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Sex hormone levels and intraocular pressure in postmenopausal Nigerian women

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Abstract

Background: A number of hormones are known to affect intra ocular pressure (IOP). Of these, the female sex hormones are the predominant ones to cause variations in IOP. During menopause, a changing hormone profile in the body causes important shifts in the levels of these hormones. Studies on the effect of menopause on visual function, cardiovascular and ocular hemodynamics showed that menopausal women had significantly higher IOP as compared to premenopausal women. The purpose of this study was to determine the influence of serum levels of sex hormones on IOP in postmenopausal Nigerian women.

Method: This study was an experimental, cross sectional study. Twenty postmenopausal women aged 50 to 55 years (mean age 52±2. 32) and twenty premenopausal women aged 45 to 50 years (mean age 50±2.13) were selected by systematic random sampling. The women were free from systemic or ocular diseases. IOP was measured and serum levels of progesterone, estradiol and testosterone were determined by hormone assay for all subjects. Data was analyzed by correlation analysis.

Results: Mean IOP between the postmenopausal (16.00±5.81 mmHg) and premenopausal women (15.50±3.28 mmHg, p=0.24) was not statistically significant. Although there was a positive correlation between IOP and estradiol level in the post-menopausal women (r=0.567, p=0.009), no significant correlation was found between IOP and serum levels of sex hormones among the premenopausal women.

Conclusion: Our result suggests a relation between levels of estradiol and IOP in postmenopausal Nigerian women. However further studies may be required to determine a direct cause and effect relationship.

Keywords: *Menopause, hormone; intraocular pressure; estradiol; testosterone.*

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Résumé

Contexte: Certains hormones sont connus comme étant la cause de la pression intraoculaire (PIO). Parmi ceux-ci, les hormones du genre féminin sont les plus prédominants à provoquer des variations de la PIO. Pendant la ménopause, un changement de profil hormonal dans le corps provoque des changements importants aux niveaux de ces hormones. Les études sur l'effet de la ménopause sur la fonction visuelle, hémodynamique cardio-vasculaires et oculaires ont montré que les femmes en ménopause ont la plus sensiblement élevée PIO que chez celles qui ne sont pas en ménopause. Le but de cette étude était de déterminer l'influence des niveaux d'hormones sexuelles de sérum sur la PIO chez les femmes ménopausées nigérians.

Méthode: C'est une étude expérimentale transversale. Vingt femmes en ménopause, âgées de 50 ans à 55 ans (52 ± 2. Âge de 32 ans moyenne) et vingt femmes pré ménopausées âgées de 45 à 50 ans (50 ± 2.13 femmes d'âge moyen) ont été sélectionnés par échantillonnage aléatoire systématique. Celles-ci sont exceptées des maladies systémiques ou oculaires. La PIO a été diagnostiquée et les niveaux de progestérone, de l'œstradiol et de la testostérone sérique ont été déterminées par dosage hormonal chez tous les sujets. Les données ont été analysées par analyse de corrélation.

Résultats: La moyenne entre le post-ménopausique (16,00 ± 5,81 mm Hg) et les femmes pré ménopausées (15,50 ± 3,28 mmHg, p = 0,24) n'était pas statistiquement importante. Bien qu'il y ait une corrélation positive entre la PIO et le niveau d'estradiol chez les femmes post-ménopausées (r = 0,567, p = 0,009), aucune corrélation importante n'a été trouvée entre les niveaux de sérum d'hormones sexuelles chez les femmes pré ménopausées et la PIO

Conclusion: Nos résultats suggèrent une relation entre les niveaux d'œstradiol et la PIO chez les femmes nigérianes en ménopause. Toutefois, d'autres études s'avèrent indispensables pour déterminer la cause directe et l'effet des relations.

Introduction

At about 40 to 50 years of age in females, the menstrual cycle usually becomes irregular and ovulation often fails to occur. After a few months to a few years, the cycle ceases altogether. The period

during which the cycle ceases and levels of the female sex hormones diminish to almost none is called menopause [1]. When a woman has not had a menstrual cycle for at least one year, she is said to be postmenopausal. A number of hormones are known to affect intra ocular pressure (IOP). Of these, the female sex hormones are the predominant ones to cause variations in IOP. Menopause has been reported to significantly affect IOP [2]. During menopause, a changing hormone profile in the body causes important shifts in the levels of sex hormones present in the female body.

