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RESEARCH ARTICLE

THE ROLE OF SERUM ESTROGEN AND NITRIC OXIDE (NO) IN POST-MENOPAUSAL KNEE OSTEOARTHRITIC FEMALE PATIENTS

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Abstract

As we are all aware the hormone estrogen is the most essential sex hormone of the female. It plays significant roles in all phases of the life of females. Osteoarthritis is the most debilitating bone disorder commonly seen in females more than males. Out of all the joints knee joint is most commonly affected as it is the weight-bearing joint. So here in this study, the main objective is to know the role of serum estrogen and Nitric oxide levels in post-menopausal knee osteoarthritic female patients. The samples were collected and the chemiluminescence and ELISA method performed the tests. Consequently, results showed decreased levels of serum Estrogen in the study group than in the control group and levels of serum nitric oxide was increased as it confirmed the inflammatory marker at the site of infection. This whole suggests that deficiency estrogen and raised nitric oxide are helpful in the diagnosis and treatment modalities of knee osteoarthritis in postmenopausal females.

Introduction:-

Osteoarthritis is the most common form of arthritis, affecting about 237 million people or 3.3% of the world population. It becomes more common as people become older. Among those over 60 years old, about 10% of males and 18% of females are affected. [1][2]

OA is a type of joint disease that results from the breakdown of joint cartilage and underlying bone. The symptoms of osteoarthritis often begin slowly and usually begin with one or a few joints. The common symptoms of osteoarthritis include Pain when using the joint, which may get better with rest. [2][3]

As we know there are multiple pathophysiological mechanisms involved in OA, those related to the sex hormone are attracting attention, among them is Estrogen. In both men and women, estrogen levels decrease with age, and lower levels can potentially lead to deficiencies such as those found in skeletal tissue. For example, bone loss, especially in postmenopausal women, is likely associated with a change in estrogen levels. Although the incidence of OA is higher in men than women until the age 50, its prevalence increases in menopausal women, which factors trigger OA in women is not clear, but lower than the normal hormone levels in both the elderly and post-menopausal women suggest an association of OA with reduced hormone.[4] . So this rise in the prevalence of OA among post-menopausal women, which is associated with the presence of the estrogen receptors (ERs) in joint tissues, suggests the link between the OA and ovarian function. Estrogen may modify the hormones that regulate ca++ balance. [5]

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At menopause in women, the acute loss of the restraining effects of E on bone cell activity leads to an accelerated phase of loss of predominantly cancellous bone that decreases after about 4–8 years and disappears after about 15–20 years when severe depletion of cancellous bone stimulates counter-regulatory forces that limit further loss. The slow phase of bone loss, which also begins at menopause, then becomes dominant. It involves loss of both cancellous and cortical bone and continues throughout the remainder of life. It is caused by the loss of E effects on extra skeletal calcium homeostasis leading to decreased intestinal calcium absorption, increased renal calcium wasting, and, perhaps also, effects on vitamin D metabolism. Age-related impairment in bone formation also contributes to the slow phase of bone loss and may be caused, at least in part, by the loss of E-stimulated synthesis of bone matrix proteins by osteoblasts. [6]

Nitric oxide acts as a mediator in various physiological and pathophysiological processes in the human body. In the inflammatory reaction, NO generated by inducible nitric oxide synthase (iNOS) has both regulatory and proinflammatory/destructive effects. Enhanced NO production along with elevated levels of other inflammatory mediators is found in osteoarthritic joints, supporting the view that osteoarthritis (OA) is a local slowly progressing inflammatory disease. Elevated levels of markers of nitric oxide (NO) production are found in osteoarthritic joints suggesting that NO is involved in the pathogenesis of osteoarthritis.[7]

In inflamed joints, NO acts principally as a proinflammatory and destructive mediator. In OA, NO mediates many of the destructive effects of interleukin-1 (IL-1) and tumor necrosis factor- alpha (TNF-α) in the cartilage. NO seems to be a destructive mediator in cartilage, although, as with the other inflammatory mediators, it may also evoke regulatory effects.[7]

The present study was aimed to find out the major role of serum Estrogen hormone & Nitric oxide in the development and pathogensis of knee osteoarthritis disease in postmenopausal females.

