

Investigations On The Biochemical Effect Associated With The Use Of Contraception In Women On Some Reproductive Hormones.

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Abstract

Contraception is the use of artificial techniques in preventing pregnancy as a consequence of sexual intercourse by many women around the world. This study was carried out to investigate the biochemical effects of contraception on some reproductive hormones in women using contraceptives. One hundred and eighty (180) women using different methods of contraception, were recruited for this study from Ekiti State University teaching hospital, Ado-Ekiti, Ekiti State, Nigeria, having obtained ethical clearance. The subjects were divided into six groups based on the contraceptive method used. Group 1 served as control (women using natural planning method), Group 2 (women using oral pills), Group 3 (women using intra uterine device, IUD), Group 4 (women using implant), Group 5(women using injection) and Group 6 (women using condoms). Parameters including Body mass index (BMI) and some major reproductive hormones were estimated in the plasma of all the groups, using Enzyme linked immunosorbent Assay (ELISA). The results showed significant increase in the BMI of women using pills, IUD, Implant and Injection ($p < 0.05$). Significant increases were observed in the concentration of Progesterone and Oestrogen in women on injection, IUD and Oral Pill users ($p < 0.05$). However, Significant decrease were observed in the levels of Prolactin, Follicle stimulated hormone and Testosterone in same women using injection, IUD and Oral Pills. Hence, it can be said that reproductive hormones are implicated with the use of contraception, especially in the methods outside the natural and the use of condoms.

Keywords: Contraception, Reproductive Hormones, Enzyme linked immunosorbent Assay, Body mass index.

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I. Introduction

Birth control, also known as fertility control, is a method or device used to prevent pregnancy. Birth control has been used since ancient times, but effective and safe methods of birth control only became available in the 20th century. At any given time, almost two-thirds of women aged 15–44 (62%; 38.5 million) are using a method of contraception; most of the remainder are pregnant or trying to become pregnant, or are not capable of becoming pregnant. Planning, making available and using birth control is called family planning. Some cultures limit or discourage access to birth control because they consider it to be morally, religiously, or politically undesirable (Hanson *et al.*, 2010).

There are several different hormonal methods of birth control. The differences among them involve

- the type of hormone,
- the amount of hormone, and
- the way the hormone enters a woman's body.

The hormones can be estrogen and/or progesterone, or preparations that contain a combination of these hormones. These hormones may be taken orally (taken by mouth), implanted into body tissue, injected under the skin, absorbed from a patch on the skin, or placed in the vagina. The mode of delivery determines whether the hormonal exposure is continuous or intermittent. (Webmed ,2020).

Hormonal contraception is available in a number of different forms, including oral pills, implants under the skin, injections, patches, IUDs and a vaginal ring. They are currently available only for women (Mackenzie and James, 2013).

There are two types of oral birth control pills, the combined oral contraceptive pills (which contain both estrogen and progestin) and the progestogen-only pills (sometimes called minipills). The minipill only

contains one hormone, progestin. Progestin thickens the cervical mucus, making it more difficult for sperm to pass through the cervix. It also makes the lining of the uterus less receptive to the implantation of a fertilized egg. The progesterone-only pill is sometimes recommended for women who have medical reasons for which they must avoid taking estrogen hormones. (These reasons can include liver disease, certain types of blood clots in the veins, breast cancer, and uterine cancer.) If either is taken during pregnancy, they do not increase the risk of miscarriage nor cause birth defects. Both types of birth control pills prevent fertilization mainly by inhibiting ovulation and thickening cervical mucus. They may also change the lining of the uterus and thus decrease implantation. Their effectiveness depends on the user's adherence to taking the pills (WHO, 2011).

Progestin-only pills may improve menstrual symptoms and can be used by breastfeeding women as they do not affect milk production. Irregular bleeding may occur with progestin-only methods, with some users reporting no periods. The progestins drospirenone and desogestrel minimize the androgenic side effects but increase the risks of blood clots and are thus not first line (Trussell and James, 2011).

Intrauterine devices

Intrauterine contraceptives (IUCs) are long-acting reversible contraceptive (LARC) methods that are used by over 150 million women worldwide. They are the most effective forms of birth control available. IUCs are small T-shaped devices that are inserted in the uterus by a health care professional in a clinic. There are two types of intrauterine contraception: the Copper intrauterine device (Cu-IUD) and the levonorgestrel-releasing intrauterine system (LNG-IUS), which contains a progestin. They are one form of long-acting reversible contraception which are the most effective types of reversible birth control (Darneyet *al.*, 2010). IUDs may reduce menstrual bleeding or stop menstruation altogether (Gabbet *al.*, 2012).

