EVALUATION OF NOR-ETHISTERONE OENANTHATE 200 mg (NET-OEN) 2 MONTHLY INJECTABLE CONTRACEPTIVE IN 12 MONTHS PERIOD

By

R. S. Misra, Preety Dubey, Ajai Bhagoliwal, P. Rohatgi and Manjubai Agarwal

SUMMARY

(NET-OEN) 200 mg, 2 monthly injections are safe contraceptives with few side effects, no adverse effects and having an efficacy rate 100%. The main side effects although, are menstrual irregullarities but an advantageous effect is amenorrhoea or scanty periods, so is highly recommended in patients having a heavy flow. They are an improvement over other long acting injectables like D.M.P.A.

Introduction

Although IUCDS and oral pills have been in use for 3-4 decades, their drawbacks are known and are not well suited for rural population of developing countries, Nor-Ethisterone oenanthate (NET-OEN) chemically 17-ethinyl oestrone-3-one-17 Heptanoate provided as an oily solution (Benzyl benzoate: eastor oil in ratio of 6:4 1 ml. contains 200 mg. of NET-OEN) given 2 monthly, intramuscularly in deep gluteal muscles between 1-5 days of menstrual cycle or within 48 hrs. of MTP, is an effective contraceptive agent. It is provided in a disposable syringe to prevent the possibility of leakage of oily solution from syringe. The preparation is formulated and manufactured by Scherring A.G. Berlin.

Material and Methods

80 patients having normal menstrual pattern (cycle 25-35 days, duration 2-3 days, flow-moderate) attending family welfare clinic and Gynaecology out patients department of U.I.S.E. Maternity Hospital, G.S.V.M. Medical College, Kanpur were studied in year 1984-85 and the cytological work was carried out in the Pathology Deptt. Menstrual record was maintained by the patient on menstrual diary card provided to her. The cases were studied and followed up regarding effects on menstrual pattern, weight B.P. and reproductive system of patients and side effects of the drug, dropouts and cause of discontinuation were analysed. Effects on haematocrit and vaginal cytology for M.I. and effect on morphology of superficial cells were also studied.

Results

The cases under study had a mean age of 27.5 years model parity of 2, mean weight, was 50.4 kg. Cases had normal menstrual pattern before start of therapy, (cycle length 25-35 days duration 2-8

From: Department of Obstetrics and Gynaecology, GSVM Medical College, Kanpur.
Accepted for publication on 21-9-87.

days, flow moderate). During administration irregularity in cycles was observed decreasing from 65%, cases after first injection to 22.22% in 12 months. Polymenorrhoea was seen in 20% cases right from start of injection but it's incidence decreased with passage of time. Irregular cycles (36-59 days) increased from 15% to 55.56% in 12 months. Amenorrhea (Cycle 60 days and more) was found from 3rd month in 10.26% and it's incidence increased to 22.22% in 12 months. Duration of flow was normal (2-8 days) in 80% cases after 1st injection but only 55.56% cases retained normal pattern in 12 months. Scanty periods (duration less than 2 days) were observed in 22.22% in 12 months in constrast to 7.5% after first injection. Bleeding more than 8 days was seen only upto first 6 months of therapy from 12.5% after 1st month to 5.88% in decreasing order. The percentage of cases having moderate bleeding decreased from 80% to 33.33% in 12 months period and flow became scanty in 48.45% compared to 15% cases after 1st month of injection. Profuse bleeding was observed only upto first 6 months. Intermenstrual bleeding and spotting was frequent with NET-OEN throughout the study period (Table I).

In majority of cases (77.5%) no

TABLE I

Showing Menstrual Pattern of Cases During 12 Months Therapy With Net—On

Menstrual Pattern	Duration of Injection in months					
	1-2	3-4	5-6	7-8	9-10	11-12
	Percentage of cases					
(A) Cycle Length (in days)						
1. 25 days (Polymenorrhoea)	20.00	12.82	8.82	4.76	5.88	—
2. 25-35 days (Regular)	65.00	43.59	35.29	33.33	29.41	22.22
3. 36-59 days (Irregular)	15.00	33.33	44.12	47.62	47.06	55.56
4. 60 days and above (Amenorrhoea)	—	10.26	11.77	14.29	17.65	22.22
(B) Duration of flow (days)						
1. 2 days	7.50	12.82	14.71	19.04	23.53	22.22
2. 2-8 days	80.00	71.79	67.65	66.67	58.82	55.56
3. 8 days	12.50	5.13	5.88	—	—	—
4. Amenorrhoea	—	10.26	11.76	14.29	17.65	22.22
(C) Amount of flow						
1. Scanty	15.00	25.64	29.41	33.33	35.29	44.45
2. Moderate	80.00	53.84	52.94	52.38	47.06	33.33
3. Profuse	5.00	10.26	5.88	—	—	—
4. Amenorrhoea	—	10.26	11.77	14.29	17.65	22.22
(D) Miscellaneous						
1. Inter menstrual bleeding	5.00	5.13	5.88	4.76	—	—
2. Spotting	27.50	23.08	20.59	14.29	11.76	11.11
3. Dysmenorrhoea	—	—	—	—	—	—

change in weight was seen, weight gain or loss was observed in a small percentage only (Table II).

