ORIGINAL ARTICLE

EFFECT OF HORMONAL CONTRACEPTIVES ON SERUM SEROTONIN IN FEMALES OF REPRODUCTIVE AGE GROUP

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Background: Many types of hormonal contraceptives are in use nowadays for example oral pills, emergency contraceptive pills, vaginal rings, implantable rods and injectable contraceptives (combined and progestogens only). The purpose of this study was to determine and compare serum serotonin levels in married fertile females of reproductive age group using hormonal contraceptives with non-contraceptive users. **Methods**: A total of 300 women were selected in the study. This cross sectional study included three groups; Group-1 (control), group-2 (combined oral contraceptive users) and group-3 (injectable contraceptive users). History and examination of subjects were recorded on pro forma. Levels of serum serotonin were measured using standard ELISA kits. Results were analysed by one way ANOVA and a *p*-value 0.05% was taken as significant, using SPSS 16.0. **Results:** The mean age of the patients in group-1 was 30.4±6.1 years, group-2 was 28.9±4.9 and in group-3 was 2.5±6.8 years. For subjects in group-1, group-2 and group 3 the mean±SD concentration of serum serotonin was 160.68±53.27 ng/dl, 227.3±63.98 ng/dl and 118.19±31.32 ng/dl. A significant (p=0.00) difference was seen among three groups, i.e., group-1, group-2 and group-3. After applying Post HOC Tukey's HSD, there was statistically no significant difference between group-1 and group-2 (p=0.956). Difference was seen between group-2 and group-3 (p=0.00), it was also significant between group-3 and group-1 (p=0.00). **Conclusion:** It was concluded that hormonal contraceptives affect the levels of serum serotonin.

Keywords: Serum serotonin, Combined oral pills, Injectable contraceptives

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INTRODUCTION

Contraception is a very important topic for reproductive age and it can improve women's health in their child bearing age.[1] Hormonal contraception is the birth control that acts on the endocrine system.[2] Nowadays, approximately about 90 million women worldwide use oral contraceptives.[3] Around 12 million women worldwide use injectable contraceptives specially progestin-only formulation over long intervals because of their efficacy and less side effects.[4] All available contraception methods have both advantages and disadvantages. It is up to the health provider and the patient to make a better choice in individual cases.[5] Serotonin which is chemically a 5-hydroxytryptamine (5-HT) derived from tryptophan, is a monoamine neurotransmitter, is mainly found in the platelets, central nervous system and gastrointestinal tract. It performs various important functions including the regulation of sleep, mood and appetite.[6] Serotonin is popularly thought to be a contributor to feelings of well-being and happiness.[7] Its deficiency is associated with low mood, lack of will power ,poor control of appetite and low levels are also have been linked to depression.[8]

Oestrogen affects the brain and behaviour through direct and indirect genomic and non-genomic actions.[9] All of which have been involved in the pathophysiology of mood disorders.[10] In addition, oestrogen modulates the functions of the hypothalamic, pituitary and adrenal glands which in turn is implicated in the pathophysiology of depression and mood regulation.[11] Elevated levels of estradiol have anti-depressive effects most probably due to its serotonin increasing property.[12] Exogenous oestrogen can also affect responses and hypothalamic-pituitary-adrenal activity, which are both implicated in the regulation of mood.[13] Such mechanisms produced by oestrogen may exert mood-regulating effects in oral contraceptive users.[14] Progestin-only contraceptives are known to deteriorate the condition of women who are already depressed.[15] The high progesterone concentration by increasing the activity of the enzyme that breaks down serotonin, will decrease the levels of serotonin in the brain.[16] In women, progesterone and progestogens used for contraception cause depression, this occurs due to increased levels of monoamine oxidase responsible for degradation of serotonin in the late secretory phase of a normal cycle or during medication.[17] Progesterone, however, may promote positive mood changes at low concentrations and negative mood changes at high concentrations due to biphasic effects on GABAergic neurons.[18] In a meta-analysis it was suggested that the progesterone/oestrogen ratio correlates to the direction of emotional changes.[19] This study was conducted to determine the effect of combined oral contraceptive pills

and injectable contraceptives on serum serotonin levels in females of reproductive age group.

