

Research Article

Activities of some liver enzymes in serum of humans receiving DMPA and Cu-IUD contraceptives

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Abstract: The use of injectable contraceptives especially depomedroxyprogesterone acetate (DMPA) is becoming increasingly popular in Nigeria probably because of its relative usage ease. Drugs, including contraceptives are metabolized in the liver, yet information on the effect of injectable contraceptives on liver function biomarkers are few among Nigerian users. In this present study, the activities of some liver enzymes: alanine transaminase (ALT), aspartate transaminase (AST) and alkaline phosphatase (ALP) were assayed in serum of patients receiving DMPA (n=15) and Cu-IUD (n=15) contraceptives. Non-contraceptive users (n=15) were included as control. Results show that DMPA contraceptive use significantly ($p<0.05$) increased serum ALT (38.40 ± 3.86 IU/L), ALP (85.50 ± 8.80 IU/L), and AST (27.18 ± 4.03 IU/L) activities when compared with levels obtained from Cu-IUD contraceptive (ALT: 13.60 ± 4.10 IU/L, ALP (36.80 ± 6.50 IU/L, AST: 13.10 ± 2.43 IU/L), and non-contraceptive (ALT: 10.43 ± 4.99 IU/L, ALP: 33.79 ± 4.49 IU/L, AST: 12.13 ± 3.06 IU/L) users. Evidence from result findings show that DMPA contraceptive increased ($p<0.05$) activities of ALT, ALP and AST in serum of users. This might be due to altered metabolism of these liver enzymes and/or compromise in liver membrane integrity. The implicating mechanism needs further elucidation.

Keywords: Contraceptive, Cu-IUD, Liver enzymes, DMPA, Alanine transaminase, Aspartate transaminase, Alkaline phosphatase

INTRODUCTION

Contraceptives are devices, drugs or methods used to prevent pregnancy. They interrupt fertilization or implantation process [1]. Contraceptives are among the various medical discoveries of the 20th century and have been used since then. Although, historical documentation shows that even ancient Egyptians used contraceptives to prevent pregnancy [2]. Different cultures created their own ways of preventing pregnancy and these methods have metamorphosed. Contraceptive methods are broadly classified into natural, barrier, and hormonal methods. In the early 1900s, researchers developed a hormonal birth control pill for women [3]. The pill comes in either a combination of oestrogen and progestin or progestin-only. The oestrogen present in oral contraceptive pill is oestradiol which is always combined with progestin, a term for any hormone (natural or synthetic) that causes progestin effect. When used through a menstrual cycle with progestin, oestrogen suppresses the action of other reproductive hormones (LH, FSH) and prevents ovulation [4]. Progestin also prevents ovulation and maintains a powerful barrier against the entry of sperm into the uterus by keeping the cervical mucus thick and sticky.

The pills, have evolved from the first to second and today, the third generation pills containing reduced amounts of the active hormones, oestrogen and

progestin [5], giving people safe and affordable brands with fewer side effects [6]. However, failure rates (9%) have been observed to be due to non-compliance [5]. In addition, common side effects and associated medical disorder have been enumerated [7-8]. Burkman *et al.* [9] observed that the metabolism of oral contraceptive pill among Nigeria users could cause disturbed liver function as suggested by increase in serum liver enzymes.

In order to reduce failure rates and non-compliance associated with pills, the injectables also containing oestrogen and progestin were introduced and marketed by various trade names. Its use appears high among Nigerians. Nevertheless, changes in serum liver enzymes of users are very scarce in literature. Therefore, this study reports the activities of liver enzymes in the serum of some Nigerian women receiving DMPA, an injectable progestin-only contraceptive. This will add to the accumulating data required for health care.

MATERIALS AND METHODS

Subjects

Thirty (30) consenting women in apparent good health between the ages of 23 and 38 years (30.0 ± 7.5 yrs), who were individuals attending the Family Planning Clinic, General Hospital, Sapele,

Delta State, were selected and divided into two groups: those receiving DMPA injectable progestin-only contraceptive (n=15), and those having Cu-IUD (non-hormonal contraceptives: n=15). The two groups have been using their associated contraceptive method for about 3-9 months. Fifteen (15) age – matched women who were not on any contraceptive or other drugs were recruited as control after seeking and obtaining informed consent. All the selected participants underwent a prequalification examination before selection and study was approved by the Hospital and our Faculty's Research Committees.

