

THE EFFECTS OF ORAL CONTRACEPTIVES ON CARBOHYDRATE, LIPID, AND PROTEIN METABOLISM IN SUBJECTS WITH ALTERED NUTRITIONAL STATUS AND IN ASSOCIATION WITH LACTATION

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SUMMARY

The effect of levo-norgestrel (150 µg) combined with 30 or 50 µg of ethynyl oestradiol (EE₂) on serum lipids (cholesterol and triglycerides) serum proteins (total and albumin) and on glucose tolerance was studied in relatively undernourished women. Changes in lipids and proteins were transitory and within the physiological range, and occurred earlier with the 50 µg EE₂ pill. About 10% women in the 30 µg EE₂ group, and 17% in the 50 µg EE₂ group developed a diabetic curve (but the fasting glucose level was normal). The curve returned to normal within 3 months of discontinuation of oral contraception.

A study of metabolic effects of steroidal contraceptives is important since it provides useful guidelines for the development of safer, more effective preparations and for adapting suitable preparations for the respective populations. There have been several such studies reported on relatively well-nourished populations of the developed nations. Data on the interaction of malnutrition, infection and other health variables with the steroidal contraceptives are relatively few. A three centre trial, linked with an external quality control programme was started in 1975, by WHO.

In Bombay, 311 subjects recruited between June 1975 and April 1977, were randomly distributed into two groups, after an initial physical and biochemical investigation, anthropometry—weight, height, upper arm circumference, triceps skin fold thickness and blood parameters for carbohydrate, lipid protein metabolism, trace elements, vitamin status and haematology.

They were randomly distributed into two groups, Group 1 receiving a pill containing 150 µg laevo norgestrel (Ng) and 30 µg ethynyl estradiol (EE₂) (Pill A), and Group 2 receiving a pill (B) containing 150 µg Ng and 50 µg EE₂. The details regarding follow-up visits, status of lactation (always > 8 months) drop out, etc. are given in Tables 1 and 2. Since most of the drop-outs before completion of the study were unrelated to contraceptive *per se*, the data on only those who completed the study is discussed here.

The anthropometric parameters and some blood parameters indicated that the study population was relatively undernourished as compared to a reference population derived from Staff-members and their relatives (Table 3).

Fasting glucose levels remained the same after the contraceptives. Levels at 1 and 2 hours after a glucose load of 1 g/Kg body weight were significantly elevated in pill users. The effect was progressive with duration

Table 1. Number of women studied

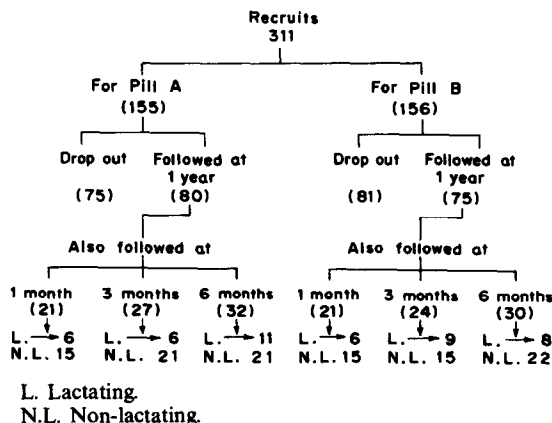


Table 2. Reasons for termination of cases enrolled for oral A and B pills

	A (155)	B (156)
Pregnancies*	21	22
Side effects†	9	12
Medical Reasons‡	5	6
Other (non-medical) reasons	40	41
Total	75	81

* Most pregnancies occurred before starting pills. Only 1 woman in pill 1 and 2 in pill B group became pregnant either because of irregular intake or in spite of regular intake.

† Not related to contraception.

‡ Minor side effects such as nausea, vomiting.

|| Hypertension viral hepatitis etc.

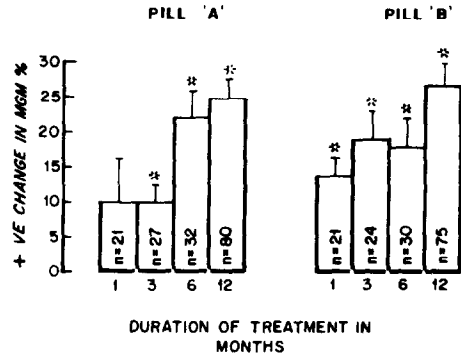


Fig. 2. Changes (mean \pm SEM) in plasma glucose (120 min after glucose load) in women on pill "A" and women on pill "B". * = Statistically significant.

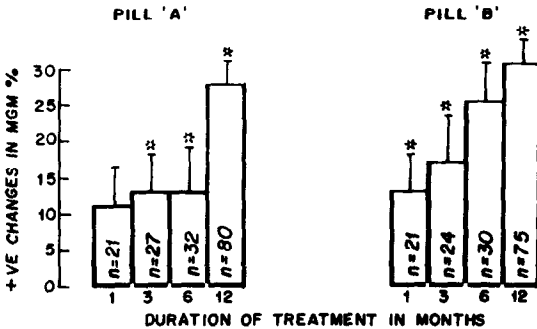


Fig. 1. Changes (mean \pm SEM) in plasma glucose (60 min after glucose load) in women on pill "A" and women on pill "B". * = Statistically significant.

