Parenteral Medroxyprogesterone as a Contraceptive Agent

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DEPOT-medroxyprogesterone acetate is a long-acting steroid supplied for parenteral administration as Depo-Provera (*A*). DMPA has been used since 1958 for the treatment of endometriosis and threatened or habitual abortion. In 1962, it was observed to produce post partum sterility in women treated for threatened abortion. Based on this observation, Coutinho and co-workers began clinical trials with DMPA as a female contraceptive (*1*). Mishell and associates (*2*) and Zanartu and associates (*3*) also reported on its effectiveness and side effects. [This drug has not yet been approved by the Federal Drug Administration, Consumer Protection and Environmental Health Service. Ed.] Prompted by these reports, we began to administer 150 mg. of DMPA every 3 months to women attending the Emory University Family Planning Clinic at Grady Memorial Hospital, Atlanta, Ga.

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Clinic Setting

The Family Planning Program of Emory University, a grant-supported program, has operated a service at Grady Memorial Hospital since the 1930's. It primarily provides for the initiation of contraception for women receiving 6-week post partum examinations. It also, however, provides contraceptive services for women who are eligible for treatment at Grady Memorial Hospital, the charity hospital for Fulton and De Kalb Counties.

Methods

In April 1967, 150 mg. of depot-medroxyprogesterone every 3 months was introduced as a contraceptive method in this clinic. Initially, we gave DMPA only to those women who had experienced contraceptive failures with oral contraceptives, intrauterine devices, or both. Later it was also given to other women whom staff physicians considered unlikely to be able to use pills or intrauterine devices successfully.

We reviewed the charts of women entering the study between April 1967 and December 1968 for demographic data and information on the contraceptive and medical difficulties en-

countered with this form of contraception. Review of the charts was delayed until February 1969 to allow time for the resolution of questions pertaining to events which occurred during the period of the study. Our method of analysis was a modification of the life table that Tietze used for analysis of the effectiveness of intrauterine devices (*4*). Since DMPA was available only at Grady Hospital, we assumed that patients lost to followup had discontinued this method 3 months after their last injection.

Results

None of the 723 patients for whom treatment with medroxyprogesterone was begun between April 1967 and December 1968 became pregnant. Seventy-three received DMPA for contraception until they could have either a tubal ligation or a hysterectomy. These 73 were eliminated from further analysis. The remaining 650 patients had a total of 5,082 woman-months of experience with this method of contraception. Table 1 shows the distribution of the 650 by age, number of living children, and marital status.

The cumulative net discontinuance rates at the end of 1 year for the 650 women, according to reason for termination of the drug, were as follows:

Reason for termination	*Rate per 100 women*
Irregular vaginal bleeding	13.5±1.8
Amenorrhea	2.8± .8
Other medical	5.5±1.2
Nonmedical	14.6±1.9
Unkown (lost to followup)	6.8±1.3
Total terminated at end of year	43.2
Active at end of year	56.8±2.6

Bleeding and amenorrhea. At the end of 1 year, 71 women, or 13.5 per 100 who began use of DMPA, had stopped using the drug because of abnormal bleeding. Fifty-one women required treatment at least once for abnormal bleeding. Only three patients needed treatment more than twice. Some of the women who needed such treatment are included in the 71 who discontinued use of DMPA. The rates of first treatment with estrogens among the women using DMPA are shown in table 2, by ordinal months from the first injection with DMPA. Calculations based on life tables were used to arrive at the denominator data for these rates.

The net cumulative rate of discontinuance of DMPA on account of amenorrhea was 2.8 per 100 women who began the use of medroxyprogesterone. In addition, four women required treatment with estrogens to produce withdrawal bleeding.

Other medical reasons for stopping DMPA. A total of 31 patients stopped using DMPA for medical reasons other than bleeding and amenorrhea. Although some of these reasons may not necessarily be related to the medication, they are included here for data analysis. These other medical reasons for discontinuance, according to the number of patients affected, were as follows:

Reason for stopping DMPA	*Number of patients*
Nausea	11
Excessive weight gain	5
Nervousness	4
Headache	3
Pregnant at time of first injection	3
Rash	2
Pelvic inflammatory disease	1
Hypertension	1
Vaginitis	1
Total	31

Table 1. Demographic characteristics of 650 patients using depot-medroxyprogesterone as a contraceptive

Characteristics	Number of patients	Percent of total
Age (years):		
0–14	13	2.0
15–19	110	16.9
20–24	174	26.7
25–29	136	20.8
30–34	121	18.7
35–39	68	10.6
40–44	26	4.0
45 and over	2	.3
Living children (number):		
0	38	5.8
1	91	14.0
2	126	19.3
3	96	14.7
4	70	10.7
5	70	10.7
6	32	5.1
7	47	7.4
8 or more	80	12.3
Marital status:		
Married	325	50.2
Single	160	24.5
Separated	136	20.9
Divorced	21	3.2
Widowed	8	1.2

Table 2. Rate of estrogen treatment for bleeding among women using depot-medroxyprogesterone acetate