Studies [3,4] on the effect of menopause on visual function, cardiovascular and ocular hemodynamics showed that menopausal women had significantly higher IOP as compared to premenopausal women. A number of studies [5, 6] provide clinical evidence that aging is associated with increases in IOP. IOP does not change significantly until the fourth decade and then increases in both sexes [3]. This impact of aging varies however according to gender. Male – female differences in IOP are small until the 40–49 years age group, after which women begin to develop significantly higher IOP than men. This may be attributed to hormonal difference between them [7]. Mean IOP in post-menopausal women have been reported to be higher than that in men and menstruating women of the same age group [7, 8].

The relationship between days of the menstrual cycle and variations in IOP findings are not consistent. Although previous studies [9,10] have demonstrated that IOP decreases during pregnancy and as compared to menstruating women, it is higher in postmenopausal women but the degree of the reported change in IOP values, differs from study to study. Although this data points out the possible influence of sex hormones on IOP, other studies [10, 11] report that pharmacological doses of progesterone and estrogen (alone or in combination) can influence IOP. It has been reported that 5mg progesterone injected intramuscularly into various subjects caused a fall in IOP. Similarly, estrogen or combined estrogen progestin treatment has been shown to induce reduction in IOP both in normal eyes and in eyes with glaucoma [12, 13]. At the time of menopause a woman must readjust her life from one that has been physiologically stimulated by estrogen and progesterone production to one devoid of these hormones. There is also a reported increase in the serum levels of testosterone [14]. It has been established that higher testosterone levels in postmenopausal women receiving hormone replacement therapy (HRT) and those not receiving were associated with higher intraocular pressures [4,14]. With increasing rate of ocular hypertension and consequently glaucoma amongst women aged 50 years and above, which is the period during which menopause occurs, this study is imperative. Increased IOP is a significant risk factor for visual impairment in glaucoma patients.

The most common type of glaucoma is primary (open – angle) glaucoma which occurs in approximately 14% of people aged over 50 years, with higher frequencies in women than in men [15]. As a diagnosis of glaucoma is usually only performed at the onset of presbyopia i.e. at an age where the majority of menopausal symptoms occur, it leads to a relationship between IOP and a reduction in estrogen and progesterone levels in postmenopausal women [15].

Since no work like this has been done previously on Nigerian women, to the best of our knowledge, this study aims to determine if any correlation exist between serum levels of estradiol, testosterone and progesterone and intraocular pressure in postmenopausal women so as to provide baseline data and for comparison with previous studies in the literature.

Materials and methods

This study was an experimental, cross sectional study. A total of forty (40) women were recruited by systematic random selection. Every third woman reporting to the clinic was selected and among them those who met our inclusion criteria were recruited into the study. Twenty of the women were postmenopausal and had not had a menstrual cycle for at least one year. They had also attained menopause naturally. They were aged 50 to 55 years (mean age 52±2. 32) while the other 20 women between 45 to 50 years were premenopausal (mean age 50±2.13), who were still having their menstrual cycle. Informed consent was obtained from the women after the purpose of the study was explained to them. Ethical approval for the study was obtained from the University of Benin Ethics Committee. The study was conducted in line with the principle of the declaration of Helsinki.

The women recruited were members of staff of the University community, primary and secondary school teachers attending the University of Benin Optometry Clinic. The women were free from systemic and ocular diseases. A short medical history from the women revealed they were not on medication for any systemic or ocular diseases. The subjects' ocular health and general health history were obtained. Visual acuity test was carried out

using the standard Snellen chart. External eye examination was carried out, using the slit lamp biomicroscope to rule out ocular surface and anterior segment abnormalities. The internal structures of the eyes were examined using the keeler professional monocular direct ophthalmoscope in dim illumination to rule out diseases of the posterior segment. Blood pressure was measured with a manual mercury sphygmomanometer in a sitting position at the right upper arm using the right cuff size. Two readings were taken and the average recorded. Blood sugar level was also measured using the Acuchek Active Pack. The standard Goldman applanation tonometer mounted on the slitlamp biomicroscope was not functional at the time of this study, hence intraocular pressure was measured with the handheld Kowa applanation tonometer. The eyes were anaesthetized with 0.5% proparacaine and fluorescein strips impregnated with 1 mg of sodium, were used to stain the eyes. The average of two readings was recorded per subjects. The test was carried out between 10 am and 12 noon each day to avoid diurnal variation. No statistical difference was found between IOP measurements of fellow eyes by unpaired *t* test (p = 0.37), so the mean value for right and left eyes of each subject was used for further statistical comparisons.

