

COMPARATIVE EVALUATION OF TWO ONCE - A - MONTH CONTRACEPTIVE INJECTIONS

Pages with reference to book, From 98 To 102

Afroze I. Kazi (National Research Institute of Fertility Control, Population Welfare Division, Karachi.)

Abstract

Two once-a-month preparations cyclo provera (Depo-medroxy Progesterone Acetate 25 mg and Estradiol Cypionate 5 mg) and HRP - 102 (Norethisterone enanthate 50 mg and Estradiol Valerate 5 mg) Were tried in two groups of Women by random allocation, and their effectiveness, complaints and reasons for discontinuation were studied. A total of 206 women were admitted (104 Dn cyclo provera and 102 on HRP-102) and studied for one year. There was little difference in the efficacy and side-effects between the two preparations. One pregnancy occurred with HRP-102 giving a pregnancy rate of 1.4%. The overall discontinuation rates at 1 year were 57.6% for cycloprovera and 54.9% for HRP - 102. The discontinuation rates for bleeding irregularities, were 21.2% and 21.8% respectively for cycloprovera and HRP - 102. Five women discontinued due to lack of bleeding or amenorrhoea. The respective figures were 4 and 1 for cyclo provera and HRP-102. Both products were highly effective and, if introduced in the national Family Planning Programme, they will fulfill an important role (JPMA 39 ;98, 1989).

INTRODUCTION

Injectable steroids are being used as contraceptives since the last 25 years. The two most widely used preparations are Depo-provera and Norigest. These injections are given three monthly in doses of 150 mg and 200 mg respectively. One of the major side-effects of these Progestogen only contraceptives is disruption of the bleeding pattern. The' subjects experience unpredictable bleeding episodes or amenorrhoea¹. To counteract this problem some investigators started to incorporate oestrogen. To avoid large doses of long-acting oestrogens small amount was used resulting in reduction of the acting time to one month. The shorter acting oestrogens together with progestogens were thus supposed to give better cycle control. This combination was tried by certain investigators in mid seventies^{2,3}. The WHO decided to have a multicentered trial in which efficacy and side-effects of two once a month preparations — cyclo-provera and HRP— 102 were studied. In this paper the experience in Paldstan is being presented.

MATERIAL AND METHODS

Cyclo-provera manufactured by Upjohn Company, micro-crystalline suspension containing Medroxy progesterone acetate 25 gm and Oestradiol cypionate 5 mg. HRP-102 contains Norethisterone enanthate 50 gin and estradiol valerate 5 mg and is manufactured by the Schering A.G. Berlin. Both preparations were given every 30 ± 3 days as deep intramuscular injections. Normal healthy women between the ages of 10-35 years were selected. They were not pregnant, not lactating and had regular menstrual cycles. Women having diabetes, pap smear of grade-III or higher, history of thromboembolisin, irregular vaginal bleeding, confirmed hypertension or severe and recent liver disease or suspected malignancy were excluded. Women Who had received DMPA or Net-en injections 6 months prior were also excluded. The women were asked to come for injections during the first five days of their menstrual cycle and after a screening interview and a proper physical examination they

were given the first injection by random allocation to any of the treatment groups. For follow-up they were asked to return after 30 ± 3 days. Every 3 months they had a physical examination and their weight and blood pressure were recorded. The subjects were also given a card to record their menses. At every visit their complaints were also elicited and recorded.

RESULTS

Admissions were started in October, 1984. Two hundred and six women were admitted and followed up for one year.

Admission Characteristics (Table I).

TABLE – 1 . Admission Characteristics by Injection Type.

		Injection type		All Women
		Cyclo- provera	HRP-T02	
Age in years	N	104	102	206
	Mean	27.0	27.1	27.0
	SD	3.9	3.8	3.8
Weight in Kg.	Mean	50.7	50.5	50.6
	SD	10.9	9.4	10.2
Height in m.	Mean	1.53	1.53	1.53
	SD	0.06	0.05	0.06
Ponderal Index	Mean	2.15	2.15	2.15
	SD	0.44	0.39	0.42
Systolic blood pressure	Mean	110.0	109.2	109.6
	SD	9.9	10.9	10.4
Diastolic blood pressure	Mean	71.3	72.0	71.6
	SD	8.1	8.7	8.4

The 2 groups were very similar with respect to age, weight, height and blood pressure. The average age was 27 years, weight 50.6kg, height 1.53 meters and mean systolic and diastolic blood pressure was 109.6 and 71.6 mm Hg/respectively.

Previous use of Contraceptive (Table-II)

TABLE II. Previous use of Contraceptives by Injection Type.