Materials & Method:-

The study was conducted (with institutional ethical committee approval) in 100 female patients suffering from knee joint osteoarthritis with age group of 50 - 80 years. They are clinically and radiologically diagnosed osteoarthritis patients, attending OPD of orthopaedic department UPUMS, Saifai, Etawah (U.P.) for regular checkup. 100 normal healthy female control subjects of same age group have also been included in our study for statistical comparison. 5 ml of blood was collected from all the subjects in fasting condition and the serum was separated and stored at -20° C until used. The estrogen hormone & Nitric Oxide were estimated by Chemiluminescese& ELISA technique respectively in Biochemistry department. All estimations were done in duplicate and the mean values were calculated. The student independent 't' test was used for the statistical analysis of the data. The written consent was also taken from patients prior to study.

Result:-

Table 1 and figure 1 shows the status of **Serum Estrogen** in postmenopausal knee osteoarthritic patients (13.27 ± 6.40) and normal healthy female subjects (83.01 ± 44.99) of the study, **Serum NO** in postmenopausal knee osteoarthritic patients (88.47 ± 36.48) and normal healthy female subjects (26.67 ± 7.09) of the study.

Table 2 shows the Correlation of study Parameters in Knee osteoarthritic female subjects. As it can be seen that there was the negative correlation of age with both of the study parameters and serum estrogen hormone shows the highly negative correlation with the age.

Table 1:- Showing the Status of serum Estrogen & Nitric Oxide in Postmenopausal knee osteoarthritic female patients and normal healthy postmenopausal female subjects.

Study Group		**ESTROGEN (pg/mL)**	**NO (µmol/L)**
Normal healthy Postmenopausal Female subjects (n=100)	**Min Range Max.**	15.7 206	10 40.9
	Mean ± SD	83.01 ± 44.99	26.67 ± 7.09
	SE	4.499	0.709

Postmenopausal Knee osteoarthritic female patients (n=100)	**Min** **Range** **Max.**	4 28	24 180
	Mean ± SD	13.27 ± 6.40***	88.47 ± 36.48***
	SE	0.64	3.64