Inclusion criteria

Only women who agreed to give blood samples were included in the study. Other criteria met by the subjects were absence of any history of eye disease or surgery, absence of diabetes mellitus (fasting blood glucose < 110 mg/dl), hypertension (blood pressure < 140/85 mmHg), smoking, hypercholesterolemia (total cholesterol > 200 mg/dl), cardiovascular, or peripheral vascular disease. No subject had received any exogenous sex steroid since the time of menopause.

Collection of blood sample

Simultaneous blood samples (10 mL) were collected for the assessment of serum sex hormone levels by a laboratory assistant into pre labeled specimen tubes (non anticoagulant). The blood sample was centrifuged and the resultant serum was stored at "20°C prior to analysis.

Hormone assay

Serum estradiol levels were evaluated using chemiluminescent immunoassay by Immulite analyzer (Diagnostic Products Corp., Los Angeles, CA). Serum testosterone levels were determined with the radioimmunoassay by Count-A-Count analyzer (Diagnostic Products Corp., Los Angeles, CA). Serum progesterone levels were measured by the electrochemiluminescent immunoassay by Elecsys 1010/2010 Modular analytics E170 analyzer (Roche Diagnostics GmbH, Mannheim, Germany).

Statistical analysis

Data obtained was analyzed with Pearson's correlation analysis and unpaired student t-test using SPSS Ver. 16.00. (SPSS Inc. Chicago, IL). Level of significance was set at $p<0.05$.

Results

Mean intraocular pressure between the postmenopausal (16.00±5.81 mmHg) and premenopausal women (15.50±3.28 mmHg, p=0.24) was not statistically significant (Fig. 1).

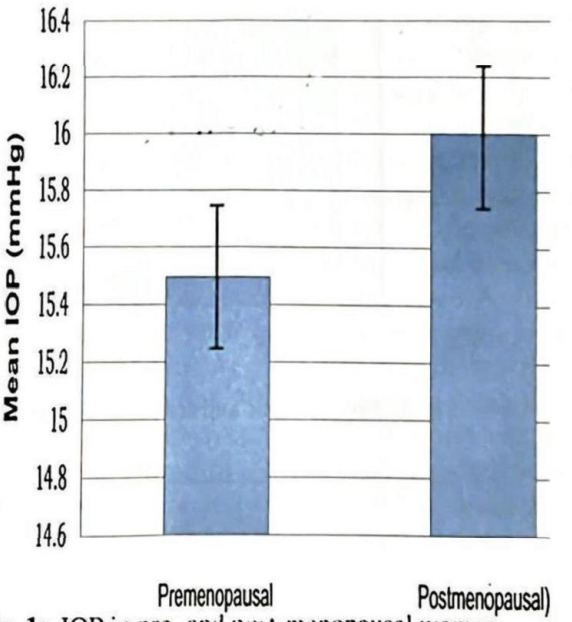

Fig. 1: IOP in pre- and post-menopausal women

Table 1: Mean Intraocular pressure (IOP) and Sex hormone levels among postmenopausal women

Statistics	n	Mean	SD	SEM
IOP (mmHg)	20	16.00	5.81	1.30
Progesterone (nmol/L)	20	4.61	3.42	0.76
Testosterone (nmol/L)	20	0.92	1.09	0.24
Estradiol (pg/mol)	20	85.65	28.39	6.34

n= Sample size, S.D=Standard deviation, S.E.M=Standard error of mean

Table 1 shows the mean values of intraocular pressure and sex hormones in postmenopausal women. There was a statistically significant difference in levels of progesterone between the pre- and post- menopausal women (t=11.07, $p<0.05$).

Table 2: Mean intraocular pressure (IOP) and hormone level among pre-menopausal women

Statistics	n	Mean	SD	SEM
IOP (mmHg)	20	15.50	3.28	0.73
Progesterone (nmol/L)	20	9.42	8.91	1.99
Testosterone (nmol/L)	20	0.76	0.53	0.12
Estradiol (pg/mol)	20	100.43	15.62	3.49

in the post-menopausal women (r=0.567, p=0.009), no significant correlation was observed between IOP and progesterone (r=0.204, p>0.05) or IOP and testosterone (r=0.05, p>0.05) in the postmenopausal women. No significant correlation was found between IOP and serum levels of estradiol (r= 0.126, p>0.05), progesterone (r =0.262, p>0.05) or testosterone (r =0.234, p>0.05) among the premenopausal women.

