CONCEPTION CONTROL BY MONTHLY INJECTABLE CONTRACEPTIVE

(A One Year Clinical Trial)

By

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SUMMARY

NET-OEN monthly injections have a contraceptice efficacy of 100%. Only minor changes in menstrual pattern were seen. Weight gain was seen in a few patients. Dropouts were mainly in first 2 months of therapy (7 cases), reasons being menstrual irregularity, cramps and pain in legs, chest pain and personal reasons. No effect on lactation was seen. Progestational effect was seen on vaginal cytology.

Introduction

Since the ideal contraceptive, one which is completely acceptable to all people has not yet been devised, the search for the same continues. A contraceptive administered as an injection each month, could provide a desirable alternative to daily oral medication, should it prove to be equally effective, safe, and accompanied by minimal side effects. This report will record our experiences with an injectable contraceptive regimen containing Nor-ethisterone Oenanthate (50 mg) (NET-OEN: pharmacologically 17 ethinyl-4 oestrone 3 one 17 ß Heptanoate) and Oestradiol Valerate (E_2 val) 5 mg given intramuscularly every 30 ± 2 days starting within first 5 days of menstrual cycle or within 48 hours of MTP. This preparation is prepared by Scherring A.G. Berlin and has been supplied to us by I.C.M.R. for country wide trial in connection with fertility control.

Material and Methods

Study was conducted on 80 patients selected by Systematic Random sampling method. (Every alternate case motivated for contraception was included in the study) from family welfare clinic and out patient department of Obstetrics and Gynaecology, U.I.S.E. Maternity Hospital, G.S.V.M. Medical College, Kanpur in the year 1984-85. All the cases were taken from urban locality keeping in mind the convenience of follow-up and regular visits of the cases. Intramuscular injections were given as per schedule. The cases were studied and followed-up regarding effects on menstrual pattern, weight B.P., reproductive system of patients and haematocrit. Side effects of the drug were analysed. Vaginal smear from lateral fornix was taken on 10th day of injection for assessment of cytohormonal pattern.

Results

Mean age of patients was 29.2 years, model parity was 2 and per capita income was Rs. 205.50 per month. 65% patients were educated upto college level. 20% upto High School level and rest less than this. Mean weight of cases was 50.5 kg. All the cases had normal menstrual pattern (cycle 25-35 days, duration—2-8

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days) before starting therapy, Menstrual cycle was classified as regular (between 25-35 days), irregular (36-59 days) amenorrhoea (60 days and above) polymenorrhoea (less than 25 days). During therapy 90-95% cases showed regular cycles and 10% cases showed polymenorrhoea in first and second months, which decreased to 5-13% during 3-4 months. Irregular cycles were seen in 5.13% and 6.45% cases in 3-4 months and 5-6 months respectively. Amenorrhoea occurred in 4.35% cases (1 case) at 7-10 months of therapy.

Majority of cases (95%) showed normal duration of flow in 1-2 months, this gradually decreased to 87% in 5-6 months, again increasing to 100% in 12 months. Duration less than 2 days was met with after first injection in 2.5% gradually increasing to 12.9% only upto 6 months and then no case was found. Bleeding more than 8 days was seen off and on from 2.5% to 7.69%.

Moderate flow was seen in 82.05% to 100% cases and scanty flow from 7.5% to 15.39% during the study. Profuse bleeding was seeni n 2.56% during 3-4 months and inter-menstrual bleeding was seen in 2.5% cases. Spotting was seen right from the start of therapy in 12.5% which gradually decreased to 5% in 10 months and

TABLE I

Showing Menstrual Patterns of Cases Taking 1 Monthly Injectable Contraceptive During 12 Months Period

Menstrual pattern	Duration of injection (months) per cent of cases					
	1-2	3-4	5-6	7-8	9-10	11-12
A. *Cycle length (days)*						
1. Less than 25 days (Polymen.)	10.00	5.13	—	—	—	7.69
2. 25-35 days (Reg. cycles)	90.00	89.74	93.55	95.65	95.00	92.31
3. 36-59 days (Irreg. cycles)	—	5.13	6.45	—	—	—
4. 60 and above (Amen.)	—	—	—	4.35	5.00	—
B. *Duration of flow*						
1. <2 days	2.50	10.26	12.90	—		4
2. 2-8 days	95.00	82.05	87.10	95.65	90.00	100.00
3. >8 days	2.50	7.69	—	—	5.00	—
4. Amen.	—	—	—	4.35	5.00	—
C. *Amount of flow:*						
1. Scanty	7.50	15.39	9.68	8.69	5.00	—
2. Moderate	92.50	82.05	90.32	86.96	90.00	100.00
3. Profuse	—	2.56	—	—	—	—
4. Amenorrhoea	—	—	—	4.35	5.00	—
D.						
1. Intermenstrual bleeding	2.50	—	—	—	—	—
2. Spotting	12.50	7.69	6.45	4.35	5.00	—
3. Dysmenorrhoea	—	—	—	—	5.00	—

no case having spotting was seen at 12 months. Dysmenorrhoea was seen in 1 case (5%) during 9-10 months (Table I).