MATERIAL AND METHODS

This cross sectional study was done at Hazara University, Mansehra. A total of 300 women were selected in the study. This cross sectional study included three groups: Group-1 (control), group-2 (combined oral contraceptive users) and group-3 (injectable contraceptive users). History and examination of subjects were recorded on *pro forma*. Levels of serum serotonin were measured using standard kits. Informed consent was taken from all the subjects. All women were married fertile females in reproductive age group (15–49 years) who had not used any kind of hormonal contraceptives and were not pregnant and non-lactating. Group-1 (controls) were not using any contraceptive, group-2 (combined oral contraceptive users) were using combined oral pills at least for the last one year, and group-3 (injectable contraceptive users) were using injectable contraceptive users (progestogen only) at least for the last one year. Women having hypertension, liver disease, abnormal nipple discharge, cardio-vascular disease, diabetes mellitus, and undiagnosed vaginal bleeding were excluded. Serum Serotonin was measured by using ELISA kit. Data was analysed using SPSS 16.0. One way ANOVA was used to compare the means among the three groups. A *p*-value of ≤0.05 was taken as significant.

RESULTS

A total of 300 women were included in this study and divided into three groups. Group-1 comprised 100 women who were not using any kind of hormonal contraceptive methods (controls). Group-2 comprised 100 women using combined oral pills (lofeminal-ethinyl estradiol+norgestrel). Group-3 comprised 100 women using injectable contraceptives (3 monthly injectable-depoprovera-depotmedroxy progesterone acetate, 2 monthly injectable-norigest-norethisterone enanthate).

The mean age of the patients in group 1 was 30.47±6.16 years, 28.95±4.96 year in group-2 and 32.57±6.84 years in in group-3. Majority of the patients in the three groups were in age range from 20 to 40 years. The mean±SD concentration of serum serotonin for group-1 (control), group-2 (COCs) and group-3 (ICs) is shown in table-1. The difference was statistically significant.

After applying Post HOC Tukey's HSD, there was no statistically significant difference between group-1 and group-2 (p=0.956). The honestly significant difference was seen between group-2 and group-3 (p=0.00) and between group-3 and group-1 (p=0.00).

Table-1: Serum Serotonin Levels by study groups

Variable	*Group 1 mean±SD	**Group 2 mean±SD	***Group 3mean±SD	*p*-value
Serum Serotonin	160.68±53.27	227.37±63.98	118.19±31.32	0.00

Key:*Group-1: Controls,**Group-2: Subjects using Combined Oral Contraceptives (COCs) and ***Group-3 : Subjects using Injectable Contraceptives (ICs)

DISCUSSION

All over the world, the use of hormonal contraceptives by women is increasing, especially in the past few years when various organizations and governments are campaigning for its use in order to space pregnancies especially in developing countries like Pakistan.[20]

Present study included three groups: controls, COCs users and Injectable contraceptive users. In our study a significant (p=0.00) difference of serum serotonin levels was seen among three groups. It was raised in combined oral pills users as compared to injectable contraceptive users and control. Our results were in accordance to a randomized clinical trial of postpartum healthy women using injectable contraceptives (progestin only). These women showed higher depression scores which are suggestive of low serotonin levels.[21] Most of the women who are on contraceptive pills experience mood swings but they do not feel depressed and can continue life normally.[22] On the other hand, some women can experience depression, especially if they already have a previous history of the disease.[23] Another study also revealed the same results, i.e., women who were on progestin-only contraceptives had increased risks of antidepressant use.[24] However, some studies provide evidence to contradict this last statement.[25] In our study we found lower levels of serum serotonin in injectable users as compared to combined oral pill users that was in accordance to an observational study, it found that there were lower levels of positive mood among injectable contraceptive (specially DMPA) users as compared to barrier method users.[26] Whereas studies in another populations reported no such association which was contradicted to the present study.[27] Another study showed consistent finding that there is less variation in mood among women taking hormonal contraceptives, which corresponds to clinical research showing that women who experience severe mood problems during the menstrual cycle (e.g., premenstrual dysphoric disorder) demonstrate improvement on hormonal contraceptives due to a more stable mood across the cycle.[28] In recent years, many studies have suggested that depression is related to women who use oral contraceptives for long-term.[29]

CONCLUSION

This study was conducted to evaluate the effect of hormonal contraceptives including combined oral pills and injectable contraceptives on serum serotonin levels.

The levels of serotonin were compared among controls, COCs users and ICs users and it was observed that serum serotonin levels were increased in combined pill users as compared to injectable contraceptive users and controls. This study is very helpful to find out the safe and beneficial hormonal contraceptive.

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AUTHOR'S CONTRIBUTION

UF, MH: Study design, MH: Supervised. UF, SR, BH write-up and proof reading. JS and MAA: Statistical analysis.

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