

An Assessment of Hormonal Contraceptives on Plasma Glucose and Lipid Profile of Women Attending Family Planning Clinic at Keffi, Nasarawa State, Nigeria

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Abstract: This study seeks to determine the influence of the type, duration of contraceptive used and the age of users on Biochemical parameters such as glucose and lipid amongst women in Keffi, Nasarawastate of Nigeria. The study group consisted of 400 women (age range 18-41 years) who were equally distributed into four groups based on contraceptive used (Noristerate =100, Depo-provera=100, Oral pills= 100 and Norplant =100) for a period of two (2) years, while 50 are control groups. Glucose, triglyceride, total cholesterol, LDL-Cholesterol and HDL-Cholesterol were determined using standard colorimetric methods. There were significant increase in the mean value of total cholesterol (4.82 ± 0.46), triglyceride (1.67 ± 0.11), LDL-Cholesterol (2.37 ± 0.23) and glucose (5.21 ± 0.22) in test group when compared with the control groups with total cholesterol (3.34 ± 0.12), triglyceride (0.89 ± 0.04), LDL-cholesterol (1.89 ± 0.05) and glucose (3.94 ± 0.20) ($p<0.05$). Results also showed monthly significant increase ($p>0.05$) in the levels of glucose, Total cholesterol, triglyceride and LDL-Cholesterol following administration of Noristerate, Depo-provera and Oral pill while the level of HDL- Cholesterol significantly decreased ($p<0.05$) within the duration of contraceptives used when compared with the control group. However, for women taking Norplant, there was monthly significant decrease ($p<0.05$) in the levels of glucose, Total cholesterol, triglyceride and LDL-Cholesterol while the HDL-Cholesterol levels were significantly increased suggesting that Norplant could be the most preferred hormonal contraceptive to others under this study. The levels of Glucose, Total cholesterol, Triglyceride and LDL-Cholesterol in this study, were significantly ($p>0.05$) increased as the age range of the users increases from 18-23 to 36-41 indicating that age has a direct influence on contraceptive used. Similarly, there was a significant increase in BMI by 8.6% between women using contraceptives and the non-users. It could be concluded that hormonal contraceptives alter lipid metabolism and induced dyslipidemia.

Keywords: Hormonal, Contraceptives, Plasma, Glucose, Lipid Profile, Family Planning

I. INTRODUCTION

Attempts to control fertility have always depended on social factors as much as on research and religious beliefs have played a large part in the provision or prohibition of contraception. Before the 20th century most references to contraception were linked to illicit sexual relations. It was not

until the early 20th century that birth control became available for married couple.

The earliest method of contraceptives was probably coitus interruptus. Barrier methods of contraception were later developed. The use of goat's bladder as a female sheath was described in Roman literature and ancient Egyptian texts describe the use of vaginal pessaries. In 1920s research confirmed the timing of ovulation and the role of the ovarian hormones, Oestrogen and progesterone, in reproduction. This led to the development of the calendar method of contraception based on the woman's monthly variation in body temperature and the development of the contraceptive pills. The First Large scale trial of the pill took place in 1956 by Dr. Gregory Goodwin Pircus was an American Biologist and Researcher who was the first inventor.

Contraceptive are means of family planning, they are classified into the modern and traditional methods. Traditional methods of contraceptives include withdrawal of penis from vaginal and breast-feeding methods while modern methods include use of condoms, hormonal contraceptive (oral pills and injections): intrauterine contraceptive device (IUCD), implants and contraceptive surgery such as tubal ligation and vasectomy. Hormonal contraceptive are agents or drugs used to prevent 0 pregnancy, however, their use is not without side effects.

Glucose is required by the body to create ATP. On a daily basis, the body changes food-containing carbohydrate to glucose and transport it into the blood. The insulin moves the glucose from the blood to the cells. The cells burn the glucose to produce energy. Its normal range 3.9 – 5.6mmol/L.

Lipids play an important role in virtually all aspect of biological life serving as hormone or hormone precursor, aiding in digestion, providing energy storage and metabolic fuels, acting as functional and structural components in bio membranes and forming insulations to allow nerves conduction or prevent heat loss (Carl and Edward, 2001). Serum lipid include cholesterol, high density lipoprotein cholesterol (HDL – C) low density lipoprotein cholesterol (LDL-C) and triglycerides. Uptake of chylomicron remnants

by liver, as the triacylglycerols of chylomicrons and VLDL are degraded, they lose the apo C II which is returned to HDL. The chylomicron remnants are taken up by receptors present on the hepatocytes of liver (Satyanarayana *al.*, 2015).

Conversion of VLDL to LDL, during the course of VLDL metabolism, intermediate density lipoprotein (IDL) is formed which lose apo-E and get converted to LDL. The apo E is returned to HDL. LDL contains high cholesterol (free and esterified) and less triacylglycerol. (Satyanarayana *al.*, 2015). Since the use of available hormonal contraceptive is by no means without side effects, it seems reasonable to assess some of the metabolic effects of the contraceptive in common use by women in Keffi, Nasarawa State.

In Nigeria, women lipid status is not known before a contraceptive is recommended according to Sperraff and Darney (1996) suggest that “because low dose oral contraceptives have negligible impact on the lipoprotein profile, hyperlipidemia is not an absolute contraindication, with the exception of very high level of triglyceride (which can be made worse by estrogen). Their text also repeated the recommendation of Knoop *et al* (1994) that dyslipidaemia patients who begin oral contraceptive should have their lipoprotein levels monitored monthly for a few visit to ensure no adverse effects (Speroff and Darney, 1996).

It is important to assess the levels of cholesterol, triglyceride, high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C) and glucose in blood of women attending family planning clinic in Keffi in order to advise gynecologist and physician on the best way to administer the contraceptive.

Statement of the Problem

Despite the level of awareness of the effect of Hormonal contraceptive on plasma glucose and lipid profile of women attending family planning clinic there are still an increase in glucose and lipid profile in Keffi Metropolis (Meliset *al.*, 2016).

Justification

Contraceptives generally increase the rate of non-communicable disease such as cardiovascular disease (CVD) (Clifford *al.*, 1997). They alter several metabolic pathways leading to unwanted increase in body weight also lead to irregular menses. This study therefore seeks to assess some of these negative effects in women on contraceptives in Keffi, Nasarawastate of Nigeria.

Aims of Research

- To determine which contraceptive(s) has the greatest effect on the plasma total cholesterol, triglyceride HDL – cholesterol, LDL – cholesterol and fasting blood glucose.

Specific Objectives

- To measure the level of plasma total cholesterol, triglyceride, HDL cholesterol, LDL cholesterol and fasting glucose in women using hormonal contraceptives and control groups.
- To compare the result of the analysis obtain in test group with those of the control groups.
- To compare our finding with those obtained in Nigeria and globally.
- To compare the anthropometrics indices with the analytical variables.

Null Hypothesis

Hormonal contraceptives have effect on plasma glucose and lipid profile of women on family planning.

II. LITERATURE REVIEW

The two major endogenous hormones in women are estrogen and progesterone. Each has a specific physiologic role in development, pregnancy, lactation, and other functions. Levels of both hormones alter at different stages of growth by prepubertal, reproductive age, and after menopause (Mani, 1998).

Mani, (1998) reported that the varying levels cause different changes in the organ system including the heart and blood vessels, some of which may increase or decrease the risks of disease. The author also pointed out that the hormones may be administered in medication (Exogenous). The most common source of exogenous hormones is in the oral contraceptive pills.

These contraceptives works through three mechanisms

- They block ovulation
- They make cervical mucus impenetrable to sperm cells, and
- By changing the lining of the uterus (Allen, 1999)

Ever since birth control pills were introduced in 1960, there have been reports suggesting an increased risk of heart attacks and stroke.

The earlier pills contained high doses around 150 micrograms – of estradiol in contrast, pills in 1988 contain only 35 micrograms. (Karam, 2001).

Also addition of progesterone derivatives further altered the effects of the pills (Mani, 1998).

Depo-Provera

Depo-Provera CI is a progestin hormone birth control method that is given by injection (a shot) to prevent pregnancy.