Implants

The contraceptive implant is hormone-based and highly effective, approved in more than 60 countries and used by millions of women around the world. The typical implant is a small flexible tube measuring about 40mm in length and is inserted under the skin (typically in the upper arm) by a health care professional. After it is inserted it prevents pregnancy by releasing hormones that prevent ovaries from releasing eggs and thicken cervical mucous. The two most common versions are the single-rod etonogestrel implant and the two-rod levonorgestrel implant (French *et al.*, 2016).

Injectable contraceptive

Injectable contraceptives are a form of hormonal birth control for women. They consist of monthly injections of combined formulations containing an estrogen and a progestin to prevent pregnancy. Depot medroxyprogesterone acetate (DMPA) is a different injectable contraceptive, containing just a progestin, given every three months. It is a progestogen-only injectable contraceptive. Hormonal contraception works primarily by preventing ovulation, but it may also thicken the cervical mucus inhibiting sperm penetration (Tamara, 2013). Hormonal contraceptives also have effects on the endometrium (Petrie *et al.*, 2007), that theoretically could affect implantation (Buggeet *al.*, 2007)

Oral contraceptive

The oral contraceptive pill, also known as birth control pill, is suitable for most healthy women, regardless of age, and can be used long-term. It is one of the world's most prescribed medications. There are two kinds of oral contraceptives, the combined oral contraceptive (COC), which contains both estrogen and progestin, and the progestin-only contraceptive (POP). The Pill is available at pharmacies but requires a prescription. (Daweet *al.*, 2004)

II. Materials and Method

Subjects used for this study are made of 180 women using different contraceptive methods. The subjects are made up of 6 different groups. And 30 women in each group.

SAMPLE COLLECTION

All subjects in each group while resting had 10ml of their venous fasting blood samples drawn by venipuncture from each of the women into a lithium heparinized anticoagulant bottles. The blood was collected from the site of puncture and was immediately centrifuged at 4000 revolutions per minute (ppm) for 15 minutes, and separated to obtain plasma. The samples were then analyzed to obtain the concentrations of all the desired parameters in this study.

DETERMINATION OF HORMONES

FOLLICLE STIMULATING HORMONE (FSH)

Plasma FSH was determined by using Randox FSH ELISA test kit described by Perlmann and Engvall (1971).

DETERMINATION OF PROLACTIN

Plasma FSH was determined by using Randox PROLACTIN ELISA test kit described by Perlmann and Engvall (1971).

DETERMINATION OF PROSTAGLANDIN ASSAY

Measurement of the various levels of prostaglandins in the plasma of the subjects were determined by the method of ELISA (Van Weemen and Schuurs, 1972).

DETERMINATION OF LUTEINIZING HORMONE (LH)

Plasma LH was determined by using Randox LH ELISA test kit described by Perlmann and Engvall (1971).

STATISTICAL ANALYSIS

The data was analyzed using one analysis of variance (ANOVA) to compare the data obtained from the experiment to those of the control subjects.

III. Results and Discussion

Table 1 below shows the anthropometric measurement of the women using various contraceptive methods. It was observed that there was significant ($P < 0.05$) increase in the body mass index of the women using of Oral, IUD, Implant, Injection and condoms compared to the group of women using natural contraceptive method. And, there was no significant difference ($P < 0.05$) between the group using condoms in comparison to the groups using natural contraceptives.

Also, It was observed that there was significant increase ($P < 0.05$) in the duration of usage of women using natural, oral, IUD, Implant and condom compared to the women using injection. Also, there was significant difference ($P < 0.05$) between the group using condoms in comparison to the groups using natural contraceptives

Table 1: ANTHROPOMETRIC MEASUREMENT OF FEMALES USING CONTRACEPTIVE.

GROUPS	BODY MASS INDEX(Kg/m ²)	AGE RANGE	DURATION OF USAGE
NATURAL	24.61± 0.30 ^a	38 – 48yrs	4.02±0.01 ^a
ORAL	27.11 ± 0.31 ^b	38 – 48yrs	4.71 ± 0.02 ^a
INTRA-UTERINE DEVICE	31.01 ± 0.29 ^b	38 – 48yrs	5.99 ± 0.01 ^b
IMPLANT	30.05 ± 0.3 ^b	38 – 48yrs	4.10 ± 0.01 ^a
INJECTION	28.90 ± 0.32 ^a	38 – 48yrs	3.19± 0.02 ^{ab}
CONDOMS	24.87 ± 0.28 ^a	38 – 48yrs	6.89± 0.02 ^b

Values are expressed as mean±SD. Values that are of the same superscript within the same column are not significantly different ($P < 0.05$) while values with different superscripts are significantly different ($P < 0.05$).