	Injection type		All Women
	Cyclo-provera	HRP-102	
All Women	104	102	206
Previous contraception			
... None	79	68	147
... Pill	3	1	4
... IUD	9	10	19
... Injectable	2	4	6
... Condom	11	19	30

One hundred and forty seven women had not used any contraceptive previously and only 59 had used some contraceptive before the injections. Among them 19 used IUD, 30 condoms and 4 used oral pills. Only 6 women had used injections.

Contraceptive efficacy:

There was one pregnancy due failure in a woman of 30 years using The woman became pregnant 3 days second injection was due. She received her third injectiontras she had a bleeding episode after 2nd injection and pregnancy was not suspected at that time. This woman was followed up and she gave birth to a normal healthy infant at term. The pearl index calculated was J.4 per 100 women years for HRP-102 (Table-III).

TABLE III. Experience and Pearl Index for Pregnancy .

Experience Measured As:	Injection type		All Women
	Cyclo- provera	HRP-102	
Women	104	102	206
Months	823	837	1661
Average Months	7.9	8.2	8.0
Years	68.6	69.8	138.4
Pregnancies	0	1	1
Pearl Index	0.000	1.432	0.722
Lower CI Bound	.	0.000	0.000
Upper CI Bound	.	4.240	2.138

Reasons and Rates for Discontinuation

Two hundred and six women were admitted to the study, 104 on cyclo-provera and 102 on HRP-102. Ninety women reached the end of study which was at 12 months. 11 women were lost to follow-up and 3 women were discontinued as they came late for injection. The remaining women discontinued use for reasons given in Table-IV.

TABLE-IV. Study Termination Reasons.

Termination Reason	Injection type		All Women
	Cyclo-provera	HRP-102	
end of Study	44	46	90
... Amenorrhoea	4	1	5
... Bleeding - Heavy	1	4	5
... Bleeding - Prolonged	5	2	7
... Bleeding - Heavy/ Prolonged	3	3	6
... Bleeding-Irregular	4	3	7
... Spotting	1	2	3
... Other Bleeding Problem	3	4	7
... Pregnancy - Involuntary	.	1	1
... Other Medical Reasons	10	12	22
... Desires Pregnancy	1	2	3
... No Longer Needs	.	2	2
... Other Personal Reasons	15	9	24
... Moved Away	6	2	8
... N.P. - Too late to FUP	3	-	3
... Lost-to-FUP	3	8	11
... N.P.-Medication	1	1	2
All Terminations	104	102	206

The cumulative discontinuation rates were 57.6% for cyclo-provera and 54.9% for HRP- 102. 21.2% cyclo-provera users discontinued due to bleeding irregularities while 6.1% discontinued due to amenorrhoea. Among HRP-102 users 21.8% discontinued due to bleeding disturbances and 1.9% due to amenorrhoea. There were no pregnancies in cyclo-provera users while 0.9% of HRP - 102 users discontinued due to involuntary pregnancy. 3.3% of cyclo-provera users and 10.2% of HRP users were

lost to follow-up. The discontinuation rates are given in Table-V.

TABLE V. Cumulative Discontinuation Rates % Main Categories.

Discontinuation Reason	CENTRE			
	All Centres		Karachi	
	Cyclo-provera	HRP-102	Cyclo-provera	HRP-102
...Involuntary Pregnancy		0.9		0.9
...Bleeding irregularities	21.2	21.8	21.2	21.8
...Amenorrhoea	6.1	1.9	6.1	1.9
...other medical reasons	12.1	15.2	12.1	15.2
...Non medical reasons	32.4	21.7	32.4	21.7
...Lost to follow-up	3.3	10.2	3.3	10.2
...Overall	57.6	54.9	57.6	54.9

Bleeding Irregularities and Amenorrhoea

Thirty five women discontinued due to bleeding problems. Among them 17 were using cyclo-provera and 18 HRP - 102. These women complained of heavy bleeding, prolonged bleeding, heavy and prolonged bleeding, irregular bleeding and spotting. The discontinuation rates for this reason were 21.2% and 21.8% respectively for cycloprovera and HRP respectively. A total of women discontinued due to lack of bleeding or amenorrhoea. Of these women, 4 had received cycloprovera and 1 HRP-102. Thus 6.1% cycloprovera users. 1.9% HRP-102 users discontinued the method due to amenorrhoea.

Other Reasons

A total of 22 women discontinued for other medical reasons, which included weight gain, hypertension and giddiness. 53 women discontinued due to personal reasons which included desire for pregnancy, no further need for contraception, leaving the city, or being late for follow-up. In addition 11 women were lost to follow-up and could not be traced.