Depo-Provera CI contains medroxyprogesterone acetate, a derivative of progesterone, as its active ingredient. Medroxyprogesterone acetate is active by the parenteral and oral routes of administration. It is a white to off-white; odorless crystalline powder that is stable in air and that melts

between 200°C and 210°C. It is freely soluble in chloroform, soluble in acetone and dioxane, sparingly soluble in alcohol and methanol, slightly soluble in ether, and insoluble in water. The chemical name for medroxyprogesterone acetate is pregn-4-ene-3,20-dione, 17-(acetyloxy)-6-methyl-, (6 α -) (Meliset *al.*, 2016).

Depo-Provera CI for intramuscular (IM) injection is available in vials and prefilled syringes, each containing 1 mL of medroxyprogesterone acetate sterile aqueous suspension 150 mg/mL.

Each mL contains:

Medroxyprogesterone acetate 28.9 mg

Polyethylene glycol 2.41 mg

Polysorbate 8.68 mg

Sodium chloride 1.37 mg

MethylparabenPropylparaben 0.150 mg quantity sufficient

Water for injection 150 mg

When necessary, pH is adjusted with sodium hydroxide or hydrochloric acid, or both.

Mechanism of Action

Depo-Provera CI (medroxyprogesterone acetate [MPA]), when administered at the recommended dose to women every 3 months, inhibits the secretion of gonadotropins which, in turn, prevents follicular maturation and ovulation and results in endometrial thinning. These actions produce its contraceptive effect (Meliset *al.*, 2016).

Pharmacodynamics

No specific pharmacodynamic studies were conducted with Depo-Provera CI.

Pharmacokinetics:

Absorption

Following a single 150 mg IM dose of Depo-Provera CI in eight women between the ages of 28 and 36 years old, medroxyprogesterone acetate concentrations, measured by an extracted radioimmunoassay procedure, increase for approximately 3 weeks to reach peak plasma concentrations of 1 to 7 ng/mL (Meliset *al.*, 2016).

Distribution

Plasma protein binding of MPA averages 86%. MPA binding occurs primarily to serum albumin. No binding of MPA occurs with sex-hormone-binding globulin (SHBG).

Metabolism

MPA is extensively metabolized in the liver by P450 enzymes. Its metabolism primarily involves ring A and/or side-chain reduction, loss of the acetyl group, hydroxylation in the 2-, 6-, and 21-positions or a combination of these

positions, resulting in more than 10 metabolites (Meliset *al.*, 2016).

Excretion

The concentrations of medroxyprogesterone acetate decrease exponentially until they become undetectable (<100 pg/mL) between 120 to 200 days following injection. Using an unextracted radioimmunoassay procedure for the assay of medroxyprogesterone acetate in serum, the apparent half-life for medroxyprogesterone acetate following IM administration of Depo-Provera CI is approximately 50 days. Most medroxyprogesterone acetate metabolites are excreted in the urine as glucuronide conjugates with only minor amounts excreted as sulfates (Meliset *al.*, 2016).

Who Should Not Use Depo-Provera CI?

Do not use Depo-Provera CI if you

- Are pregnant or think you might be pregnant
- Have bleeding from the vagina that has not been explained
- Have breast cancer now or in the past, or think you have breast cancer
- Have had a stroke
- Ever had blood clots in your arms, legs or lungs
- Have problems with your liver or liver disease

Are allergic to medroxyprogesterone acetate or any of the other ingredients in Depo-Provera CI.

What should I tell my healthcare provider before taking Depo-Provera CI?

Before taking Depo-Provera CI, tell your healthcare provider if you have:

- Risk factors for weak bones (osteoporosis) such as bone disease, use alcohol or smoke regularly, anorexia nervosa, or a strong family history of osteoporosis
- Irregular or lighter than usual menstrual periods
- Breast cancer now or in the past, or think you have breast cancer
- A family history of breast cancer
- An abnormal mammogram (breast X-ray), fibrocystic breast disease, breast nodules or lumps, or bleeding from your nipples
- Kidney problems
- High blood pressure
- Had a stroke
- Had blood clots in your arms, legs or lungs
- Migraine headaches
- Asthma
- Epilepsy (convulsions or seizures)
- Diabetes
- Depression or a history of depression
- Any other medical conditions

The most common side effects of Depo-Provera Contraceptive Injection include:

- Irregular vaginal bleeding, such as lighter or heavier menstrual bleeding, or bleeding that does not stop
- Weight gain: You may experience weight gain while you are using Depo-Provera
- CI. About two-thirds of the women who used Depo-Provera CI in the clinical trials reported a weight gain of about 5 pounds during the first year of use. You may continue to gain weight after the first year. Women who used Depo-Provera CI for 2 years gained an average of 8 pounds over those 2 years.
- Abdominal pain
- Headache
- Weakness
- Tiredness
- Nervousness
- Dizziness

Norplant (Levonorgestrel-Releasing Implant)

Norplant is 99% – 99.95% effective at preventing pregnancy, and is one of the most reliable, though not the most available, forms of birth control. Norplant prevents pregnancy through multiple methods: by preventing ovulation, which means that no eggs are released for fertilization; by thickening the mucus of the cervix, which prevents sperm from entering; and by thinning the lining of the uterus, which makes implantation of an embryo less likely (FDA, 2000).

Contraindications

Norplant should not be used in women with liver disease, breast cancer, or blood clots. Women who believe they may already be pregnant or those with vaginal bleeding should first see a physician. However, since it does not contain estrogen like some birth control pills, older women, women who smoke, and women with high blood pressure are not restricted from using the system (FDA, 2000).

Side effects

Side effects may include irregular menstrual periods for the first approximately three months, including periods lasting longer than normal, bleeding or spotting between periods, heavy bleeding, or going with no period for the mentioned period of time. Common side effects include weight gain, nervousness, anxiety, nausea, vomiting, mastalgia, dizziness, dermatitis/rash, hirsutism, scalp-hair loss, headache, depression, and acne. Sometimes, pain, itching or infection at the site of the implant will occur. Ovarian cysts may also occur, but usually do not require treatment, although they can cause pain even if benign (FDA, 2000).

Insertion

Norplant is implanted under the skin in the upper arm of a woman, by creating a small incision and inserting the capsules in a fanlike shape. Insertion usually takes 15 minutes and the capsules can sometimes be seen under the skin, although

usually they look like small veins. They can also be felt under the skin. Once inserted, the contraceptive works within 24 hours and lasts up to five years (FDA, 2000).

Removal

Norplant can be removed by creating a second incision and withdrawing the capsules. It is normally removed when the five-year period is over, or if:

- Pregnancy is desired
- Different birth control is preferred
- Complications arise

Normally removal is not complicated; removal difficulties have been reported with a frequency of 6.2%, based on 849 removals. Removal difficulties include: multiple incisions, capsule fragments remaining, pain, multiple visits, deep placement, lengthy removal procedure, or other (FDA, 2000).

Mechanism of action

Norplant releases constant low doses of the hormone progesterone and estrogen over a period of several years. The Norplant exerts its contraceptive action by causing changes in the cervical mucus, by inhibiting ovulation and by promoting ovulatory dysfunction. Cervical mucus becomes viscous and scanty. Postcoital studies and sperm penetration tests in vitro have shown that few sperm penetrate the mucus and that this effect persists, even in cycles with high endogenous estradiol production. Ovulation is inhibited in over 85% of the cycles in the first year of use, when the release rate of Norplant is highest. The percentage of ovulation inhibition decreases to near 65% of the cycles in years 2 and 3, while luteal activity occurs in around 50% of the cycles in the last 2 years of use. However, in these apparently ovulatory cycles, a dissociation of the normal ovulatory process has been observed. The peak of follicle stimulating hormone present in non-users does not occur, and the luteinizing hormone peak is blunted and of short duration. It is known that the mid-cycle gonadotropin surge plays a major role in the maturation of the oocyte; it is therefore possible that, due to this inadequate gonadotropin surge, the oocyte may not be capable of fertilization in the event of follicular rupture. Luteal phase defect has also been reported. Ultrasound evaluation of follicular activity during Norplant use has shown that luteinization of unruptured follicles occurs in nearly 30% of the cycles with luteal activity. Persistent follicles are also a common observation among implant users. Since low-dose progestins do not completely inhibit the gonadotropin stimulus, follicular growth occurs. However, the positive feedback of estradiol on the mid-cycle gonadotropin surge is frequently blocked, thus preventing follicular rupture. This dominant follicle remains functional for about 21 days, but the anatomic structure remains echographically visible for around 1-2 months before spontaneously disappearing. Hypoestrogenism is not a concern in women with Norplant since mean estradiol levels in samples taken twice weekly for

4-5 weeks were not significantly different in women using implants from those acting as controls (FDA, 2000).