No change in weight was seen in 75% cases, increase in weight in 22.5%, weight loss in 2.5% from 6 months and in 12 months, no change in 70%, weight gain in 25%, weight loss in 5% cases was observed (Table II).

TABLE II
Showing Change in Weight of Cases in 12 Months Period of Therapy

Change in weight	0-6 months percentage of cases	0-12 months percentage of cases
1. No change	75.0	70.0
2. *Weight gain*		
0-0.5	5.0	—
0.5-1.0	15.0	15.0
1.1-1.5	—	2.5
1.6-2.0	2.5	5.0
2.1-2.5	—	2.5
3. *Weight loss*		
0-0.5	—	—
0.5-1.0	2.5	2.5
1.1-1.5	—	2.5
1.6-2.0	—	—
2.1-2.5	—	—

B.P. was unchanged in 95%, increased in 5% cases in 12 months and did not decrease in any case. No adverse effect on reproductive system was seen. Main side effects complained by the patient were dizziness (25%), nervousness (17.5%), weekness (15%), cramps and pain in legs (15%), backache (15%), pain in chest (5%), nausea (5%), vague abdominal pain (2.5%) and breast tenderness in only 1 case (2.5%). No deleterious effect on lactation was seen (Table III).

22.5% (9 cases) dropped out during the study, 5 cases due to menstrual irregularity, 1 case due to cramps and pain in legs, 1 case due to chest pain and 2 cases for personal reasons.

None of the cases became pregnant during treatment indicating (100%) contraceptive efficacy.

Vaginal cytology showed shift to midzone (progestational change throughout the study, superficial cells were less in number and showed poor formation and dysplastic cells were not seen (Table III).

TABLE III
Showing Side Effects of Net OEN+E2 VAL During 12 Month Period

No.	Side Effects	No. of cases	%age
1.	Headache	8	10.0
2.	Dizziness	20	25.0
3.	Weakness	12	15.0
4.	Nervousness	4	17.5
5.	Cramps	12	15.0
6.	Pain in legs	2	2.5
7.	Vague abdominal pain	4	5.0
8.	Pain Chest	12	15.0
9.	Backache	4	5.0
10.	Nausea	—	—
11.	Leucorrhoea	2	2.5
12.	Breast tenderness	—	—
13.	Effects on Lactation	—	—

TABLE IV

Showing Vaginal Cytological Pattern During 12 Months Therapy with Net —OEN + E2 VAL. Injection

No. of cases	Time month	Intermediate Cells		Superficial cells		M.I.	Other
		Range	Mean	Range	Mean		
30	Before Therapy	30-42	37	58-70	63	0/37/63	Leukocytes
30	2 months	54-62	58	38-46	42	0/58/42	„
30	4 „	68-80	75	20-32	25	0/75/25	„
25	6 „	74-82	78	18-26	22	0/78/22	„
20	8 „	78-86	81	14-22	19	0/81/19	„
15	10 „	82-92	86	8-18	14	0/86/14	„
9	12 „	86-94	90	6-14	10	0/90/10	„

Discussion

There was good patient acceptance in clinic patients as the patients preferred to have the doctor to take the responsibility for her conception control. One can speculate that in many of the under developed areas, such control may be necessary and perhaps culturally desirable. In this study the cycle length was regular in majority of the cases, duration and amount of flow were normal in most of the cases. Polymenorrhoea, irregular cycles, amenorrhoea and spotting off and on were present in only a few cases. These findings are in accordance with those of Continhe and D'Souze (1968), Block and Davies (1978) and Koestsawang *et al* (1978-79).

Weight gain from 0.6-1.5 Kg was seen in 25 cases and weight loss of 0.6-1.5 Kg in 5% cases. These findings co-incide with those of Koetswang *et al* (1978-79) and Block and Davies (1978). No significant change was found in B.P. in our cases as also observed by Block and Davies (1978). Koetsawang *et al* (1978-79). Pregnancy was not seen in any case in our study Block and Davies (1978), Scommegna *et al* (1970) also observed this during trial with cycloprovera and Depoprovera respectively (monthly injections). No adverse effect was seen on lactation. Similar findings were observed by Continhe *et al* (1968) and Population reports (1983).

Only a few of our patients had side effects like dizziness, nervousness, weakness, cramps and pain in legs backache, pain in chest, nausea and breast tenderness as also observed by Scommegna *et al* (1970), where as Flores *et al* (1984) could only notice side effects like nausea, vomiting and break through bleeding in their study and the reason they suggested was rapid absorption of E_2 resulting in oestrogen induced bleeding.

Vaginal smear showed a mid zone shift (progestational effect) with poorly formed few superficial cells suggesting low oestrogen production (through gonadotrophic inhibition) or due to exogenous progestogen overwhelming end organ effect of normal levels of circulating oestrogen. Nieves and Andino (1981) found an abolished FSH and LH peaks, with a normal basal level. There is an initial inhibition of ovulation co-inciding with very high plasma progesterone levels. The major action probably is suppression of oestrogen induced positive feed back mechanism.

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