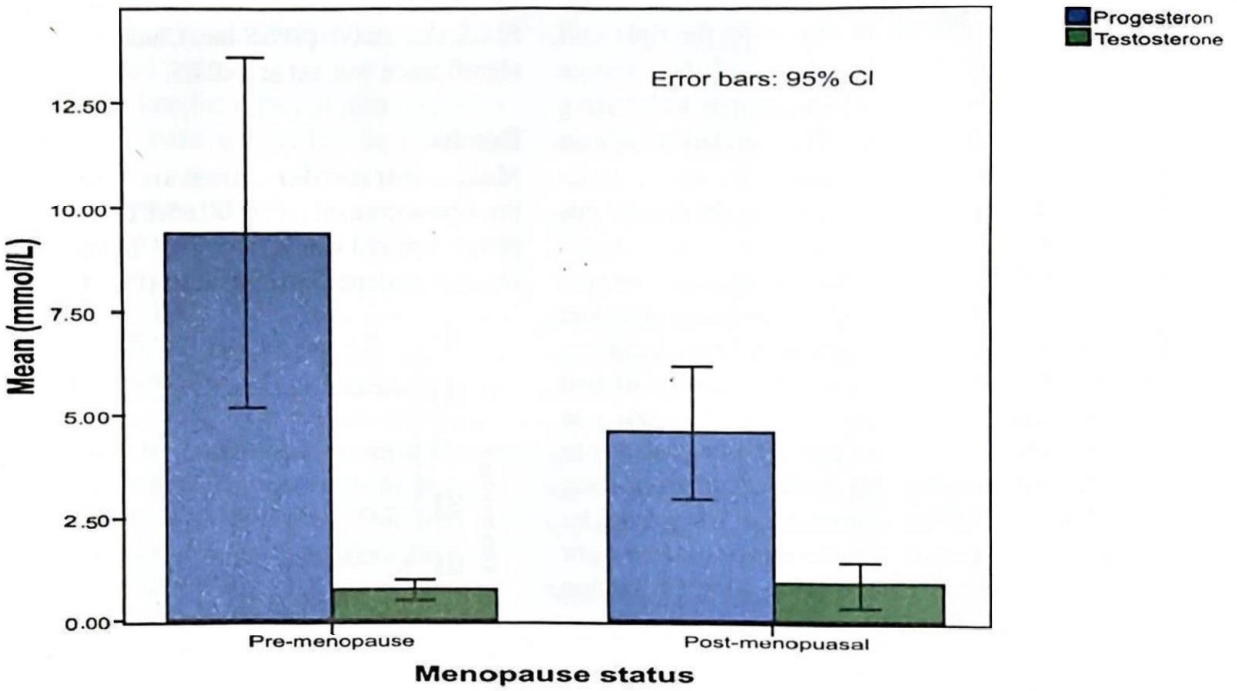

Fig. 2: Progesterone and testosterone in pre- and post-menopausal women

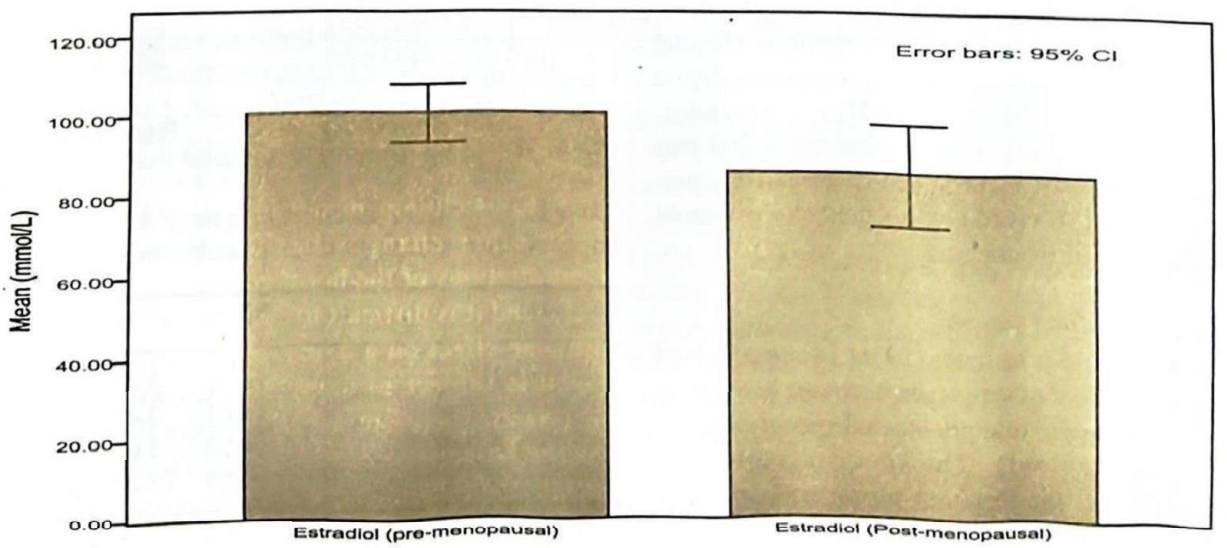

Fig.3: Estradiol in pre- and post-menopausal women

However the difference in levels of testosterone (t=-0.351, p>0.05) and estradiol (t=0.242, p>0.05) between the premenopausal and postmenopausal women was not significant. Although there was a positive correlation between IOP and estradiol level

