

The Effect of Implanon on Liver Function Tests

AK Hussain¹, GA Modawe² and AA Abdrabo^{1*}

¹Department of Clinical Chemistry, Faculty of Medical Laboratory Sciences, Alneelain University, Khartoum, Sudan

² Department of Biochemistry, Faculty of Medicine, Omdurman Islamic University, Omdurman, Sudan

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Back ground: Implanon is a type of birth control Implanon receiving FDA – approval in July 2006. Sudanese women used the Implanon insert.

Objective: This study was conducted to evaluate the effect of Implanon on liver function among Sudanese Woman receiving the drug.

Methodology: This case control hospital based study, conducted in Omdurman maternal hospital during January to May 2015. The study included 75 married women with reproductive age, received from family planning clinics of maternal hospital. The age ranged between (18 – 50 years), the control group includes 25 married women not using any contraceptive method and 25 single women match age. The serum biochemical parameters were measured using spectrophotometric methods using an automated chemistry analyzer (Mindray BS 200) all result were analyzed using Computerized Program (SPSS), all result were expressed in mean and standard deviation (SD).

Result: The (mean \pm SD) of total protein, Albumin, total bilirubin, direct bilirubin, transaminases (AST and ALT), and ALP in patients, respectively were (7.22 \pm 1.12)g/dl, (4.46 \pm 4.77)g/dl, (0.61 \pm 0.57)mg/dl, (1.15 \pm 6.84)mg/dl, (41.62 \pm 51.85)u/l, (47.49 \pm 29.44)u/l, (109.72 \pm 56.50) u/l. The (mean \pm SD) of total protein, Albumin, total bilirubin, direct bilirubin, AST, ALT, ALP in control subject respectively were (7.7 \pm 5.45), .89 \pm .78, 0.66 \pm 0.22, 0.29 \pm 0.18, 71.34 \pm 6.66, 32.80 \pm 21.21, 48.62 \pm 32.76). There is significant increase of ALT (P=0.000) and also ALP (P=0.000)). There is in woman used Contraceptive significant decreased of albumin (P=0.000) and also AST (0.014).

Conclusion: These studies concluded that, there is significant increasing ALT and ALP, and significances decreased in Albumin and AST.

Key words: Implanon, women, liver function, Sudanese.

INTRODUCTION

Implanon is a subdermal contraceptive it has recently been approved by the US Food and Drug Administration to provide effective forgettable contraception for 3 years. It is composed of a single nonbiodegradable rod, 40mm long and 2mm in diameter, containing a core of 68 mg of etonogestrel (ENG). Inhibition of ovulation occurs within 1day of insertion ⁽¹⁾ it also enjoys excellent reversibility with return or fertility within 1 month after removal. Among those not using other contraceptives, 14% became pregnant within 90 days after removal ⁽²⁾. Additional advantages of Implanon include an estrogen-sparing effect, safety ^(3,4). It is a good choice for adolescents and woman with systemic hypertension, bleeding problems are the most common side effects through direct and indirect effects on the endometrium ⁽⁵⁻⁶⁾.

ENG is approximately 32% bound to sex hormone-binding globulin (SHBG) and 66% bound to albumin in blood. ENG is metabolized in liver microsomes by the cytochrome

P450 3A4 isoenzyme and is rapidly transformed in the body to 3 keto-desogestrel, a low androgenic third-generation progestin ⁽⁷⁾. The Effect on liver functions has also been studied whereas total bilirubin and were reported to increase ⁽⁸⁻⁹⁾, serum levels of (AST), and aspartate aminotransferase-ase (AST) were found either to decrease ⁽⁸⁾ or to remain unchanged ⁽⁹⁾. The effect of Implanon on hepatic perfusion has not been previously studied.

Implanon is a viable contraception option for Sudanese women providing long-term contraception. The impact of Implanon on the Liver is of paramount importance in Sudan a country where many individuals are afflicted with chronic liver disease. This study was conducted to evaluate the effect of Implanon on liver function among Sudanese Women.