Values expressed as Mean ± SD, ***P<0.0001, NS = Non-significant

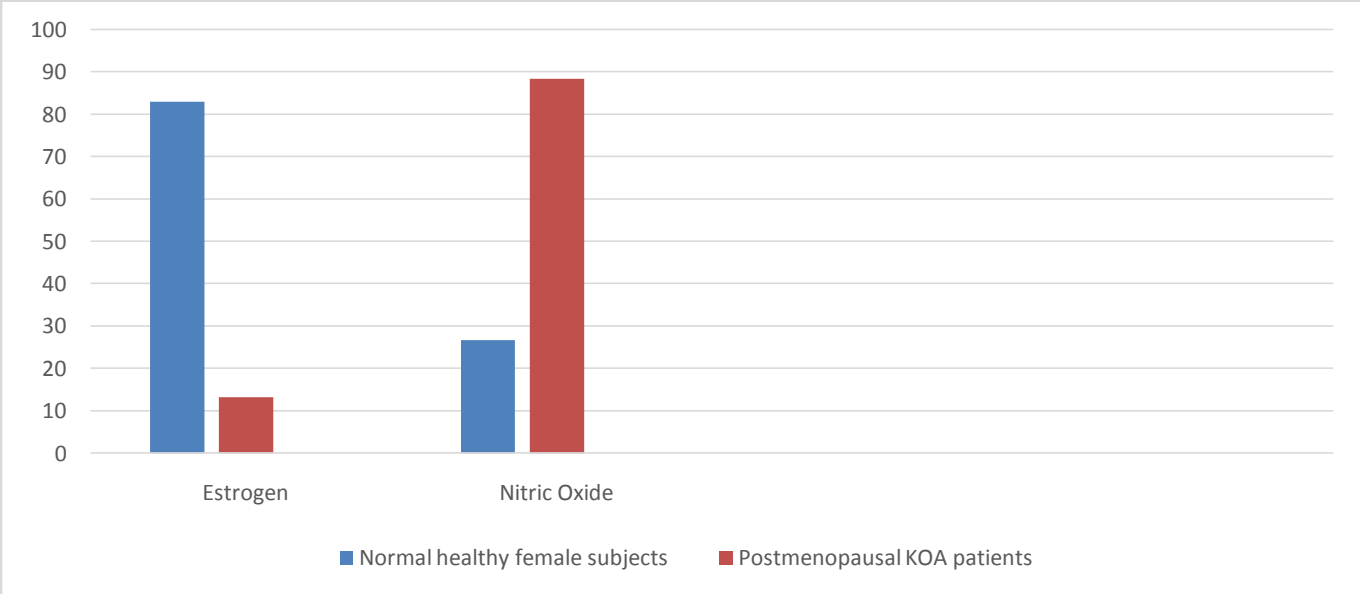

Fig 1:- Showing the status of Mean values of serum Estrogen & Nitric Oxide in Postmenopausal knee osteoarthritic female patients and normal healthy postmenopausal female subjects.

Table 5:- Showing the correlation of serum Estrogen & Nitric Oxide in Postmenopausal Knee osteoarthritic patients.

VARIABLE	ESTROGEN	NO
AGE	-0.71***	- 0.13*
ESTROGEN	-	-0.56**

Pearson correlation

Values expressed as correlation coefficient (r), *low correlation, **moderate correlation, ***high correlation

Discussion:-

OA of the knee is a major cause of mobility impairment, particularly among females. OA was estimated to be the 10th leading cause of non-fatal burden. Osteoarthritis is mainly disease of later age onset which is around 50 to 60 years of age.[8]

Serum Estrogen, as we all aware that it is a steroid hormone and the major female sex hormone. It is involved in the regulation of the estrous and menstrual female reproductive cycles. Estradiol is responsible for the development of female secondary sexual characteristics, which was studied and found to be significantly ($p<0.0001$) decreased among the postmenopausal KOA patients (13.27 ± 6.40) compared to the Normal healthy female subjects (83.01 ± 44.99). These values were corresponded to the several studies out of which one was led by Dipanshu Sur, RatnabaliChakravorty in which it was found that Mean serum estrogen levels in the OA and control samples were 29.53 ± 3.27 and 49.21 ± 2.18 ($P < 0.0001$) which were significantly lower in OA patients compared with controls.[9] In the study done by Jie Xu et.al done in china showed the changes of FSH, LH and E2 in the postmenopausal women and indicates that FSH level may have an effect on the development of osteoarthritis.[10]

Similarly in the study done by the Jorge A Roman-Blas, it was concluded that Both experimental and observational evidence support a relevant role for estrogens in the homeostasis of joint tissues and, hence, in the health status of joints.[7]

Serum NO, found to be significantly ($p<0.0001$) increased among the cases (88.47 ± 36.48) compared to the controls (26.67 ± 7.09). These values corresponded to the several studies out of which one was done by Salvieterra J et.al and results showed that increased NO levels in joint cartilage of patients with hip OA. This increase was not homogeneously distributed, but the higher NO levels were found in macroscopically deteriorated areas. The data also suggest that high NO serum levels found in patients with hip OA may be due to joint cartilage destruction.[11]In this study the raised levels of the serum Nitric Oxide was found to be increased and can be used as the one of the investigatory biochemical parameter of the OA patients, irrespective of the mechanism and pathway followed by NO and due to its complex biochemistry in our body & various studies had not been elucidated. When Pearson correlation was used it was observed that it had negative correlation with the age & estrogen when done in postmenopausal KOA female patients.

So according the studies and the result of my study its being evident that estrogen deficiency affects the bone health of the postmenopausal females whereas increased serum levels of the NO was seeming to be the destructive mediator in cartilage leading to the pathology and osteoarthritic changes in the bones and affecting the functioning of the joints involved.

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