The Combined Oral Contraceptive Pill (Cocp)

The **combined oral contraceptive pill (COCP)**, often referred to as the **birth control pill** or colloquially as "**the pill**", is a birth control method that includes a combination of an estrogen (estradiol) and a progestogen (progestin). When taken by mouth every day, these pills reversibly inhibit female fertility. They were first approved for contraceptive use in the United States in 1960, and are a very popular form of birth control. They are currently used by more than 100 million women worldwide and by almost 12 million women in the United States. As of 2012, 16% of U.S. women aged 15–44 reported being on the birth control pill; making it the most widely used contraceptive method among women of that age range. Use varies widely by country, age, education, and marital status. One third of women aged 16–49 in the United Kingdom currently use either the combined pill or progestogen-only pill, compared with only 1% of women in Japan (Taylor *et al.*, 2006)

Medical use

Combined oral contraceptive pills should be taken at the same time each day. If one or more tablets are forgotten for more than 12 hours, contraceptive protection will be reduced. Most brands of combined pills are packaged in one of two different packet sizes, with days marked off for a 28-day cycle. For the 21-pill packet, a pill is consumed daily for three weeks, followed by a week of no pills. For the 28-pill packet, 21 pills are taken, followed by a week of placebo or sugar pills. A woman on the pill will have a withdrawal bleed sometime during the placebo week, and is still protected from pregnancy during this week. There are also two newer combination birth control pills (Yaz 28 and Loestrin 24 Fe) that have 24 days of active hormone pills, followed by 4 days of placebo (Stacey and Dawn 2009).

Effectiveness

The estimated probability of pregnancy during the first year of perfect use of the pill is 0.3%, and the estimated probability of pregnancy during the first year of typical use of the pill is 9%. The perfect use failure rate is based on a review of pregnancy rates in clinical trials, the typical use failure rate is based on a weighted average of estimates from the 1995 and 2002 U.S. National Surveys of Family Growth (NSFG), corrected for underreporting of abortions (Trussel and James 2011).

Several factors account for typical use effectiveness being lower than perfect use effectiveness:

- Mistakes on the part of those providing instructions on how to use the method
- Mistakes on the part of the user
- Conscious user non-compliance with instructions.

Hormonal Contraceptive and Lipid Profile

Allen, (1999). reported that the progestin components of contraceptives can alter the level of lipids such as cholesterol in the blood. Although estrogen works against this effect by increasing beneficial high density lipoprotein (HDL) and lowering harmful low density lipoprotein (LDL).

Allen (1999) also reported that the progestin component opposed the estrogen and does the opposite. Because high levels of LDL and depressed levels of HDL can cause fatty plaque to build up in the arteries, progestins have been implicated as a risk factor for coronary heart disease. On the other hand, oral estrogen increase triglyceride levels, which is an undesirable effect (Carrie, 2001).

In however in women with LDL – cholesterol greater than 160mg/dl multiple risk factors for coronary artery disease including smoking, diabetes, obesity, hypertension, family history of premature coronary artery disease, HDL level less than 36mg/dl or triglyceride level greater than 120mg/dl use of alternative contraceptive should be considered (Knoop, 1994).

The world health organization medical eligibility criteria suggest that women with known hyperlipidemia may initiate any of the progestin only contraceptives (progestin –only pill, depo – provera, implants), or combined oral contraceptives.

Each of these methods receives a “2” means that a woman can use the method and that the advantage of that method generally outweigh theoretical or proven risks (WHO, 2000).

The disruption of insulin secretion results in enhanced metabolism of lipids from the adipose tissue to the plasma. It has been shown that insulin resistance in contraceptives users leads to a variety of derangements in metabolic and regulatory process, which in turn leads to accumulation of lipids such as cholesterol and triglyceride. Accumulation of triglycerides is one of the risk factors in coronary heart disease. The abnormal high concentration of serum lipids in the contraceptives users are due mainly to increase in mobilization of free fatty acid from the peripheral fat depots (Bopanna *et al.*, 1997).

The increase in the production of VLDL and, consequently, triglycerides, contributes to increase the clearance of the VLDL particles, since these are rapidly converted into LDL (Campos and Walse 1997).

Hormonal Contraceptive and Plasma Glucose

The use of oral contraceptive pills may be associated with the development of a reversible insulin resistance and subsequent impairment of glucose tolerance. This altered glucose metabolism is believed to be mainly due to the effects of progesterone (Allen, 1999).

Most expert, believe that increase blood sugar levels due to oral contraceptives are usually very slight at best and they have no clinical significance.

The current use of traditional methods of family planning is 30 percent while 32 percent are currently using modern contraceptives.

They also found out that the choice of a particular method depends on the age, education, religion, ethnicity, marital status, and family planning approval. Education and religion are determinants of modern methods use.

Method of hormonal contraceptive

In the last 50 years, the number of contraception methods has dramatically increased. You can differentiate between different types of contraception based on how they work: there are barrier methods (e.g. condoms or a cervical cap), hormonal methods (example the pill), intrauterine devices (IUD) and sterilization (Allen, 1999).

Most types of contraceptives work by:

- Preventing an egg from being released every month (hormones)
- Preventing sperms from reaching the egg (barrier and some IUD methods)
- Blocking the reproductive function – in men or women (sterilization)
- Preventing a fertilized egg from implanting in the uterus (hormones).

The pill

The contraceptive pill was invented in 1960. Fifty years on, many new inventions have been added to the list of available contraception methods, but the pill remains the most popular form of female contraception. The contraceptive pill will prevent individual from getting pregnant in 95% of cases and it comes close to providing 99% protection if you take one pill every day as prescribed (Carrie, 2001).

The pill can come in two forms: the combined contraceptive pill (containing the hormones estrogen and progestin) or the mini-pill (only progestin). In the case of the mini-pill, it is important that women should take their pills every day at the same time you should not be late by more than three hours.

The female condom

Just like the male condom, the female condom is one of the few types of contraception that you can buy over-the-counter at pharmaceutical and grocery stores without a prescription.

It was first introduced twenty years ago and offers 95% effective protection for pregnancy, as well as some protection against STIs. Female condoms are generally more expensive than the male ones but they are less likely to burst. They can be inserted up to eight hours before sex (Carrie, 2001).

The diaphragm

The diaphragm is placed inside the vagina so that it prevents the sperm from getting into the uterus. Despite being a barrier method, it doesn't protect against STIs (Clifford, 1997).

The diaphragm must be coated with spermicide each time before sex it is inserted at least six hours before sex and it needs to be removed after 24 hours for cleaning. Depending on the material and type of the diaphragm, it can be reused many times.

The cervical cap Femcap

The cervical cap (sold as Femcap) is a thimble-shaped latex cup, basically like a diaphragm but smaller. It also needs to be used with a spermicide. The cervical cap must remain in the vagina at least 6 hours after sex, but it also has to be taken out within 48 hours after sex.

Because some women get cystitis (bladder infection) from using a diaphragm, the cervical cap is a useful replacement because it has less contact with the vagina (it only covers the cervix).

The problem with types of contraceptives such as the Femcap or the diaphragm is that their effectiveness - 92 to 95% protection in ideal use - is lower than other types (98-99%) and that they offer only partial protection against STIs (example no HIV protection) (Clifford, 1997)

The intrauterine device (IUD)

There are two types of IUDs: hormonal and copper-based devices. Hormonal and copper IUDs are part of the few long-term solutions, meaning that can keep them inside the vagina for up to five or ten years respectively.