Materials and Methods

Study population

Case control study, Conducted in Omdurman Maternity Hospital during the period January to May 2015, 75 women using hormonal contraceptive methods, compared with 50 women that don't use contraceptive as control. The Study includes married women using hormonal contraceptive methods, including (combined contraceptive pills, progestin-only pills, injectable birth control hormones and implantable rods). Married women not using hormonal contraceptive methods

Women with known previous history liver disease were excluded

Sample collection

Samples collected in heparinised sample collection tubes. Women with Reproductive age were enrolled into this prospective observational study. Divided in tow group one used hormonal contraceptive (75) case and other (50) women as negative control (do not use contraceptive), they were followed-up for five months. Questionnaire (including age, type

Discussion

Implanon is a long-term Implanon contraceptive containing ENG that is both safe and effective⁽⁵⁾ the pharmacokinetics and pharmacodynamic of Implanon indicate that it's high contraceptive efficacy, as reflected in a zero pregnancy rate over 5629 women – years of use. Its excellent reliability, ease of use, and reversibility make Implanon a valuable addition to current contraceptive⁽¹⁰⁾ in Sudan the need for long-term contraception could not be overemphasized. Due to the prevalence of chronic liver disease in Sudan and the growing popularity of Implanon its impact on liver perfusion and liver functions is of particular importance. The splanchnic pharmacodynamic effect of the drugs was poorly clarified until some years ago, the introduction of Doppler ultrasound provided a powerful tool to investigate such hemodynamic effect and brought new insights into this field⁽¹¹⁾.

In our study found serum total protein is non significant (P.value 0.151), i suggested that Implanon does not cause inflammation. In our study also found serum albumin significantly decreased differ from previous study reported⁽¹²⁾. In our study found serum total bilirubin slightly increased (p value 0.121) similar to the previous study reported⁽¹²⁾. In our study, we found out that direct bilirubin has significantly

of contraceptive used and duration of usage) .serum biochemical parameters were measured using spectrophotometric methods.

Statistical analysis

These data were analyzed using SPSS Program, results are represented as mean±SD and were considered significant when p was <0.05.

Ethical approval

This study will be approved by the Faculty of Medical Laboratory Science- Alneelain University. An informed consent will be obtained from each participant before sample collection.

Result

Seventy five women with a mean age of 33.02±8.7 years (patients) and fifty women with a mean age of 33.16±9.0 years (control) were enrolled into this prospective observational study, after placement of an Implanon rod in patients. They were followed-up for five months and end-of-study values of serum a mean Total protein of patients 7.22±1.12 and in the control 7.7±5.45 which is insignificant.

decreased, because the implanon not foreign substance and also affected in the liver cells. AST in our study found similar to previous study and also significant decrease⁽¹²⁾, in our study ALT found is highly significant increased differs to pervious study significant decreased⁽¹²⁾ ALP in our study

Found that highly significant similar in previous study⁽¹²⁾. ENG is bound to Implanon and 66% is bound to albumin in blood in vitro data showed that ENG is metabolized in liver microsomes by the cytochrome p450⁽⁷⁾, the biological activity of ENG metabolites is unknown. The impact of ENG on liver functions has been studied by a number of investigators^(8,9), whereas total bilirubin were reported to decrease⁽⁸⁾, serum concentration of AST was found to decrease⁽⁸⁾ rise in ALT and ALP occur without liver disease, perhaps because of microsomal enzyme induction⁽¹³⁾ some investigators could that there may mild hepatocellular dysfunction associated with use of implanon which is possibly of no clinical significance to the healthy acceptor⁽⁹⁾. The over all finding of the present study conform to such a statement.

Conclusion

These studies were concluded that significant increase of ALT and ALP, and significances decreased of Albumin and AST.

Table 1: The mean \pm SD of serum biochemical parameter in liver on study population

Parameter	Means \pm SD		p- value
	Patients No. =(75)	Control No. =(50)	
Age/years	33.02 \pm 8.7*	33.16 \pm 9.0*	0.181
Total protein	7.22 \pm 1.12*	7.7 \pm 5.45*	0.151
Albumin	4.46 \pm 4.7740**	0.89 \pm 0.78**	0.000
TBI	0.61 \pm 0.57*	0.66 \pm 0.22*	0.121
DI	1.15 \pm 6.84	0.29 \pm 0.18	0.091
ALT	41.62 \pm 51.85**	32.80 \pm 21.21**	0.000
ALP	109.72 \pm 56.50**	48.62 \pm 32.76**	0.000
AST	47.49 \pm 29.44*	71.34 \pm 6.66*	0.014

* = Sig

** = highly Sig

Table 2: showed the period of implanon rod insertion in women

period	Frequency	Percent
0-1 years	12	9.6
1-2 years	28	22.4
2-3 years	35	28.0

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