Complaints

At the followup visits the subjects were asked if they had any complaints. A total of 1647 visits were made and the complaints recorded. On the 1st and 2nd follow-up visits, in order of importance, 140 and 126 women or 683% and 663 % had no complaints while the remaining complained of bleeding, amenorrhoea, dizziness and headache and other medical problems. Thirty nine women on 1st visit and 34 women on 2nd visit complained of bleeding irregularity but this may be due to the clinic personnel not explaining to them that the 1st period comes 15-16 days after the 1st injection. The number of those complaining of this problem decreased with the passage of time. When the two drugs are compared with regards to complaints there is hardly any difference between the two. With HRP - 102, 20 women had some bleeding problem on 1st visit while with cyclo-provera 19 women had similar complaints. With HRP 1 woman complained of amenorrhoea on 1st visit and 5 on 12th visit while with cyclo-provera the number was 2 and 2 respectively. On 3rd visit one woman complained of reduction in the size of breasts (Table VI).

TABLE -VI. Complaints at Follow-up Visits.

1st Complaint at each visit		Follow-up Visit												
		S01	S02	S03	S04	S05	S06	S07	S08	S09	S10	S11	S12	UV1
Dosages Together	All Visits	205	190	172	160	146	134	126	118	109	99	94	91	3
	Complaint This Visit?													
	...None	140	126	117	103	101	75	89	77	73	70	67	67	.
	...Bleeding	39	34	28	26	24	30	17	15	16	16	12	15	1
	...Other Medical	16	21	15	17	11	18	11	12	10	4	6	2	1
	.. Amenorrhoea	3	5	6	6	4	7	4	5	6	7	6	7	.
	...Headaches/dizziness	7	4	5	8	6	4	5	9	4	2	3	.	1
	...Breast related	.	.	1
HRP 102	All Visits	101	95	87	82	75	69	64	60	53	50	48	46	.
	Complaint This Visit?													
	...None	69	65	59	53	51	41	46	42	36	39	34	31	.
	...Bleeding	20	14	17	14	15	17	10	7	7	6	7	9	.
	...Other Medical	8	11	7	7	6	9	5	5	5	2	2	1	.
	...Amenorrhoea	1	3	3	4	2	2	1	2	2	3	4	5	.
	...Headaches/dizziness	3	2	1	4	1	.	2	4	3	.	1	.	.
Cycloprovera	All Visits	104	95	85	78	71	65	62	58	56	49	46	45	3
	Complaint This Visit?													
	...None	71	61	58	50	50	34	43	35	37	31	33	36	.
	...Bleeding	19	20	11	12	9	13	7	8	9	10	5	6	1
	...Other Medical	8	10	8	10	5	9	6	7	5	2	4	1	1
	...Amenorrhoea	2	2	3	2	2	5	3	3	4	4	2	2	-

DISCUSSION

206 women were admitted to the study and followed for 12 months. The two types of drugs were similar in their efficacy and side-effects. One pregnancy occurred in a subject using HRP-102 giving a pregnancy rate of 1.4 per 100 women years. Both drugs are, therefore, highly effective contraceptives. When ' overall discontinuation rates are compared there is no difference between the two types of drugs. Similar studies were conducted in 16 other countries. Discontinuation rates due to bleeding

problems were highest in Karachi, Rome and San Luis, while no discontinuations were reported for these reasons in Jakarta and Valdivia. This negates the presumption that Karachi subjects being Muslims cannot tolerate irregular bleeding, as the population of Jakarta is also predominantly Muslim. Amenorrhoea as a cause for discontinuation was high in Alexandria, Karachi and Durango while no subjects discontinued for amenorrhoea in Bangkok, Jakarta and Mexico city. ⁴ While cultural attitudes play an important role in the use of different contraceptive methods, the behaviour of clinic staff, the time given to the subjects and the counselling given to them also contribute in the continuation of any method. Comparing the overall discontinuation rates of the two once a month preparation with the discontinuation rates in women using Depomedroxy progesterone acetate 3 monthly and Norethisterone enanthate 2 monthly, we find that the overall discontinuation rates were lower with once-a-month preparations⁵. The discontinuation rates at 12 months for Depo-provera and Norethisterone enanthate were 69.8% and 65.8% respectively. One of the major reasons for adding Oestrogen was to see if there was any improvement in the control of vaginal bleeding. Though the subjects do not have normal bleeding there was some improvement in the overall bleeding pattern. The once-a-month preparations are highly effective and they significantly reduce the bleeding problems associated with long acting progestogen only contraceptives. They have a drawback of monthly visits to the clinic. It is hoped that if introduced in the Family Planning Programme of the country they will fulfil an important role.

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