TABLE II

Showing Change in Weight of Cases During 12 Months Therapy With Net-Oen

Change in Weight (Kg.)	0-6 months %	0-12 months %
1. No change	77.5	77.5
2. *Wt. Gain*		
0-0.5	2.5	2.5
0.6-1.0	15.0	15.0
1.1-1.5	—	5.0
1.6-2.0	—	—
2.1-2.5	—	—
3. *Wt. Less*		
0-0.5	—	—
0.6-1.0	2.5	—
1.1-1.5	—	—
1.6-2.0	2.5	—
2.1-2.5	—	—

No significant change in B.P. was seen in any of the cases and no adverse effect was seen on the reproductive system. Main side effects encountered were dizziness in 22.5% cases, weakness (12.5%) nervousness (7.5%), cramps and pain in legs (in 10%) cases, vague abdominal pain (in 10% cases), backache (in 10% cases). Other side effects like headache, pain in chest, (in 1 case), leucorrhoea were seen in a few cases only. The drug had no effect on lactation in any cases. Breast tenderness was not observed in any case. 8 cases dropped out during the study period, reasons for discontinuation were menstrual irregularities in 6 cases. Pain in chest 1 case, personal reasons in 1 case (Table III).

Significant changes in Hb%, platelet count, BT, CT, was observed in the study period, none of the cases became

TABLE III

Showing Side Effects of Injectable Contraceptive (Net-Oen) Under Study During 12 Months Period

S. No.	Side effects	No. of cases	%
1.	Headache	2	2.5
2.	Dizziness	18	22.5
3.	Weakness	10	12.5
4.	Nervousness	6	7.5
5.	Cramps pain in legs	8	10.0
6.	Vague abdominal pain	8	10.0
7.	Pain in chest	2	2.5
8.	Backache	8	10.0
9.	Nausea	—	—
10.	Leucorrhoea	2	2.5
11.	Breast tenderness	—	—
12.	Effect on lactation	—	—

pregnant during study period (100% contraceptive efficacy). Vaginal cytology showed a mid zone shift in MI with a preponderance of intermediate cells, superficial cells were less in number and showed poor formation. No dysplastic cell was seen in any case (Table IV).

Discussion

NET-OEN injection given at 60-65 days interval were 100% effective contraceptive agents in our study as seen by I.C.M.R. (1984) with the same schedule, W.H.O. (1978) and W.H.O. (1983) found 3.6 pregnancy/100 women years, when injections were given at 90 days and 84 days respectively.

Menstrual period with NET-OEN in our study showed decreasing percentage of regular cycles, with increasing incidence of irregular cycle (36-59) days amenorrhoea (60 days) and scanty flow (2 days) and decreasing incidence of polymenorrhoea, intermenstrual bleeding and spotting. Our findings are consistent with those of W.H.O. (78-83) and population reports (1983). The decrease

TABLE IV

Showing Vaginal Cytological Pattern During 12 Months Therapy With Net-Oen

No. of cases	Time (months)	Intermediate Cell		Superficial cells		M.I.	Other cells
		Range	Mean	Range	Mean		
60	Before therapy	30-42	35	58-70	65	0/35/65	Leuco-cytes
60	2 months	55-65	60	35-45	40	0/60/40	„
60	4 months	62-78	71	22-38	29	0/71/29	„
50	6 months	70-86	80	14-30	20	0/80/20	„
40	8 months	76-90	84	10-24	16	0/84/16	„
30	10 months	84-96	91	4-16	9	0/91/9	„
10	12 months	94-98	96	2-6	4	0/96/4	„

in amount of bleeding and increased tendency towards amenorrhoea can be explained easily by the fact that endometrium becomes thin and atrophic with continued use of progestins.

No adverse effect was seen on weight B.P. haematocrit, reproductive system, lactation. Side effects were few like menstrual irregularity, dizziness weakness, nervousness, cramps, pain in legs, vague abdominal pain, headache, backache, leucorrhoea and chest pain. Drop-outs in our study were due to menstrual irregularity mainly chest pain in 1 case, Virutamasen *et al* (1980) however observed vertigo, vomiting nausea, vagina discomfort, insomnia, which were not seen in any of our cases.

Vaginal smear in our study showed a midzone shift suggestive of progestational change with poorly formed superficial cells, and no dysplastic cell. Same findings were observed by Zanartu and Navano (1968) and Mitra *et al* (1976). This effect is probably due to high plasma progesterone which possibly is associated with ovulation inhibition caused by suppression of oestrogen induced positive feed back mechanism as evidenced by low percentage of superficial cells in vaginal smears through out the study.

This hypoestrogenism may also produce atrophic endometrium, so nidation cannot take place.

References

1. Mitra, R. and Bai, K. Sunanda: J. Obstet. Gynec. India, 26: 70, 1976.
2. Population reports: Long acting progestins promise and prospects—Population reports series K. No. 2, May 1983 p. 18.
3. Virutamasen, P., Nisichai, V., Tang Keow, P., Kankeerati, W., Riem Prayuran, P. and Doon Siri, B.: Contraception, 22: 397, 1980.
4. W.H.O., Contraception, 17: 395, 1978.
5. W.H.O., Contraception, 28: 1, 1983.
6. Zanartu, J. and Navaro, C. J.: Obstet. Gynec. 31: 627, 1968.