ORIGINAL ARTICLE

Evaluation of Progesterone and Testosterone in Surgical Menopause

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Abstract:

Background and objectives: Natural menopause is a physiological process which occurs around the age of 45 – 55 years. Surgical menopause is not physiological, occurs through an operative procedure which leads to sudden hormonal imbalances. Both the groups whether natural or surgical menopause experience hot flushes and mood swings, but this happens gradually in natural menopause and suddenly in surgical menopause. These symptoms may be correlated to the sudden hormonal imbalances. *Aim:* To study and compare hormonal levels of progesterone and testosterone in surgical and natural menopause. *Material and Methods:* The present study is case control study consisting of 50 women belongs to surgical menopausal group and 50 women belong to natural menopausal group. The hormonal parameters such as Progesterone and Testosterone were measured by Solid Phase Competitive Chemilumniscence Enzyme Immunoassay. Student's t-test was used to compare mean serum concentrations of Progesterone. Mann-Whitney U Rank Test was used to compare mean testosterone values. *Results:* The mean level of progesterone hormone in case group was found to be 0.71±0.57 while that in control group was 2.074±0.42. Mann- Whitney U Rank Test was used to compare mean testosterone values which showed significant difference between both the groups of surgical and natural menopause. *Conclusion:* In natural menopause the hormonal imbalance occurs gradually over a period of time but in surgical menopause the hormonal levels change abruptly. These sudden changes in the hormonal level may be responsible for severe hot flushes, headaches, mood swings and atherosclerosis.

Keywords: Serum testosterone, serum progesterone, surgical menopause, natural menopause, Chemiluminiscence.

Introduction:

Progesterone is secreted mainly by corpus luteum and partly metabolized to estrogen and partly to totestosterone. It also have many significant actions such as secretory hypertrophy of endometrium, myohyperplasia of uterus, inhibit production of FSH and causes sodium retention and relaxation of smooth muscles.[1] Fifty percent testosterone is secreted by adrenal gland and remaining secreted in ovaries by all three types of cells i.e stroma, theca and granulosa but mainly by the theca interna cells of ovarian follicles. 80-85% testosterone are bound to sex – hormone binding protein , 10 -15 % to albumin and remaining 1- 2% remains free which is responsible for its action at peripheral targets mainly hair growth and acne.[1] Menopause is defined as that point in time when permanent cessation of menstruation occurs following loss of ovarian activity.[2] It takes 12 months of amenorrhoea to confirm that menopause has set in and so it is retrospective diagnosis. [3] Surgical menopause was defined as a condition in which there occurs a cessation of menses resulting from surgical removal of the uterus, leaving one or both ovaries, or the removal of both ovaries.[4]

Material and Methods:

This research study was conducted in department of biochemistry of grant medical college & JJ hospital Mumbai from september 2012 to april 2013. The study is case control study consisting of 50 women belong to surgical menopausal (Cases group) and 50 women belong to natural menopausal (Control group). Women having age between 44 to 50 years who undergone total hysterectomy in past one to two years and Women having age between 44 to 52 years who are experiencing natural menopause since past one to two years were included in the study. Women having endocrine disorders, testosterone secreting tumors and on hormonal intake in any form were excluded from the study. All the women who were enrolled in the study were duly informed and written consent was taken. Blood samples were collected and were sent for hormonal evaluation in special investigation laboratory working under

department of biochemistry. In this study fully automated enzyme amplified chemiluminescent immunoassay based Immulite 1000 analyzer was used. The solid phase(bead) is coated with rabbit anti-hormonal polyclonal antibody. The reagent contains alkaline phosphatase conjugated to respective hormone. This hormone-enzyme conjugate competes with respective hormone in patients' blood sample for limited antibody binding sites on bead. The excess sample and reagent are removed by centrifugal wash. Finally chemiluminiscent substrate is added to the bead and signal is generated in proportion to the bound enzyme. The results of hormonal evaluation were subjected to statistical analysis using Mann-Whitney U Rank test and unpaired sample t – test. The reported *p* value < 0.05 was considered as statistical significant.

Results:

Table 1: Reference values of serum Progesterone & Testosterone

Reference Values as per Siemens diagnostic kit insert	
Total Testosterone	ND – 43 ng/dl
Progesterone	ND – 11 ng/ml

(ND- non detectable, ng – nanogram, dl – decilitre, ml – millilitre) On applying independent (Unpaired) sample t – test, the difference in mean progesterone level between both the groups was found to be very significant with p value < 0.001. (Table – 2 & Figure – 1)

Table 2: Mean Serum Progesterone Level of surgical and natural menopausal females

Serum mean Progesterone Level of surgical and natural menopausal females				
Menopause	N	Mean Progesterone [ng/ml]	Standard Deviation [ng/ml]	Standard Error [ng/ml]
Surgical	50	0.71	0.57	0.08
Natural	50	2.074	0.42	0.06
Mean Difference= -1.364 [ng/ml]				
Independent Sample t test:- t value -13.63, df-98, p value <0.001				