The effectiveness rate for IUDs is above 99%, however they provide no protection against STIs. Note that IUDs can be a form of emergency contraception if the device is inserted within 5 days after unprotected sex. You will nonetheless need to visit a doctor to have it properly inserted and follow the prescription (e.g. a few follow-ups and check-ups for possible infection in the first weeks (Clifford, 1997).

The contraceptive Implant

The implant is another option among the types of contraceptives that offer long term protection. It lasts for about three years on average. Just like IUDs, the implant does not protect against STIs.

Contraceptive Implant

The contraceptive implant contains progestin (progesterone), the same hormone as the contraceptive pill. The hormone is released into your body at a steady, slow pace for three years, producing the same effects as the pill.

The implant is inserted in the arm by a healthcare specialist and must be removed after three years. Since the risk of human mistake is ruled out, the implant has a much higher effectiveness rate than the pill – around 99.99% (Clifford, 1997).

The contraceptive sponge

The sponge is small, round-shaped foam (polyurethane) placed deep inside the vagina. It contains spermicide so that sperm does not get past the foam. You should leave the sponge inside the vagina for at least six hours after sex, but remove it within 24 hours following sexual intercourse (to lessen the risk of toxic shock).

The sponge does not protect past those 24 hours and does not provide any STI protection. It is sometimes used as a backup for other contraception methods (e.g. when you forgot to take the pill) and you can buy it without a prescription from the pharmacy.

Spermicide

Spermicide is a recurrent "ingredient" in contraception because it proves very effective when used in combination with other methods (e.g. diaphragm, sponge). In itself spermicide doesn't always offer the best protection against pregnancy, although this is also due to inconsistent use of the product.

You don't need a prescription to buy spermicide and it has very few associated side-effects, but keeps in mind that it does not protect against STIs (Carrie, 2001).

Natural family planning

Natural family planning relies on knowing the menstrual cycle (periods) so that couples avoid having sex when the woman is fertile.

Three techniques (basal body temperature, cervical mucus and rhythm/calendar method) can be used for this, with higher protection rates when all three methods are used in combination. The effectiveness of this type of contraception varies between 75% to 99% (but 85% on average) with the higher uncertainty due to the fact that most women do not have a perfectly regular menstrual cycle (Clifford, 1997).

Chemistry of Carbohydrates

Carbohydrates are aldehydes or ketone derivatives of polyhydric alcohols. They are sugars containing three, four, five and six carbon atoms known as trioses, tetroses, pentoses and hexoses respectively (Sacks, 1987).

Carbohydrate is a very important source of energy for the body; it is the major component of the diet in many area of the world (Kaplan, 1999). It is ingested mainly in the form of polysaccharides starch and disaccharides. Monosaccharides are minor components of the diet, as di and polysaccharides are majority the dietary form (Nduka, 1999).

There are three main groups of carbohydrate namely: monosaccharide, example are hexoses ($C_6H_{12}O_6$) that is fructose and Galactose, disaccharide ($C_{12}H_{22}O_{11}$). These cannot be absorbed directly but must be hydrolyzed to monosaccharide by their appropriate enzyme. Examples are sucrose, lactose and maltose. The third group is the

polysaccharide ($C_6H_{10}O_5$). Considerable amount of digestion is required before they can be absorbed. The most important polysaccharide is starch, glycogen and cellulose.

Carbohydrate digestion

Carbohydrate in their undigested or partly digested state cannot pass through the mucosa of the gut into the body, but its form of glucose can permeate through the minute projections in the wall of the small intestine called villi. The villi create an enormous surface area for absorption which is said to be about five times that of the skin surface of the body. Glucose is absorbed into the blood capillaries (Baker, 1985).

Carbohydrate metabolism

The carbohydrate in the food appears in the blood after digestion and absorption as glucose ($C_6H_{12}O_6$). The normal blood glucose level (using glucose oxides method) is between 60 – 100mg per 100ml of blood (3.9 – 5.6mmol/L). With a blood volume of 5 litres, there will be 5g of glucose in the blood. Glucose diffuses readily into the tissue fluid and into capillary with a uniform concentration throughout the whole body and water is assumed to be 45 litres, and then there will be 45g of glucose in the intracellular fluid (ICF).

Glycogen is the storage form of glucose-usually in the liver and muscles. Glycogen is a high molecular weight component and is insoluble in water. The conversion of glucose into glycogen is facilitated by insulin a hormone synthesized in the islet cells of the pancreas, and is inhibited by pituitary and adrenocortical hormones (Green, 2005).

Glucose is the principal carbohydrate in the plasma; it is derived from the hydrolysis of dietary starch, from conversion of other dietary hexoses in the liver and from glycogen it is referred to as glycogenesis. When blood glucose level depletes glycogen is converted to glucose by a different set of enzymes in a process known as glycogenolysis. The liver is the main storage organ for excess carbohydrate, which stores glycogen, other skeletal and heart muscles can store limited amounts of muscles glycogen. When the capacity to storage is saturated, glucose is converted to fat (Davidson, 1989).

The energy stored in the glucose molecule is being utilized by the organism through several catabolic pathways, which generated ATP, these pathways consist of anaerobic phase, and in glycolysis the glucose – 6 – phosphate is converted through various steps to a triosephosphate and then to pyruvate, which can either be converted back to glucose to glucose – 6 – phosphate in a process known as gluconeogenesis and this can be carried out only in the liver but not necessary by the same enzymatic steps (Kaplan, 1999).

The brain depends largely upon carbohydrates as a source of energy and quickly ceases to function properly when the blood glucose level falls much below normal (Kaplan, 1999).

Glucose is the major source of the energy for human body; it is derived primarily from dietary carbohydrates (grains, starch and legumes) and may be synthesized from proteins, glycerol

moieties and triglycerides. The level of blood glucose is maintained by the action of some hormones e.g. insulin, glycogen (Whitby *et al.*, 1991).

Hypoglycemia is defined as a plasma glucose concentration of less than 2.5mmol/L (45mg/dl) in a specimen collected into a tube containing an inhibitor of glycolysis (Green, 2005).

A rapid fall of plasma glucose usually triggers the release of epinephrine, which accounts for the signs and symptoms like weakness, hunger and epigastric discomfort (Whitby *et al.*, 1991).

Muscles glycogen provides the glucose for muscular activity. Excess glucose is oxidized to fatty acids and stored as fat in the tissues.

Glucose Metabolism

Glucose metabolism can take several pathways such as in adipose tissue, including oxidation to CO₂ via the citric acid, oxidation in the pentose phosphate pathway, conversion to a long chain fatty acids and formations of acyl glycerol via glycerol 3 – phosphate.

Blood glucose regulation

In the fasting state; however, the blood glucose level is maintained by drawing upon glycogen stores of the liver and slight amounts may be contributed to the kidneys. Both organs contain specific enzymes glucose – 6 – phosphate dehydrogenase, necessary for the conversion of glucose – 6 – phosphate to glucose. For obvious reasons, skeletal muscles, which lack such enzyme, cannot directly contribute glucose to the even though it stores glycogen. As blood glucose level increase, usually by absorption of carbohydrate from the intestine, (the process of glycogenesis) the excess blood glucose is converted into the liver and muscle glycogen in normal situation (Tiezet *al* 2001).

A number of hormones are essential in the regulation of blood glucose concentration insulin produced by β-cell of the islet of langerhans in the pancreas promotes glycogenesis and lipogenesis (formation of fats from carbohydrates, with resultant decrease in blood glucose level. When insulin is deficient, hyperglycemia sets in and the body shows less ability to metabolize carbohydrates. At the other extreme, an islet cells tumor can produce excess insulin resulting in a very low level of blood glucose (hypoglycemia).

Other hormones responsible for the regulation of blood glucose are catecholamines (epinephrine and norepinephrine), thyroxin (somatotrophin) (Cryer and Gerich, 1986).