Number of injections	Ordinal months from first injection	Woman-months of experience in period	Number of women requiring treatment for bleeding	Rate of treatment per 100 woman-months	Rate of treatment by number of injections per 100 woman-months
1	1	638. 0	6	0. 94	5. 31
	2	596. 5	15	2. 51	
	3	535. 5	10	1. 86	
2	4	472. 5	8	1. 96	3. 72
	5	418. 5	4	. 95	
	6	369. 5	4	1. 08	
3	7	326. 0	0	0	. 35
	8	283. 5	1	. 35	
	9	246. 5	0	0	
4	10	207. 0	0	0	1. 26
	11	169. 5	1	. 58	
	12	146. 0	1	. 68	

Nonmedical reasons for stopping DMPA. Seventy-six of the 650 women studied discontinued depot-medroxyprogesterone acetate for such nonmedical reasons as spouse's objection to the method, fear of sterility, and change of marital status. The cumulative net rate of discontinuance for nonmedical reasons per 100 women at the end of 1 year was 14.6. A tabulation of the nonmedical reasons for discontinuance follows.

Reason	*Number of patients*
Moved from Atlanta area	23
Lack of transportation	11
Doesn't need birth control	8
Fear of sterility	6
Desires another method	4
Unable to leave job	3
Unable to obtain babysitter	3
Cannot afford clinic visit	3
Spouse objects to method	3
Forgot appointment	2
Decreased libido	2
Loss of hospital eligibility	2
Miscellaneous	6
Total	76

Patients lost to followup. We were unable to contact 28 patients. For Grady patients, the only source of DMPA is Grady Hospital. For this reason, any patient lost to followup was assumed, for the purpose of data collection, to have discontinued the drug 3 months after her last injection.

Discussion

The cumulative net continuance rate for depot-medroxyprogesterone at the end of 1 year was 56.8 per 100 women with first injections of DMPA. Moreover, P. C. Schwallie, M.D., has pointed out, in a personal communication in August 1967, that the net cumulative continuance rate probably understates the total demographic effectiveness of this method since the lower limit of action of one injection is 3 months. Also, the largest number of our patients who discontinued the drug did so for nonmedical reasons. Approximately 28 of the 76 women who discontinued for nonmedical reasons probably would have continued taking DMPA if it had been widely available. To our knowledge, ours is the first analysis of this method of contraception with calculations based on life tables.

No conceptions occurred in 5,082 woman-months of use of DMPA. Other authors have reported a pregnancy rate of 0.5 pregnancies per 100 woman-years (*2*, *3*). Probably none of the women in our study who were lost to followup became pregnant either, since all of them who had been pregnant previously came to Grady Memorial Hospital for obstetrical care. In addition, Wright has pointed out that, of 424 visits to physicians by patients who were using a method of contraception originally obtained at Grady Hospital, only two visits, or 0.5 percent, were made to private physicians (*4*).

The primary medical reason that patients stopped using DMPA was abnormal bleeding. Of our 650 patients, 51, or 7.8 percent, required treatment at least once for this complication, Treatment consisted of diethylstilbesterol, 0.1 mg. per day for 20 days. This result is consistent with Schwallie's observation, in his August 1967 communication, that the amount of abnormal bleeding a patient experiences after receiving

DMPA decreases with each injection. Bleeding is the most important block to acceptance of DMPA by either physicians or patients.

The other frequent medical complaint is amenorrhea. Mishell indicated that with continuous progesterone stimulation, endometrial atrophy will eventually occur (*5*). In our patients, amenorrhea was less common than irregular menses. As mentioned previously, some patients discontinued DMPA because of medical reasons which were perhaps not related to this drug. Apparently, however, nausea and vomiting, as well as "nervousness," may well be related to its use. The discontinuance of DMPA by two patients because of a possibly allergic rash indicates that this etiology should be considered in the differential diagnosis of women with allergic dermatitis. The cumulative net rate of continuance of DMPA compares favorably with the rate of 63.8 calculated by Wright for the Lippes Loop D in the same population (*6*). It is better than the 51 percent 1-year continuance rate for oral contraceptives cited by Wright in an earlier publication (*7*).

Conclusion

Although abnormal menses, including amenorrhea, limit the use of depot-medroxyprogesterone acetate as a contraceptive, its high rate of effectiveness—comparable to the theoretical effectiveness of oral contraceptives—and its high continuance rate make DMPA an excellent drug for use in family planning clinics.

Summary

As a contraceptive, depot-medroxyprogesterone acetate (DMPA) was given intramuscularly in 150 mg. doses every 3 months to 650 women in a family planning clinic. This treatment represents 5,082 woman-months of experience. To date, there have been no pregnancies.

Calculations based on life tables show that, at the end of 1 year, 56.8 of every 100 women who started using DMPA, continued to use it. Of the 43.2 per 100 who stopped using it, 13.5 did so because of abnormal bleeding, 2.8 because of amenorrhea, 5.5 because of other medical problems, and 14.6 because of nonmedical problems; 6.8 were lost to followup.

Since there have been no pregnancies with this method and the continuance rate is high, we consider DMPA to be an effective and acceptable method of contraception.

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EQUIPMENT REFERENCE

(A) Depo-Provera. Upjohn Pharmaceutical Company. Kalamazoo, Mich.

Tearsheet Requests

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