

MEDROXYPROGESTERONE ACETATE AS AN INJECTABLE CONTRACEPTIVE—ITS UTILITY IN INDIAN WOMEN

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Medroxyprogesterone Acetate (DMPA) is a compound which has been used in over 500,000 patients in the United States for a variety of indications. Recently it is under clinical trials where its contraceptive efficacy and acceptability are being evaluated. This compound, popularly known as Depo-Provera or DMPA is a potent, long acting progestational agent with the following formula -17 α hydroxy -6 α methylprogesterone Acetate. A single injection of DMPA had a dramatic effect of producing prolonged amenorrhoea.

Mode of administration and action of DMPA

DMPA is injected intramuscularly in the dose of 50 mg in combination with 10 mg of estradiol-17 β -cyclopentyl propionate every five weeks by some workers (Scomegna, 1970), while most of the others used an i.m. dose of 150 mg DMPA every three months. It is absorbed slowly from the injection site and hence it has a prolonged action (Lee 1969). Repeated doses result in endometrial suppression, thus creating an endometrium hostile to nidation (Rubin 1969). It has been shown to be a powerful inhibitor of gonadotropin (Epstein 1962, Laron 1963, Schultz 1963). Serial studies of vaginal

cytology, cervical mucus and postcoital tests as well as endometrial histology and urinary pregnanediol excretion demonstrate an intense and prolonged effect of DMPA with ovulation inhibition (Zanartu *et al*, 1968). However, because of the prolonged action of this steroid on the hypothalamo-pituitary axis, it is certainly not the contraceptive of choice (Maqueo 1970).

Pregnancy Rate with DMPA

In the hands of most of the workers, there were no pregnancies when the women were taking DMPA injections. Table I shows the comparative pregnancy rates per hundred women, per year. It is this high rate of effectiveness of this drug compared to that of other conventional contraceptives, makes it an excellent drug for use in family planning clinics.

Return of Ovulatory Cycles after Discontinuation of DMPA

An ideal contraceptive drug should not cause abnormally long periods of suppressed ovulation after its use is discontinued. Neither should it exert any effect on the subsequent pregnancy and the foetus. Medroxyprogesterone acetate has been found to produce prolonged period of anovulation following discontinuation of injections. However, even after several years of use, fertility was resumed in the majority of the subjects. In those previously fertile subjects in whom preg-

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Received for Publication on 14-3-1972.

TABLE I
Comparative Pregnancy Rates Per 100 Women Per Year

Method	Method failure	All pregnancies
DMPA*	0.085	0.3
Oral contraceptives @		
Combined	0.1	0.7
Sequential	0.5	1.4
Intrauterine device @		
Large Lippes loop	1.9	2.7
Saf-T-Coil	1.9	2.8
Condom or Diaphragm @	2.6	

* Source—Powell & Seymour, Amer. J. Obst. & Gynec. May 1, 1971.

@ Source—Second Report on Oral contraceptives, Food and Drug administration, August 1, 1969.

nancy was not established upto 8-14 months after discontinuation of DMPA therapy, and who were anxious of having another child, ovulation could be successfully induced by clomiphene and human chorionic gonadotropin and pregnancy immediately followed (Zanartu 1968).

The end results of pregnancies that occurred after the use of DMPA were similar to what one would expect in a regular clinic. There was no evidence of any masculinization in the female foetus or congenital abnormalities in the foetuses born from pregnancies that occurred after use of DMPA.

Endometrial Histology During DMPA Injections

For the first two months after injection of DMPA the proliferative activity of the glandular epithelium was still seen. After six months of treatment the endometrial glands regressed, the stroma was locally or diffusely oedematous. Bizarre or abnormal endometrial changes suggestive of neoplasia were never seen (Scomegna 1970). Mequeo *et al*, 1970 noted that three weeks after the injection of DMPA there was always marked regression and thinning of the endometrium.

Papanicolaou smears were found to be normal and all the patients had a secretory endometrium within 12 months after the last injection or within 9 months after the effect of the last injection had worn off.

Acceptability of Contraceptive Injections of DMPA

The main advantage of this method which would make it the most acceptable family planning method is the infrequent need of injection. Patient failure is rarely a problem. Patients will have to bother about birth control only once in three months! It provides freedom from the strict regimen of oral contraceptives and the annoyance of a diaphragm. The sterilization is not permanent like after tubectomy, but can be reversed just after stopping the injections. Some women reported increased libido and orgasm due to confidence in the drug (Soichet 1969). However, because of its high incidence of alteration in bleeding pattern, disagreeable side-effects during therapy, prolonged inhibition of hypothalamo-pituitary axis, prolonged period of amenorrhoea and anovulation after discontinuation of the therapy, the use of such a drug in the

general population might not be desirable. For those who have already had enough number of children and do not wish for any more, amenorrhoea may be a blessing! Therefore, use of DMPA should be reserved for such patients and to others who can not use any other conventional methods of contraception due to certain reasons.

Drop out Rate with DMPA and Reasons For it

Unfortunately, the out rate with this method of contraception is quite high. Table II shows the drop out rate

TABLE II

Drop out Rate With DMPA From Various Clinics

Source	Drop out rate
Seymour et al. 1970	16.9 per cent
Scommegna et al. 1970	32 per cent
Soichet et al. 1969	21 per cent
Maqueo, et al 1970	43.2 per cent

from various clinics. The reasons put forward by the women for their unwillingness to use this contraceptive were as follows:

Frequent spotting, headache, dysmenorrhoea, prolonged bleeding, backache, diminution of orgasm, need for menses, nausea, vomiting, etc.

However, in well motivated patients there were no complaints of emotional instability, nausea, vomiting or breast soreness. Occurrence of spotting was erratic but tended to decrease as the treatment continued.

Role of DMPA as an Injectable Contraceptive in Indian Women

We, in India, are facing a situation where there is an enormous population to be served with meagre resources. If

the population explosion is not controlled effectively, the country's economy will be seriously overburdened. We need a method of birth control which is less expensive, which does not require constant vigilance of medical personnel, which is absolutely safe and which could be easily reversed if such a need arises. Medroxyprogesterone acetate fulfills all these requirements. The only draw back with the drug is the unfavourable side-effects occurring during its use. Hence it is very essential to hold enthusiastic clinical trials with this drug in our country and to search for ways and means by which the side-effects of the drug could be reduced to a minimum.

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