Carbohydrate metabolism disorders

The common disease related to carbohydrate metabolism disorder is diabetes mellitus, which is characterized by insufficient blood levels of active insulin. Deficiency of insulin results in inability of glucose to enter the muscles and the liver cells thereby given rise to hyperglycemia, impaired metabolism of fats, protein and secondary changes in fat

metabolism leading eventually to ketosis, diabetic and perhaps coma (Tiezet *al.*,2001).

When the plasma glucose concentration falls below the lower limits of normal range greater than 2 standard deviations (below 55mg/L), a condition known as hypoglycemia occurs. Since the brain is dependent upon an adequate supply of glucose for its energy, the clinical symptoms of hypoglycemia reassemble those of cerebral anoxia, which may include one or more of the following faintness, weakness, dizziness, tremors, anxiety, hunger, palpitation of the heart of “cold sweat”. There may even be mental confusion and motor-incoordination. The lower the plasma glucose level, the deeper is the coma for both adults and infants (Kaplan, 1999).

The various disorders in carbohydrate metabolism may be grouped into several categories which are dependent primarily upon laboratory findings; these are: high levels of glucose which is indicative of diabetes mellitus, which occur when the effectiveness of insulin is inadequate.

III. MATERIALS AND METHODS

Keffi is a Local Government Area in Nasarawa State, Nigeria. Its headquarters are in the town of Keffi. It has an area of 138 km² and a population of 92,664 at the 2006 census. The postal code of the area is 961All participants/subjects must fall within the ages of 18-41 years and be free from hyperglycemia, and hypercholesterolemia from Keffi.

Four hundred (400) apparently healthy women of aged between 18-41 years, attending family planning clinics in three different hospitals namely; General hospital Keffi, Federal medical hospital Keffi and Danbal Hospital Keffi.

Fifty (50) apparently healthy women were recruited as control. These women were nonsmoking volunteers, who are not aware of their blood lipid status and fasting glucose level. All subjects gave an informed consent to participate after a pretested, interviewer-administered questionnaire was served on them

Formula For Sample

$$X = \frac{Z_{\frac{\alpha}{2}}^2 * p * (1-P)}{2}$$

MOE² and $Z_{\frac{\alpha}{2}}$

Where

$Z_{\frac{\alpha}{2}}$ is the critical value of the Normal distribution at $\frac{\alpha}{2}$

MOE is the margin of error

P is the sample proportion

N is populations Size

Sample Collection

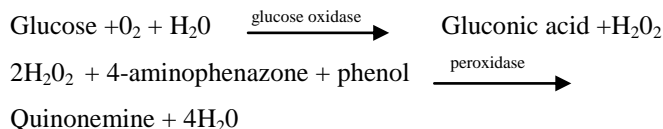
Five (5) miles of fasting blood was subsequently collected from each of the test subjects and controls via the antecubital Fossa by vene puncture after swabbing the site with 70%

methanol. The blood was transferred into lithium heparin. Plasma was extracted after centrifuging at 3,000 revolutions for 5min.

Determination of Plasma Glucose (Trinder, 1969) as Modified by Randox

Principle:

Glucose is determined after enzymatic oxidation in the presence of glucose oxidase. The hydrogen peroxide formed reacts under catalysis of peroxidase with phenol and 4-aminophenazone to form a red-violet quinoneimine dye as indicator. And read at 546nm



Procedure:

Three test tubes labeled T, S and B were set for test, standard and blank respectively to each of the three tubes, 1000ul of phenol reagent was added. To the test tube labeled ‘T’ 10ul of serum was added, to the test tube labeled ‘S’ 10ul of glucose standard was added. To the blank Test tube ‘B’ 10ul of distilled water was added. The test tubes were mixed and incubated for 10 minutes at 37°C. The absorbance of test and standard were then read against the blank spectrophotometrically within 60 minutes at 546nm.

Calculation:

$$\text{Glucose Concentration (mmol/L)} \times \frac{A \text{ sample}}{A \text{ standard}} \times 5.55$$

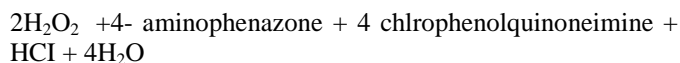
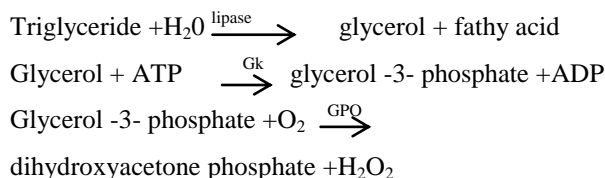
Where;

A sample = absorbance of test (sample), A standard = absorbance of standard

Determination of Plasma Triglyceride (Sullivan, 1985) as Modified by Randox

Principle:

Triglyceride is hydrolyzed by lipase to yield glycerol and free fatty acid. The glycerol is phosphate by glycerol kinase to produce glycerol -3-phosphate which is further oxidized to hydro acetone phosphate and hydrogen peroxide by the enzyme glycerol -3- phosphate oxidase. Oxygen from the peroxide is transferred to an acceptor (4-amino phenazone) in the presence of 4-chlorophenol under the catalytic influence of peroxide to form a coloured product. (Quinonimine) which can be measured calorimetrically. The intensity of which is proportional to the concentration of triglyceride in the sample.



Procedure:

The test tubes labelled “test” ‘standard’ and blank. 0.01ml of serum, 0.01ml of standard and 0.01ml of distilled water were added separately into the test tubes as test, standard and blank respectively. 1ml of the reagent was dispensed into each of the test tubes.

The content of the test tubes were mixed, incubated at 37°C for 5 minutes. Absorbance of the sample and standard was measured against the reagent blank at 500nm within 60 minutes.

Calculation:

$$\begin{aligned} \text{concentration: of triglyceride in sample} \\ = \frac{A \text{ sample}}{A \text{ standard}} \times 2.29 \text{mmol/l} \end{aligned}$$

Determination of HDL- Cholesterol (Demacker, 1997) as Modified by Randox

Principle:

Using precipitant method, low density lipoprotein (LDL and VLDL) and chylomicron fractions are precipitated quantitatively by the addition of phosphotungstic acid in the presence of magnesium ions. After centrifugation, the cholesterol concentration in the HDL fraction, which remains in the supernatant, is determined.

Procedure:

Serum (200ul) was pipetted into a centrifuge tube and 500ul of phosphotungstic acid (precipitant) was added and mixed thoroughly and allowed to stand for 10 minutes at room temperature, then it was centrifuged for 10 minutes at 400 rpm or 2 minutes at 12,000 rpm separated clear supernatant (sample) and 100 ul was pipetted into a test tube labeled: ‘T’, distilled water; 100 ul into the test tube ‘B’ for 1000 ul of HDL cholesterol reagent was added into all the test tube mixed, incubated for 5 minutes at 37°C then measure spectrophotometrically at 546nm the absorbance of sample and standard against blank.

Reagent was Constituted by the Manufacturer As Follows

Materials required

- Level 1 LE 2661 or LE 2668
- Level 2 LE 2662 or LE 2669
- Level 3 LE 2663 or LE 2670

Randox Aqueous cholesterol standard cat no ST 1590

Calculation:

$$\begin{aligned} \text{concentration: of HDL cholesterol} \\ = \frac{A \text{ sample}}{A \text{ standard}} \times 8.27 \text{mmol} \end{aligned}$$

Determination Of Plasma LDL-Cholesterol (Okazaki,1997) as Modified by Randox

Principle

The LDL Direct Cholesterol assay is a homogeneous method for directly measuring LDL-C levels in plasma. Without the need any off–line pretreatment or centrifugation steps.

Procedure

The method is in a two reagent format and depends on the properties of a unique detergent. The detergent (Reagent 1) solubilizes only the nonLDL lipoprotein particles. The cholesterol released is consumed by cholesterol esterase and cholesterol oxidase in a noncolor forming reaction.

A second detergent (Reagent 2) solubilizes the remaining LDL particles and a chromogenic coupler allows for color formation. The enzyme reaction with LDL in the presence of coupler produces color that is proportional to the amount of LDL cholesterol present in the sample.