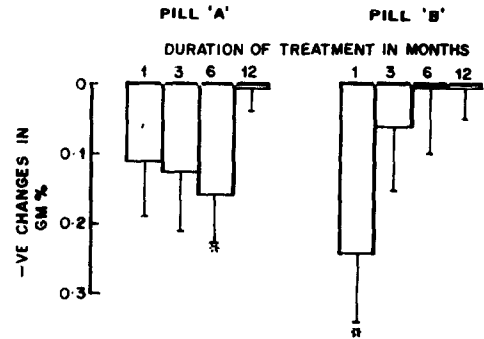


Fig. 3. Changes (mean \pm SEM) in total proteins in serum of women on pill "A" and women on pill "B". * = Statistically significant.

Table 3. Parameters showing statistically significant differences between reference and patient population

Parameter	Reference subjects (63)	Results in (mean \pm SD)	
		Lactating women (46)	Non-lactating women (109)
Plasma glucose (mg%) (2 Hr after glucose load)	106.2 \pm 22	88.8 \pm 17.3‡	89.8 \pm 18.0‡
Plasma triglycerides (mg%)	79.6 \pm 30.0	59.2 \pm 22.3†	67.5 \pm 26.0*
Erythrocyte glutathione reductase activity (Basal)	97.6 \pm 31.3 n = 48	58.4 \pm 20.2† n = 13	68.1 \pm 16.2‡ n = 34
Erythrocyte glutathione reductase activity % stimulation	18.8 \pm 19.2 n = 48	65.5 \pm 36.4‡ n = 13	47.8 \pm 41.6‡ n = 34
Wt/ht ² \times 100	0.207 \pm 0.02	0.188 \pm 0.02‡	0.180 \pm 0.02‡
Upper arm circumference (cm)	25.2 \pm 2.75	23.5 \pm 2.11*	23.2 \pm 2.14*
Triceps skinfold thickness (mm)	17.5 \pm 5.2	13.1 \pm 4.6†	12.0 \pm 4.1†

* $P < 0.05$.

† $P < 0.01$.

‡ $P < 0.001$.

Table 4. Glucose tolerance test results in women who developed a Diabetic curve during Levo-Norgestrel + Ethinyl oestradiol administration

Women studied at visit	No.	Serum glucose (Mean ± S.D.) in mg% at		
		0 hr	1 hr	2 hr
Initial	26	94 ± 10	133 ± 26*	98 ± 19†
Intermediate (1, 3 or 6 months)	26	93 ± 13	172 ± 28‡	129 ± 27§
Yearly	22	94 ± 9	192 ± 27	156 ± 27¶
3 months post-O.C.	11	93 ± 11	147 ± 42††	119 ± 26**

‡ and || significantly different from *.
 || significantly different from ‡.
 §, ¶ and ** significantly different from †.
 ¶ significantly different from §.

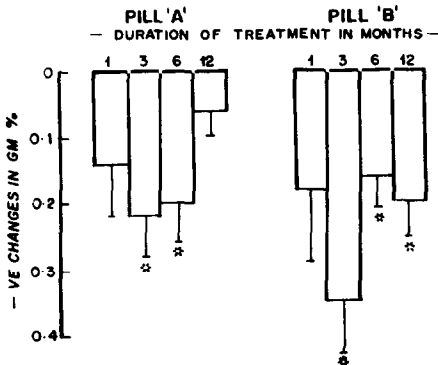


Fig. 4. Changes (mean ± SEM) in serum albumin in women on pill "A" and women on pill "B". * = Statistically significant.

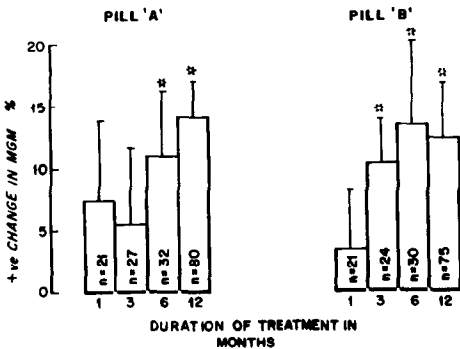


Fig. 5. Changes (mean ± SEM) in plasma triglycerides in women on pill "A" and women on pill "B". * = Statistically significant.

of time and was seen earlier in pill B users than in pill A users (Figs 1 and 2).

Eight out of 80 women on pill A and 13 out of 75 women on pill B developed a diabetic curve at

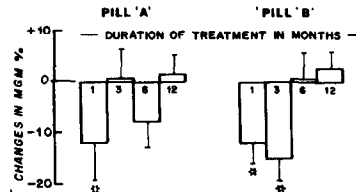


Fig. 6. Changes (mean ± SEM) in plasma cholesterol in women on pill "A" and women on pill "B". * = Statistically significant.

one time or other during treatment. Table 4 shows that the deterioration is progressive with time. However, values promptly returned to normal within 3 months of discontinuation of treatment.

Total proteins remained constant except for a transitory decrease which occurred earlier in pill B than in pill A users (Fig. 3). The decrease in albumin persisted in pill B users and returned to normal in pill A users at the end of 1 year (Fig. 4).

Plasma triglycerides were elevated, the rise being apparent earlier in pill B users (Fig. 5). The decrease in cholesterol was transitory (Fig. 6).

In conclusion, transitory changes in proteins and lipids may take place with the laevo-norgestrel and ethinyl oestradiol pills. The change is earlier with higher dose oestrogen oral contraceptives. However, the changes are within normal physiological limits. The incidence of abnormal glucose tolerance tests may be brought down by reducing the dose of oestrogens.

Acknowledgement—This report is on a part of work on a World Health Organization Task Force on 'Interaction of Oral Contraceptives with nutrition, infections and other health variables'. The following people have actively collaborated in the work: Dr. K. D. Virkar, Dr. V. Chowdhary, Dr. U. M. Donde.