

Serum LH, FSH and Estradiol Levels in Women Using Injectable Contraceptive (Norigest) Over Long Periods of Time

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SUMMARY

Blood glucose, serum bilirubin, serum enzymes, i.e. SAP, SGPT and SGOT, sodium and potassium, LH, FSH and estradiol level were determined in 93 women (aged 25-45). These subjects were grouped according to the time of receiving intragluteal injections (200 mg NETEN 8-weeks intervals). The groups of women receiving injections for 19-24 months showed a significant decrease ($P < 0.01$) in LH, FSH and estradiol levels. The pregnancy rate was 2%. Levels of LH, FSH and estradiol were elevated in women receiving injections for 25-38 months. The pregnancy rate was 3%. The values were not significantly different when compared with controls. A significant increase in serum bilirubin, SAP, SGPT, SGOT, sodium and potassium levels were recorded in all treated groups. The control and treated groups did not show any significant difference with respect to blood glucose levels.

INTRODUCTION

Since the introduction of oral contraceptives in 1956 by Pinus, Rock and Garcia^{1,2}, the cycle administration of ovarian steroids to control fertility by inhibiting ovulation has become a very acceptable method of contraception. However, the use of these agents have introduced, several have been found to cause several side effects, of which have been attitude to estrogen component of the pills^{3,4}. In view of these side effects of currently used combination contraceptives, progesterones, both oral as well as injectable, have been the subject of investigation in the recent part. Several workers^{5,6} have reported conflicting evidences of the effect of depomedroxy-progesterone acetate (DMPA) on metabolic and hormonal changes. Many studies on women receiving injectable preparations of NET EN (Norethindrone enathate) for short period has demonstrated only minor metabolic changes^{7,8}. Recently it has been reported that there is an increase in total cholesterol, triglycerides and thyroxine levels in women receiving Norigest injections over long period of time⁹. The present study was conducted to evaluate the effects of Norigest on LH, FSH, estradiol levels and on the activity of certain serum enzymes and serum electrolytes in long-term situations in Pakistani women.

MATERIALS AND METHODS

Blood glucose, serum bilirubin, serum enzymes i.e. SAP, SGPT, SGOT, Sodium and Potassium, LH, FSH and estradiol levels were determined in 93 women, (aged 25 to 45 years), of proven fertility with two or more previous successful pregnancies. All these women were receiving intra-gluteal injections of 200 mg NETEN at 8 week intervals. Serum LH, FSH and estradiol levels were determined by radio-immunoassay using RIA kits (Amersham, U.K.). Blood glucose estimations were made using YSI Model 23A glucose analyser. Serum bilirubin was measured by the method of Gambino and 10 Freda Serum AP was determined with the method of Michel et al¹¹, while serum SGPT, SGOT were done with method of Reikman and Frankel¹². Serum sodium and potassium were determined by Flame Photometer. Pregnancy rate and blood pressure were recorded throughout the study. Statistical analysis was by students test.

RESULTS

Results of LH, FSH and estradiol are shown in Table 1. The groups of women receiving injection for 19-24 months showed a significant decrease ($P < 0.01$) in LH, FSH and estradiol levels. The pregnancy rate was

Table 1: Effect of Norgest on serum LH, FSH and estradiol levels.

Group	Duration of norgest	LH IU/ml	FSH IU/ml	Estradiol mol/L
Control	Nil	20.12±1.48	8.017±0.82	316.36±47.21
Group-I	2-6 months	18.05±2.91 (N.S)	6.147±0.401 (N.S)	309.00±74.64 (N.S.)
Group-II	7-12 months	17.65±2.83 (N.S)	8.102±1.82 (N.S)	313.83±71.19 (N.S.)
Group-III	13-18 months	16.54±1.89 (N.S)	6.54±0.973 (N.S)	315.04±45.29 (N.S.)
Group-IV	19-24 months	9.07±1.83 (P<0.01)	4.599±0.66 (P<0.01)	247.43±34.12 (P<0.01)
Group-V	25-38 months	19.65±1.32 (N.S)	10.99±1.02 (N.S)	381.34±24.83 (N.S.)