Table 2 below also shows the effect of contraceptives on follicle stimulating hormone and Prolactin in women. Significant ($P < 0.05$) increase was observed in FSH of women using IUD, Implant, Injection when compared with the control. While a non- significant increase ($P < 0.05$) was observed in the level of FSH of women using oral contraceptive and condom when compared with the control. Significant increase ($P < 0.05$).was observed in the level of Prolactin of women using Oral, IUD, Implant and Injection when compared with the control. While a non-significant decrease was observed in the level of Prolactin of women using condom compared to the control.

Table 2: THE EFFECT OF CONTRACEPTIVES ON FOLLICLE STIMULATING HORMONE AND PROLACTIN IN WOMEN

TEST PARAMETERS	CONTROL	ORAL	IUD	IMPLANT	INJECTION	CONDOM
FSH (ng/ml)	11.79±2.0 ^a	12.14±3.0 ^a	15.20±2.4 ^b	17.0±3.00 ^b	15.00±2.01 ^b	12.00±3.0 ^a
Prolactin (pg/ml)	65.24±1.40 ^a	68.14±1.3 ^b	72.00±1.7 ^b	77.04±1.00 ^b	69.71±1.50 ^b	64.00±1.40 ^a

Values are expressed as mean±SD. Values that are of the same superscript within the same column are not significantly different ($P < 0.05$) while values with different superscripts are significantly different ($P < 0.05$).

Table 3 shows the determination of the concentration of prostaglandin and luteinizing hormone in women using various methods of contraceptives. It was observed that there was significant ($P < 0.05$) increase in

the concentration of prostaglandin in the women using of Oral, IUD, Implant, Injection and condoms compared to the group of women using natural contraceptive method. Also, It was observed that there was significant increase ($P<0.05$) in the concentration of luteinizing hormone in women using, oral, IUD, injection and Implant compared to the women using natural contraceptives. Also, there was no significant difference ($P<0.05$) between the group using condoms in comparison to the groups using natural contraceptives.

Table 3: Determination of the concentration of prostaglandin and luteinizing hormone in women using various methods of contraceptives.

TEST PARAMETERS	LUTEINIZING HORMONE (ng/ml)	PROSTAGLANDIN (pg/ml)
Natural (Control)	2.10 ± 1.40^a	3.80 ± 1.0^a
Oral	2.61 ± 1.20^a	7.10 ± 1.30^b
IUD	4.72 ± 1.01^b	6.12 ± 1.00^b
Implant	6.14 ± 1.20^b	7.24 ± 1.20^b
Injection	4.94 ± 1.3^b	6.94 ± 1.00^b
Condom	2.4 ± 1.7^a	4.0 ± 1.11^a

Values are expressed as mean \pm SD. Values that are of the same superscript within the same column are not significantly different ($P<0.05$) while values with different superscripts are significantly different ($P<0.05$).

IV. Discussion

Table 1 shows the anthropometric measurement of the women using various contraceptive methods. It was observed that there was significant ($P<0.05$) increase in the body mass index of the women using of Oral (27.11 ± 0.31^b), IUD (31.01 ± 0.29^b), Implant (30.05 ± 0.3^b) and Injection (28.90 ± 0.32^a) compared to the group of women using natural contraceptive method (24.61 ± 0.30^a). And, there was no significant difference ($P<0.05$) between the group using condoms (24.87 ± 0.28^a) in comparison to the groups using natural contraceptives. This work is in agreement with previous work done by(Lopez *et al.*, 2015) who found out that there is weight gain and possible increase in body fat and decrease in lean body mass compared to the users of non- hormonal contraceptives

Also, It was observed that there was significant increase ($P<0.05$) in the duration of usage of women using natural (4.02 ± 0.01^a), oral (4.71 ± 0.02^a), IUD (5.99 ± 0.01^b), Implant (4.10 ± 0.01^a) and condom (6.89 ± 0.02^b) compared to the women using injection (3.19 ± 0.02^{ab}). Also, there was significant difference ($P<0.05$) between the group using condoms (6.89 ± 0.02^b) in comparison to the groups using natural contraceptives (4.02 ± 0.01^a).