Method of Analysis

Data obtained were analysed using Statistical Package For the Social Science (SPSS). The results were explained as Standard Error of Means (SEM). Student test was used to test significance between the mean values. P value was $P < 0.05$, Pearson Correlation studies was used to assess correlation among variable.

IV. RESULT

Results obtained in this study were expressed in table 4.1 to 4.7

Table 4.1

Shows comparism of assayed parameters of subject and control groups. There were significant different between the mean value of BMI, Glucose, TC, HDL, LDL, TG recoded in subject compared to control. The value recoded in control is significantly lower when compared with that of subject ($P < 0.05$).

Table 4.2

Shows the average influence of age and duration on contraceptive users. Making age 18 -23 as a Base line control, when compared with all ages they were significantly increased ($P > 0.05$) as the age increased throughout the parameters used from lower to higher.

Table 4.3

Shows the effect of duration on Glucose level of women on contraceptives compared with the control subject, they were significantly increased ($p > 0.05$) across the months when compared with controls except in the case of Norplant were significantly decreased ($p < 0.05$) across the month, when compared with the controls.

Table 4.4

Shows the effect of duration on total cholesterol level of women on contraceptives compared with the controls subject, they were significantly increased ($p > 0.05$) across the months when compared with control, except in the case of Norplant they were significantly decreased ($p < 0.05$) when compared with the controls.

Table 4.5

Shows the effect of duration on Triglyceride level of women on contraceptives compared with the controls subject, they were significantly increased ($p > 0.05$) across the months when compared with controls except in the case of Norplant they were significantly decreased ($p < 0.05$) when compared with controls.

Table 4.6

Shows the effect of duration on HDL-cholesterol level of women on contraceptives compared with the control subjects, they were significantly decreased ($p < 0.05$) across the months when compared with controls.

Table 4.7

Shows the effect of duration on LDL-Cholesterol level of women on contraceptive, they were significantly increased ($p > 0.05$) across the months, when compared with control except in the case of Norplant they were significantly decreased ($p < 0.05$) when compared with controls.

Table 4.1: Comparism of assayed parameters of subjects on contraceptives with those of controls

Parameters/ Variable	women on contraceptives	women without contraceptives (Control)
	mean ± SEM	mean ± SEM
Age (years)	32.00 ± 0.53 ^a	35.00 ± 0.42
BMI (Kg/m ²)	59.40 ± 0.45 ^a	54.30 ± 0.50
Glucose (mmol/L)	5.21 ± 0.22 ^a	3.94 ± 0.20
TC (mmol/L)	4.82 ± 0.46 ^a	3.34 ± 0.12
HDL-C (mmol/L)	0.97 ± 0.27 ^a	1.24 ± 0.41
LDL-C (mmol/L)	2.37 ± 0.23 ^a	1.89 ± 0.05
TG (mmol/L)	1.67 ± 0.11 ^a	0.89 ± 0.04
n	50	400

Key: (TC) = Total cholesterol, (HDL-C) = High Density Lipoprotein Cholesterol, (LDL-C) = Low Density Lipoprotein Cholesterol and TG = Triglyceride

Values are expressed as mean ± standard deviation,

^aSignificant as compared with the control (p<0.05)

Table 4.2: Average Influence of Age and Duration on Contraceptive Users

Age Range	18-23	24-29	30-35	36-41
Perimeter				
Glucose	3.42±0.012	4.58±0.002 ^{ac}	4.28±0.002 ^{abc}	6.57±0.64 ^{ab}
TC	3.05±0.007	3.12±0.022 ^{ac}	4.28±0.024 ^{abc}	4.60±0.011 ^{ab}
TG	0.77±0.007	1.40±0.010 ^{ac}	1.48±0.006 ^{abc}	1.51±0.008 ^{ab}
HDL-C	0.07±0.012	1.13±0.005 ^{ac}	1.64±0.012 ^{abc}	1.67±0.018 ^{ab}
LDL-C	1.10±0.012	1.19±0.006 ^{ac}	1.80±0.023 ^{abc}	0.73±0.014 ^{ab}

Key:

a=Significant as compared with age range 18-23

b=Significant as compared with age range 24-29

c=Significant as compared with age range 30-35

(TC) = Total cholesterol, (HDL-C) = High Density Lipoprotein Cholesterol, (LDL-C) = Low Density Lipoprotein Cholesterol and TG = Triglyceride

Table 4.3: Effect of duration on Glucose level of women on contraceptives compared with the control subjects

Contraceptives based grouping

	Control (mmol/L)	Noristerate (mmol/L)	Depo-provera (mmol/L)	Oral pill (mmol/L)	Norplant (mmol/L)
Period	mean± SEM	mean±SEM	mean±SEM	mean±SEM	mean±SEM
Month 1	3.42 ± 0.02	3.97 ± 0.01 ^a	4.03 ± 0.01 ^a	3.53 ± 0.01 ^a	2.97 ± 0.01 ^b
Month 4	3.42 ± 0.02	4.45 ± 0.01 ^a	4.27 ± 0.03 ^a	3.69 ± 0.00 ^a	3.02 ± 0.01 ^b
Month 8	3.42 ± 0.02	4.72 ± 0.01 ^a	4.46 ± 0.01 ^a	3.87 ± 0.01 ^a	3.18 ± 0.01 ^b
Month 12	3.42 ± 0.02	4.84 ± 0.01 ^a	4.63 ± 0.01 ^a	3.90 ± 0.00 ^a	3.26 ± 0.01 ^b
Month 16	3.42 ± 0.02	5.12 ± 0.04 ^a	4.73 ± 0.01 ^a	3.98 ± 0.01 ^a	3.30 ± 0.00 ^b
Month 20	3.42 ± 0.02	5.82 ± 0.01 ^a	4.85 ± 0.01 ^a	4.03 ± 0.01 ^a	3.39 ± 0.01 ^b
Month 24	3.42± 0.02	5.81±0.01 ^a	4.82± 0.01 ^a	4.08± 0.01 ^a	3.40 ± 0.01 ^b
n	50	100	100	100	100

Values are expressed as mean ± SEM, n = 4.

^aValues are significantly high when compare with control (p < 0.05)

^bValues are not significantly different when compare with control (p < 0.05)

Table 4.4: Effect of duration on Total Cholesterol level of women on contraceptives compared with the control subjects

Contraceptives based grouping

	Control (mmol/L)	Noristerate (mmol/L)	Depo-provera (mmol/L)	Oral pill (mmol/L)	Norplant (mmol/L)
Period	mean± SEM	mean±SEM	mean±SEM	mean±SEM	mean±SEM
Month 1	3.00 ± 0.02	3.37 ± 0.01 ^a	3.35 ± 0.04 ^a	3.23 ± 0.01 ^a	2.86 ± 0.01 ^b
Month 4	3.00 ± 0.02	3.68 ± 0.01 ^a	3.31 ± 0.01 ^a	3.41 ± 0.01 ^a	2.93 ± 0.01 ^b
Month 8	3.00 ± 0.02	4.92 ± 0.01 ^a	4.45 ± 0.01 ^a	3.67 ± 0.01 ^a	2.84 ± 0.02 ^b
Month 12	3.00 ± 0.02	4.97 ± 0.02 ^a	3.87 ± 0.02 ^a	3.67 ± 0.01 ^a	2.90 ± 0.02 ^b
Month 16	3.00 ± 0.02	4.99 ± 0.01 ^a	4.07 ± 0.04 ^a	3.70 ± 0.01 ^a	2.78 ± 0.01 ^b
Month 20	3.00 ± 0.02	4.99 ± 0.01 ^a	4.63 ± 0.06 ^a	3.62 ± 0.01 ^a	2.98 ± 0.00 ^b
Month 24	3.00 ± 0.02	4.98 ± 0.01 ^a	4.62 ± 0.06 ^a	3.68 ± 0.01 ^a	2.99 ± 0.00 ^b
n	50	100	100	100	100

Values are expressed as mean ± SEM, n = 4.