Values of IOP and sex hormones for the premenopausal women are shown in table 2. Figures 2 and 3 show mean levels of sex hormones in premenopausal and postmenopausal women.

Discussion

The mechanism(s) by which sex hormones may modulate intraocular pressure (IOP) are unclear. IOP is maintained as the result of a balance between the secretion of aqueous humor by the ciliary processes and the outflow of aqueous humor through the trabecular meshwork and uveoscleral pathway. The lack of change in aqueous flow rate during menstrual cycle and gestation suggests that the alterations in IOP related with hormonal changes are mainly a consequence of altered outflow facility, supported by the findings of previously mentioned studies [3,4].

Data obtained in this study did not show a statistically significant difference between the IOP of pre-menopausal and post-menopausal women, which is consistent with some studies [3, 10, 12] and contrast with others [4,11,14]. Although IOP correlated significantly with estradiol in the postmenopausal women, no significant correlation was observed between IOP and the sex hormones among the premenopausal women.

In the literature [2, 11], evidence is found for a direct effect of endogenous hormonal changes on aqueous humor circulation: Some authors [10,15-17] agree that in pregnancy, with altered hormonal status, intraocular pressure decreases significantly. This reversible effect is most likely explained by an increased outflow facility through the trabecular meshwork.

There is evidence that progesterone has the properties of a glucocorticoid antagonist [6]. Glucocorticoids are known to elevate intraocular pressure. Progesterone may inhibit the ocular hypertensive effect of endogenous glucocorticoids by competing for the receptor binding site. These receptors have been located in human trabecular meshwork cells and rabbit iris-ciliary body cells, binding both glucocorticoids and progesterone [6, 18-21].

In a population-based study, age at natural menopause was associated with the presence of open-angle glaucoma [17, 19, 22]. The relation between primary open-angle glaucoma and gender is still controversial. Several biologic mechanisms could explain the association between early menopause and open-angle glaucoma [19, 23]. It may be assumed that the decrease in estrogen and progesterone levels after menopause may play a key role, and therefore biologic mechanisms influenced by these hormones may be involved. For both etiologic and therapeutic reasons, further research into the effects of endogenous and exogenous exposure to female sex hormones would be of interest.

It had been suggested that estradiol increases endothelial nitric oxide levels by enhancing the activity of the enzyme nitric oxide synthase III [19]. Several investigators [24, 25] have reported that nitric oxide induces a decrease in intraocular pressure—for example, by relaxation of the trabecular meshwork. Moreover, as a vasodilator, nitric oxide may have an effect on the blood supply of the optic nerve and the basal vascular tone in uveal, retinal, and choroidal circulation [26, 27].

A possible limitation of the present study may be the fact that the IOP and serum sex hormone measurements were performed only once between 10:00 a.m and 12:00 o'clock. Performing serial measurements of IOP and serum level of sex hormones at different periods of the day would perhaps better define the role that these hormones may play in the regulation of the diurnal rhythm of IOP. The small sample size of women used for this study might also have brought about the results obtained. The small sample size was as a result of the fact that not many of the women enlisted were disposed to giving blood samples. Also the need to keep the age range of both the postmenopausal and premenopausal women as close as possible made it difficult to increase the sample size beyond what we used, as there were only few females over 50 years old who were still having their monthly cycle. This posed a great challenged to the Researchers. Another factor to bear in mind when considering the result of this study is that the postmenopausal and premenopausal women were not exactly matched for age.

In conclusion, menopause is associated with many other changes besides the change in concentrations of the hormones measured in this study, and it is difficult to evaluate an individual hormone effect on a dynamic function like IOP, which is subject to many acute and long-term influences. Therefore, we recommend that further studies be carried out to fully investigate and explain the relationship between serum levels of sex hormones and IOP in post-menopausal women. Also menopausal women and women approaching menopause should always be screened for increased intraocular pressure and counseled on the need to visit their eye care professional for proper ocular examination.

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