0.309, *P*=0.819 (ANOVA test)

Table 2: BMI and serum orexin levels.

S. No.	BMI (kg/m^2)	Number of women	% of total women	Serum orexin levels (pgm/ml) Mean±SD
1.	<25	89	63.57	48.22±13.33
2.	>25	51	36.42	53.26±14.37

P=0.035 (Student's '*t*'-test). BMI: Body mass index

In our study, the mean serum orexin levels were higher in women having BMI > 25 kg/m^2. Orexin-A has a close association with raised BMI and obesity[21,22] and obesity is associated with overeating, orexin-A being an appetite-inducing neuropeptide also influences the energy homeostasis.[15]

The results of our study corroborate with the findings of Tomasik *et al*.,[23] Matsumura *et al*.[24] and Heinonen *et al*.[25] who also observed a significant positive association between BMI and serum orexin level which was measured using ELISA. Elevated plasma orexin-A levels in morbid obesity measured with ELISA contrast the radio immune assay (RIA) measured data in the literature.

In a comparative study done by Gupta *et al*.[15] on premenopausal women, a negative association between waist circumference and orexin-A circulating level exists in premenopausal women with metabolic syndrome compared to premenopausal women without metabolic syndrome. In another study by Mishra *et al*.[26] in obese North Indian women, orexin-A levels were significantly lower in obese women as compared with control group. Studies done by Baranowska *et al*.[21] and Adam *et al*.[22] also found a negative correlation between plasma orexin-A levels and BMI. The negative association found in above studies could be because of the fact that women with metabolic syndrome were chosen as subjects and other factors as waist circumference and waist-hip ratio causing central obesity could have been affecting orexin levels.

In our study, mean serum orexin levels (pgm/ml) among different age groups among RAG women ranged from 46.88 ± 15.92 (>35 years) to 50.84 ± 14.53 (26–30 years). This age group was taken into account as an important aspect of addressing adverse weight transitions among fertile women, as these transitions will have deleterious effects on women's long-term health and on the risk of adverse pregnancy outcomes if pregnancy occurs.[13]

In the previous studies, there are varying levels of orexin-A detected in blood in various age groups. Arihara *et al*.[27] measured basal plasma orexin-A concentrations of 1.94 ± 0.24 pmol/l (6.9 ± 0.9 pg/ml) in healthy individuals. Plasma orexin-A levels measured with RIA have varied between 1 and 100 pg/ml. Dalal *et al*.[28] reported even higher levels of 175–847 pg/ml and Tomasik *et al*.[23] reported plasma levels of 1000 pg/ml in healthy children of varying ages.

In a study done by Tomasik *et al*.,[23] plasma orexin-A level in children and young adults varies in the age group of 0–18 years. They found higher orexin-A levels in newborns and adolescents (10–15 years) than in young adults (16–18 years). They used ELISA to detect serum orexin levels.

Not much data are available on the association of orexin-A levels and its role in women of fertile age group. Further studies are required to establish its causal relationship with metabolic risk markers.

CONCLUSION

In the present study, BMI correlated significantly with mean serum orexin levels and it did not correlate with the age of women of RAG.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

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