N.S. = Not Significant.

Table 2: Effect of norgest on SAP, SGPT, SGOT, serum bilirubin, serum sodium and serum potassium levels.

Group	Duration of Norgest	SAP IU/L	SGPT IU/L	SGOT IU/L	Total Bilirubin mg/100 ml	Serum sodium mEq/L	Serum Potassium mEq/L
Control	Nil	29.2±9.7	8.01±1.1	16.0±6.4	0.47±0.10	140.0±10.4	4.2±0.8
Group-I	2-6 months	28.4±7.9 (N.S)	7.9±1.4 (N.S)	15.8±7.3 (N.S)	0.49±0.11 (N.S)	146.7±12.3 (N.S)	4.7±0.4 (N.S)
Group-II	7-12 months	32.5±6.7 (P<0.05)	10.6±1.3 (P<0.05)	17.4±4.7 (N.S.)	0.54±0.10 (P<0.05)	155.9±11.4 (P<0.05)	5.2±0.5 (N.S.)
Group-III	13-18 months	33.7±5.8 (P<0.05)	12.7±2.1 (P<0.05)	19.6±5.3 (P<0.05)	0.63±0.14 (P<0.05)	163.0±13.1 (P<0.05)	6.5±1.2 (P<0.05)
Group-IV	19-24 months	35.9±5.9 (P<0.01)	14.8±1.8 (P<0.01)	19.9±4.6 (P<0.01)	0.79±0.13 (P<0.01)	168.3±12.6 (P<0.01)	639±0.6 (P<0.01)
Group-V	25-38 months	34.8±6.1 (P<0.05)	13.9±0.21 (P<0.05)	18.6±3.8 (P<0.05)	0.69±0.18 (P<0.05)	165.6±11.5 (P<0.05)	8.0±0.5 (P<0.05)

N.S. = Not Significant.

2%. Levels of LH, FSH and estradiol were elevated in women receiving injections for 28-38 months. The pregnancy-rate was 3%. The values were not significantly different when compared with control. A significantly increase in serum bilirubin, SAP, SGPT, SGOT, sodium and potassium levels were recorded in all treated groups as shown in Table 2. The control and experimental group did not show any difference in respect to blood glucose levels.

DISCUSSION

The present study showed that LH, FSH and estradiol levels were suppressed in women receiving injections for 19-24 months, which is in agreement with previously published reports. Nasal sprays of NET EN were well accepted and that no adverse clinical effects or menstrual disturbance occurred. NET EN inhibited ovulation and FSH and LH were also suppressed¹³.

Similarly, it has been reported earlier that FSH and LH were suppressed after the intramuscular injection of 150 mg and 30 mg of Depo-Provera in women¹⁴. Serum LH and FSH levels were suppressed during each of the six cycles of drug administration. Levels of serum estradiol were lower in women using combination of oral contraceptive contain al-norgestrel¹⁵.

The mechanism behind this suppression of gonadotrophin and estradiol in some groups is not very well understood. It could be due to individual difference in the rate of absorption at the site of injection. Another possible cause of suppressed gonadotrophin and estradiol could be high levels of NETEN in the circulation at the end of 19th months period (19-24 months group). Moreover, the occasional low values of circulating serum FSH, LH and estradiol confirms the absence of the ovulatory surge. However it is important to note that this observation can not be equaled entirely with the absence of ovulation.

A significant increase in SAP, SGPT and SGOT were noted in the present study which is contrary to the earlier findings. However a significant increase in AChE activity (acetylcholinesterase) and ACP (acid phosphatase) were recorded¹⁶. Significant alteration in blood pressure and weight gains were recorded in the present study which is again conforms the previous study¹⁷.

It is suggested that period of 19-24 months is the most effective one when the LH, FSH and estradiol levels undergo suppression and rate of pregnancy is curtailed. It appears that the duration of treatment is important as LH, FSH and estradiol levels were suppressed after 19-24 months treatment. Liver function test showed that norigest do have some adverse effect on liver. Sodium and potassium retention in the body is also a feature of this contraceptive which resulted in an increase in blood pressure and weight gains.

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