^aValues are significantly high when compare with control (p < 0.05)

^bValues are not significantly different when compare with control (p < 0.05)

Table 4.5: Effect of duration on Triglyceride level of women on contraceptives compared with the control subjects

Contraceptives based grouping

Period	Control	Noristerate	Depo-provera	Oral pill	Norplant
	(mmol/L)	(mmol/L)	(mmol/L)	(mmol/L)	(mmol/L)
	mean± SEM	mean±SEM	mean±SEM	mean±SEM	mean±SEM
Month 1	0.86 ± 0.01	1.00 ± 0.02 ^a	1.08 ± 0.01 ^a	0.91 ± 0.01 ^a	0.68 ± 0.01 ^b
Month 4	0.86 ± 0.01	1.28 ± 0.01 ^a	1.26 ± 0.01 ^a	0.95 ± 0.01 ^a	0.81 ± 0.06 ^b
Month 8	0.86 ± 0.01	1.38 ± 0.01 ^a	1.37 ± 0.01 ^a	0.98 ± 0.00 ^a	0.80 ± 0.01 ^b
Month 12	0.86 ± 0.01	1.47 ± 0.01 ^a	1.49 ± 0.01 ^a	0.99 ± 0.00 ^a	0.82 ± 0.01 ^b
Month 16	0.86 ± 0.01	1.53 ± 0.01 ^a	1.52 ± 0.01 ^a	1.03 ± 0.01 ^a	0.84 ± 0.01 ^b
Month 20	0.86 ± 0.01	1.77 ± 0.01 ^a	1.66 ± 0.02 ^a	1.02 ± 0.00 ^a	0.86 ± 0.00 ^b
Month 24	0.86 ± 0.01	1.79 ± 0.01 ^a	1.67 ± 0.02 ^a	1.04 ± 0.00 ^a	0.87 ± 0.00 ^b
n	50	100	100	100	100

Values are expressed as mean ± SEM, n = 4.

^aValues are significantly high when compare with control (p < 0.05)

^bValues are not significantly different when compare with control (p < 0.05)

Table 4.6: Effect of duration on HDL-Cholesterol level of women on contraceptives compared with the control subjects

Contraceptives based grouping

Period	Control	Noristerate	Depo-provera	Oral pill	Norplant
	(mmol/L)	(mmol/L)	(mmol/L)	(mmol/L)	(mmol/L)
	mean± SEM	mean±SEM	mean±SEM	mean±SEM	mean±SEM
Month 1	1.78 ± 0.01	1.50 ± 0.01 ^a	1.68 ± 0.01 ^a	1.67 ± 0.02 ^a	1.73 ± 0.01 ^a
Month 4	1.78 ± 0.01	1.28 ± 0.01 ^a	1.41 ± 0.01 ^a	1.51 ± 0.01 ^a	1.64 ± 0.02 ^a
Month 8	1.78 ± 0.01	1.13 ± 0.01 ^a	1.26 ± 0.01 ^a	1.43 ± 0.01 ^a	1.56 ± 0.01 ^a
Month 12	1.78 ± 0.01	0.96 ± 0.02 ^a	1.34 ± 0.01 ^a	1.34 ± 0.01 ^a	1.50 ± 0.00 ^a
Month 16	1.78 ± 0.01	0.96 ± 0.02 ^a	1.03 ± 0.02 ^a	1.29 ± 0.01 ^a	1.46 ± 0.01 ^a
Month 20	1.78 ± 0.01	0.86 ± 0.01 ^a	0.96 ± 0.01 ^a	1.22 ± 0.01 ^a	1.41 ± 0.01 ^a
Month 24	1.78 ± 0.01	0.87 ± 0.01 ^a	0.99 ± 0.01 ^a	1.24 ± 0.01 ^a	1.45 ± 0.01 ^a
n	50	100	100	100	100

Values are expressed as mean ± SEM, n = 4.

^aValues are significantly high when compare with control (p < 0.05)

Table 4.7: Effect of duration on LDL-Cholesterol level of women on contraceptives compared with the control subjects

Contraceptives based grouping

Period	Control	Noristerate	Depo-provera	Oral pill	Norplant
	(mmol/L)	(mmol/L)	(mmol/L)	(mmol/L)	(mmol/L)
	mean± SEM	mean±SEM	mean±SEM	mean±SEM	mean±SEM
Month 1	1.56 ± 0.02	1.86 ± 0.01 ^a	1.72 ± 0.01 ^b	1.82 ± 0.01 ^a	1.52 ± 0.01 ^b
Month 4	1.56 ± 0.02	1.98 ± 0.01 ^a	1.73 ± 0.01 ^a	1.87 ± 0.01 ^a	1.64 ± 0.01 ^a
Month 8	1.56 ± 0.02	2.11 ± 0.02 ^a	1.94 ± 0.01 ^a	1.92 ± 0.01 ^a	1.66 ± 0.01 ^a
Month 12	1.56 ± 0.02	2.21 ± 0.01 ^a	1.98 ± 0.01 ^a	1.98 ± 0.01 ^a	1.70 ± 0.01 ^a
Month 16	1.56 ± 0.02	2.28 ± 0.01 ^a	2.16 ± 0.01 ^a	2.02 ± 0.02 ^a	1.77 ± 0.01 ^a
Month 20	1.56 ± 0.02	2.32 ± 0.01 ^a	2.25 ± 0.01 ^a	2.17 ± 0.02 ^a	1.88 ± 0.01 ^a
Month 24	1.56 ± 0.02	2.34 ± 0.01 ^a	2.26 ± 0.01 ^a	2.19 ± 0.02 ^a	1.89 ± 0.01 ^a
n	50	100	100	100	100

Values are expressed as mean ± SEM, n = 4.

^aValues are significantly high when compare with control (p < 0.05)

V. DISCUSSION

Contraceptive agents induces substantial metabolic changes which include raised plasma triglyceride and Low Density Lipoprotein-cholesterol levels, reduced High Density Lipoprotein-cholesterol levels, impairment of glucose and elevated insulin levels (Szlendak, 2009). One of the main reported effects of combined contraceptives is an increased risk of cardiovascular disease (CVD). The progressive change in the composition and dosages in the contraceptives and more careful selection of women who are to use these products have resulted in a lower risk of CVD associated with their use (ESHRE *et al.*; 2000). The World Health Organization (WHO) study of cardiovascular heart disease (CVD) and steroid hormone contraception conducted in developing and developed countries revealed a higher overall risk of Ischemic stroke among contraceptives users in developing countries than those in developed countries of Europe. These differences were attributed to the type of contraceptives used and the frequency with which users reported that their blood pressure had been checked prior to or during contraceptives use (WHO 1999).

Even though the mean age of women on contraceptives is significantly lower than the control, the BMI of the test women were significantly higher than those of control. Biochemical parameters including glucose, TC, LDL and TG that were all significantly higher in women on contraceptives compared with control, however, the HDLC value for women on contraceptives was significantly lower than control. This is in agreement with work of WHO (1999). They reported that prolonged use of contraceptives is often linked with abnormal lipid metabolism. In this study, the rise in blood glucose was accompanied by significant increase ($p < 0.05$) in cholesterol levels by 30.7%, when compared with the normal control. Similarly, there was significant increased ($p < 0.05$) in the triglyceride levels by 46.7%, when compared with the normal control group. The disruption of insulin secretion results in enhanced metabolism of lipids from the adipose tissue to the plasma. It has been shown that insulin resistance in contraceptives users leads to a variety of derangements in metabolic and regulatory process, which in turn leads to accumulation of lipids such as cholesterol and triglyceride. Accumulation of triglycerides is one of the risk factors in coronary heart disease. The abnormal high concentration of serum lipids in the contraceptives users are due mainly to increase in mobilization of free fatty acid from the peripheral fat depots (Bopanna *et al.*, 1997).

Triglycerides measurements are used in the diagnosis and treatment of diseases involving lipid metabolism and various endocrine disorders such as diabetes mellitus, nephrosis and liver obstruction (Ju *et al.*, 2008).