In this study Mann-Whitney U Rank Test was used to compare mean testosterone values which showed significant difference between both the groups of surgical and natural menopause. (Table 3)

Figure 1: Dot Plot of serum progesterone level by type of menopause

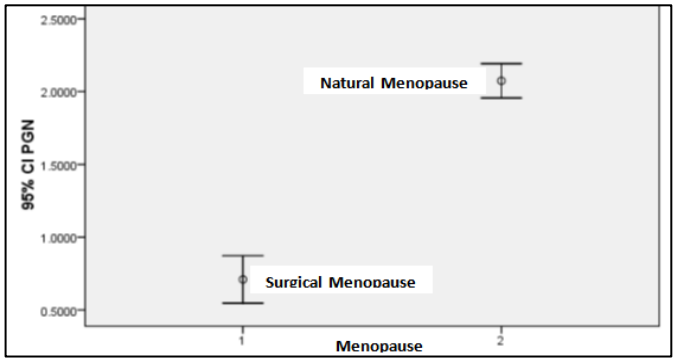

Table 3: Mean Serum Testosterone level of surgical and natural menopausal females

Serum mean Testosterone level of surgical and natural menopausal females						
Ranks Test Statistics						
Menopause	N	Mean Rank	Sum of Rank	Mann-Whitney U Rank Test Value	p Value	Inference
Surgical	50	43.05	2152.5	877.5	0.01	Significant Difference
Natural	50	57.95	2897.5			

Discussion:

In the present study, the serum progesterone levels in surgical menopausal women from 1 to 2 years after surgery was lower than that in the post-menopausal women at similar periods after natural menopause. This indicates that some ovarian progesterone may be sustained for a few years after natural menopause. Similar finding were suggested by Nobuaki Furuhashi *et al.* [5] who reported significantly decreased levels of progesterone within 2 years after surgical menopause as compared to their levels in natural menopause. The study findings were also consistent with the findings of Abraham, G.E et al[6] and J. Dinny Graham et al[7] who reported significant decrease in the blood levels of progesterone and testosterone in surgical menopausal women. As ovary is the major site of synthesis and secretion of estradiol and progesterone in the mammals, this might be the reason of significant decrease in progesterone secretion in surgical menopause than that of natural menopause as surgical menopause is characterized by faster onset of ovarian dysfunction. [8,9] Present study also reported a significant decrease in testosterone levels of surgical menopausal women as

compared to its level in natural menopausal women. This view was supported by S. L. Davison *et al.,* [10] who reported that surgical menopausal women had significantly lower testosterone levels than women in the reference group of natural menopause. Similar findings were also suggested by A. Vermeulen significant decrease in testosterone levels in surgical menopause as compared to natural menopause. [11] Gail A. Laughlin *et al.,* reported 40% decrease while Hughes. [12] CL Jr. *et al.,* reported 50% decrease in testosterone levels in surgical menopause. [13] Significant decrease in testosterone menopause was also revealed by Taylor who concluded that this decrease is associated with destabilization of psychiatric axis in women with surgical menopause. [14] In women, testosterone is produced primarily through peripheral conversion of androstenedione (50 percent) with the remainder of production concentrated in the ovary (25 percent) and adrenal cortex (25 percent). [15] Women with surgical menopause have decreased level of testosterone because production in this condition relies primarily on the adrenal cortex and peripheral conversion of androstenedione[16] while in natural menopause ovary still appears to be source of testosterone. [17] It has also been shown that testosterone levels do not fall abruptly in women undergoing natural menopause due to the preservation of androgen producing theca cells. [18] Evidence that even a simple hysterectomy hampers ovarian function has been proved in various studies.[19-23] and thus emphasized on the after effects of simple hysterectomy and need of proper consultation after the surgery. In another couple of studies conducted by Watson NR et al and Ritterband AB et al it was reported that there occurs a increased bone loss after premenopausal hysterectomy [24] as well as there has been increased incidence cardiovascular disease in such patients[25] and these findings were attributed to the evident ovarian failure in surgical menopause. Decrease in the ovarian blood supply after simple hysterectomy has also been reported by and this was attributed to the post-hysterectomy blockage in the circulation of the uterine vessels resulting in decreased ovarian blood flow. This ultimately leads in loss of follicular reserve and results in premature menopause. [26]

Conclusion:

In the present study, Progesterone and Testosterone were significantly decreased in surgical menopause as compared to natural menopause. The sudden change in these hormone levels may be responsible for the increased severity of hot flushes or mood swings seen in the surgical menopausal women as compared to natural menopausal women. Hence women with surgical menopause should consider the evaluation of both testosterone and estradiol under the consultation of a concerned doctor and inch one step closer for a healthy and happy menopause.

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Conflicts of Interest: Nil

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