Blood Sample Collection

Whole blood (about 5ml) was collected from the anterior cubital fossa by the vene puncture technique using 21 guage hypodermic needle and stringe into a clean, sterile container. It was allowed to clot and thereafter centrifuged at 1200 x g for 5 min at room temperature (29⁰-31⁰C). The supernant (serum) was decanted into bijou bottle and stored frozen until

required for assay which was done within 48 hours of collection.

Serum Assay

The transaminases: alanine and aspartate transaminases were assayed in serum using standard procedures as previously described [10]. Serum alkaline phosphatase activity was determined using the sodium thymolphthaline monophosphate method [11].

Statistics

All the data obtained were expressed as Mean±SD. Analysis of variance (ANOVA) was used to analyze the data obtained and Duncan Multiple Range Test (DMRT) was employed to compare the group mean. P – values less than 0.05 (P<0.05) was taken as statistically significant.

RESULTS

The results obtained from the investigation into the changes in liver enzymes induced by DMPA and Cu-IUD contraceptives are shown in Table 1.

Table 1: Activities of alkaline phosphatase (ALP), alamine transaminase (ALT) and aspartate transaminase (AST) in serum of some Nigerian women receiving DMPA and Cu-IUD contraceptives

Liver Enzymes	*Control (n=15)	Contraceptive users	
		DMPA(n=15)	Cu-IUD (n=15)
Alkaline phosphatase, ALP (IU/IL)	33.79±4.49 ^a	85.50±8.80 ^b	36.80±6.60 ^a
Alanine transaminase, ALT (IU/L)	10.43±4.99 ^a	38.40±3.86 ^b	13.60±4.10 ^a
Aspartate transaminase AST (IU/L)	12.13±3.06 ^a	27.18±4.03 ^b	13.90±2.43 ^a
AST: ALT Ratio	1.16	0.71	1.02

Data are written as Mean±SD for 'n' number of subjects
Values bearing another superscript on a row differ significantly (P<0.05)

Data obtained were all within the reference range, but values for the DMPA contraceptive users were significantly increased ($p<0.05$) when compared with the non-contraceptive and Cu-IUD users. The AST: ALT ratio was also reduced by DMPA contraceptive use when compared with the ratio for the control or Cu-IUD users.

Even though data were within normal range, the trend of the results indicates that DMPA contraceptive could induce a measure of hepatic dysfunction or alter the metabolism of liver enzymes.

DISCUSSION

The liver is the largest organ in the human body. It plays major roles in metabolism, and has a number of important functions in the body. Disturbed hepatic function therefore affects several vital processes in the body. In view of this, performance of liver function test (LFT) becomes pivotal in assessing liver integrity. A wide array of tests is involved in LFT but the most common in our environment is liver enzymes.

In this regard, the assay of liver parenchymal (transaminases) and membraneous (alkaline phosphatase) enzymes has remained popular.

Our present study (Table 1) shows that DMPA contraceptive significantly increase alamine/aspartate transaminases and alkaline phosphatase when compared with values obtained from either Cu-IUD users or non-contraceptive (control) users. Burkman, *et al.* [9] observed elevated values for women using oral contraceptive pills, OCPs, and concluded that OCPs could cause liver congestion, sinusoidal blockage and cellular inflammation. When the liver is compromised, liver enzymes leak into the circulating system causing increased activities. Injectable progestin-only contraceptive, DMPA (present study: Table 1) increased the activities of liver enzymes (ALT, AST and ALP) in serum of users in Nigeria.

The liver regulates the amounts of body lipids, glucose and hormones including insulin activities OCPs have been reported to induce hyperlipidaemia [12] and

insulin resistance [13]. These observed effects of OCP have been traced to the oestrogen component [14]. Oestrogen has also been observed to significantly inhibit the metabolism of liver enzymes, and this, increased the activities of liver enzymes in bloodstream [1].

The observed increase in liver enzymes: ALT, AST, and ALP (Table 1) for women receiving DMPA contraceptive may be due to either interrupted metabolism of the liver enzymes or a measure of compromise in hepatic membrane integrity. The more plausible implicating cause of the elevated activities need further verification and documentation for primary health care.

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