It is a well-established fact that in an uncontrolled hyperlipidaemia; an inverse relationship occurs between LDL-cholesterol and HDL-cholesterol levels. These fractions of cholesterol have been known to contribute to the risk of

coronary artery disease seen in some diabetic subjects and HDL-cholesterol plays an important role in the mobilization of lipids from peripheral cells to the liver where it is concentrated in the bile and excreted in the intestine (Arvind *et al.*, 2002). In this present study, the significantly increased LDL-cholesterol ($p < 0.05$) by 20.3% in the contraceptives group as compared with the normal control group was observed in the course of this study. On the other hand, there was significant decrease ($p < 0.05$) in the HDL-cholesterol levels by 27.8% of the contraceptives group, when compared with the normal control group.

Results from this study showed that the levels of glucose, triglyceride and LDL-cholesterol increased with duration of contraceptive intake in the study group. The increase in the production of VLDL and, consequently, triglycerides, contributes to increase the clearance of the VLDL particles, since these are rapidly converted into LDL (Campos and Walse 1997). After being converted into LDL, HDL will promote the efflux of the cholesterol from tissue to the liver, where LDL can be converted into bile acid and secreted through the bile (Steck and Lenge 2010). The levels of total cholesterol were found significantly higher in groups using contraceptives in relation to the control group. Total cholesterol sums the lipoproteins HDL, LDL, and VLDL, and probably presents higher levels in contraceptive users due to the increase observed in the levels of VLDL and HDL. This result is in agreement with other studies (Karam 2001). This observation is however different from that reported by other investigators (Neser *et al.*; 2007). They observed that serum triglyceride and LDL cholesterol did not show significant variations. Significant decrease ($p < 0.05$) level of HDL-cholesterol was observed within the duration of contraceptive use. HDL-cholesterol is involved in the reverse cholesterol transport from peripheral cells to the liver, prevents oxidation of LDL-cholesterol because of the presence of paraoxonase in HDL-cholesterol. Paraoxonase is synthesized in the liver and is HDL-associated enzyme that inhibits the oxidation of LDL-cholesterol (Shivaprakash 2006). The variations in the observation by the different investigators may be due to the chemical composition of the different contraceptives the women were given. Changes seen in glucose and lipid with combined contraceptives vary according to progesterone type (ESHRE *et al.*; 2000). The contraceptives induced increased triglyceride is due to increased synthesis rather than decreased clearance. These observed changes in lipid and glucose were sustained with duration of contraceptives use but the levels were still within normal or acceptable range.

This study showed significant increase ($p < 0.05$) in weight by 8.6% amongst women taking contraceptives compared to the control groups. These changes in body weight showed that administration of the contraceptives have a significant effect on body weight. The weight gains seem to be as a result of the ability of the contraceptives to reduce hypoglycemia within the period of this study (Trusselet *et al.*, 2011).

Result showed a significant increased ($p < 0.05$) in Glucose for contraceptives users within the age ranges of 24-29, 30-35 and 36-41 when compared with women with age range of 18-23. There was also a significant increase ($p < 0.05$) in Glucose between users within the range of 36-41 and those within the age range of 30-35. However, there was no significant difference in the glucose level of users within the age range of 24-29 and 30-35.

The levels of total cholesterol and triglyceride were significantly increased ($p < 0.05$) in users of age range 24-29, 30-35 and 36-41 compared with user of age range 18-23. Similarly, there was a significant increased ($p < 0.05$) in the total cholesterol and triglyceride levels in the users of age range 30-35 compared with those of age range 24-29 and between users of age range 36-41 compared with age range 30-35 respectively. This is also in tandem with the findings of (WHO, 1999) which stated that the incidence of CVD varies with age.

There was a significantly increase ($p < 0.05$) in the HDL-cholesterol for users of age ranges, 24-29, 30-35 and 36-41 compared with users of lower age range, 18-23. Similar results were obtained as there was a significant increase in the HDL-cholesterol levels for users within age range 30-35 compared with age 24-29 and 36-41 compared with age range 30-35 respectively.

The LDL-C level were significantly ($p < 0.05$) higher only in users of age range 24-29, 30-35 and 36-41 compared with users within the age range of 18-23. However, there was no significant difference in the LDL-C levels between users in the other age range.

Although it was suggested that a long term (> 6 years) current use of contraceptives may be associated with cardiovascular disease (CVD) in old women (Szlendak 2009). In this study the duration of current contraceptives use was not more than 2 years and the age of users were not more than 41 years.

This study also indicated that total lipid was not significantly increased ($p < 0.05$) beyond 2 years of contraceptives use. The contraceptives effect on total lipid was short lived and started to decline towards levels in control subjects after 2 years of administration (table 4.2). Since the effects caused by contraceptives intake are short lived, it could be said that the effects of these hormonal preparation may be physiologic rather than pathogenic (Szlendak 2009). The significant increase ($p < 0.05$) in the glucose, total cholesterol, triglycerides, HDL-C and LDL-C were highest by 47.9%, 33.6%, 49.0%, 95.0% and 33.6% respectively in the young (age groups between 18 to 23 years) contraceptives users compared to older (age groups of 36 to 41 years). This suggests that it decreases with increase in age of the women (table 4.2). Since the incidence rates of cardiovascular disease (CVD) events are low in younger women of reproductive age these observed changes are not likely to have adverse effects (WHO, 1999). The dyslipidaemia induced by contraceptives use may not be regarded as proatherogenic

since it was not observed across all the age groups and duration.

Women taking Noristerat Contraceptive over the two years of study had significant monthly increase in biochemical parameters including glucose, total cholesterol, triglyceride, LDL-cholesterol, and significant decrease in HDL cholesterol respectively compared to women without any contraceptives as shown in the table 4.3 to 4.7. Similar result from table 4.3 to table 4.7 were obtained for women taking Depo-provera and oral pills as there was a significant monthly increase in biochemical parameters such as glucose, total cholesterol, triglyceride, LDL-cholesterol respectively for the two years compared to women without any contraceptives.

Also, a significant decrease in HDL-cholesterol levels for the two years was recorded for those women as compared with the control group (Table 4.6) the women taking Norplant there was a significant decrease in biochemical parameters such as Glucose, Total Cholesterol, Triglyceride respectively for the two years when compared with the control group. However, there was no significant monthly change in HDL-cholesterol. Also significant increase was observed for women under Norplant contraceptives for the two years compared with control group as shown in table 4.3 – 4.6. In this study, significant increase ($p < 0.05$) levels of HDL by 25.6% were found in the serum of users of Norplant, in comparison to control group. This finding agrees to the literature (Machado, *et al.*, 2010) and shows that despite of the presence of the progesterone, the levels of HDL for this group are higher than the levels of this lipoprotein in the control group. Different from this finding, a study developed with 400 women treated with contraceptive containing androgenic progesterone (BLT) observed decrease in the levels of the lipoprotein HDL in comparison to basal analyses (Endrikat *et al.*, 2002). Levels of LD-CL and triglycerides, in this study, are significantly ($p < 0.05$) higher for women who use Noristerate by 17.2% and 37.90 and Depo-provera by 23.95% and 28.2% respectively in comparison to women in the control group. Similarly, there was a significant decrease in Glucose by 15.6% in women using Norplant compared to those using Noristerate, Depo-provera and oral pills suggesting that Norplant could be the most safe hormonal contraceptive to others under this study. Which is intended with the work of Segal S (2010), Norplant is not only safe and long active, it is also the most effective current reversible contraceptive method, with at least 99% rate of effectiveness.

VI. CONCLUSION

In conclusion, this study showed that contraceptives intake produces changes in Lipid metabolism in women. In respective of the contraceptive used, the levels of lipid increased with age, duration of intake and the type of contraceptive with increased been highest in total cholesterol. Norplant has minimal effect on the level of all lipid component assayed. Thus Norplant seems to be the best family planning method.

VII. RECOMMENDATION

Since hormonal contraceptive are influenced by factors such as age, duration of usage and type, it is advisable that users should carry out risk assessments assays such as lipid profile and glucose as carried out in the present study in other to determine the contraceptives that is safe.

In addition, further work on the most active components of these contraceptive and their biochemical mechanism of action need to be fully elucidated.

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