In table 2, the estimated values of follicle stimulating hormone for Oral (12.14 ± 3.0), Intra-Uterine device (15.20 ± 2.4), Injective contraceptive (17.0 ± 3.00) and implant (15.00 ± 2.01) is elevated compared to the value of control (11.79 ± 2.0) in the group. And literally, the value for the group using condom (12.00 ± 3.0) is higher than that of the control compared to the other groups. Therefore, the drastic increment in the estimated values of follicle stimulating hormone of the groups using synthetic contraceptives (Oral, IUD, Implant, Injection) is due to primary hypogonadism (Lasley *et al.*, 1975).

In table 2, the estimated values of Prolactin for Oral (68.14 ± 1.3), Intra-Uterine device (72.00 ± 1.7), Injective contraceptive (69.71 ± 1.50) and implant (77.04 ± 1.00) is elevated compared to the value of control (65.24 ± 1.40) in the group. Elevated Levels of Prolactin is due to Hyperprolactinaemia, is associated with hypoenestrogenism, unexpected lactation and loss of libido in women and erectile dysfunction and loss of libido in men (Melmed and Kleinberg, 2008).

Analysis of etymological and biochemical profile of organs are widely used as indicators to access the functional status of the animal health and the internal environment of the organism (Rehman *et al.*, 2006). Local hormone such as prostaglandin and bio-molecules such as Luteinizing hormone FSH, Prolactin have served as good bio-indicators. Literally, the value for the group using condom (64.00 ± 1.40) is lower than that of the control compared to the other groups. Studies on women taking low-dose-estrogen compounds (less than 50 micrograms of estradiol) did not show a significant elevation response as compared to pretreatment levels (De Leo *et al.*, 1991) or control patients with intrauterine devices (Hwang *et al.*, 1986). In the studies documenting hyperprolactinemia, the incidence among women on oral contraceptives is variously reported, from 12% (Luciano *et al.*, 1985) to 30% (Reyniak *et al.*, 1980)

In table 3, the calculated values of Prostaglandin for oral (7.10 ± 1.30^b), IUD (6.12 ± 1.00^b), Implant (7.24 ± 1.20^b) and Injection (6.94 ± 1.00^b) is elevated compared to the value of Natural (3.80 ± 1.0^a) in the group. And literally, the value for the group using condom (4.0 ± 1.11) is a little bit higher than that of the control compared to the other groups. Elevated level of prostaglandin can serve as contraceptives. Significant difference ($P<0.05$) was observed in prostaglandin's level in the group of women that were using implants (7.10 ± 1.30^b) compared to the groups using other contraceptive methods. Also, it was observed that there was significant

increase ($P < 0.05$) between the group using (7.10 ± 1.30^b), IUD (6.12 ± 1.00^b), Implant (7.24 ± 1.20^b) and Injection (6.94 ± 1.00^b) in comparison to the groups using natural contraceptives (4.02 ± 0.01^a). Literally, high concentration of prostaglandin in women can serve as contraceptive. i.e. high level of prostaglandin can prevent implantation of fertilized egg in the uterus. The hormonal contraceptive method can be deduced to be more effective in birth control.

In table 3, the estimated values of Luteinizing hormone for Natural (2.10 ± 1.40^a) is low in comparison to the value of Oral (2.61 ± 1.20^a), IUD (4.72 ± 1.01^b), Implants (6.14 ± 1.20^b) and Injection (4.94 ± 1.3^b) in the group. Literally, the value for the group using condoms (2.4 ± 1.7^a) is elevated than that of the women using natural contraceptives (2.61 ± 1.20^a) compared to the other groups. And explicitly, Significant difference ($P < 0.05$) was not observed in luteinizing hormone level in the group of women that were using condoms (2.4 ± 1.7^a) compared to the groups using natural contraceptive methods (2.61 ± 1.20^a). Therefore, the observed significant difference ($P < 0.05$) in the estimated values of Luteinizing hormone of the groups using synthetic contraceptives (Oral, IUD, Implant, Injection) may be due to primary hypogonadism (Lasley *et al.*, 1975).

The majority of women perceive that using birth control allows them to better care for themselves and their families, either directly or indirectly through facilitating their education and career.

These individual-level evaluations of the benefits of personal contraceptive use are generally consistent with the findings of broader economic research examining the role that contraceptive use has played in improvements in social and economic conditions for women, particularly through greater education and more workforce participation (Ananat *et al.*, 2012).

V. Conclusion

This research suggests that only natural methods of contraception and the use of condoms seem not to have effect on the reproductive hormones. Hence adequate caution and care must be taken when using other methods of contraception.

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