

## Depo-Provera associated with weight gain in Navajo women

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### Abstract

Depo-medroxyprogesterone acetate (DMPA) is an increasingly popular contraceptive choice among Navajo women. Weight gain is cited as a common side effect and major reason for discontinuation of DMPA. No controlled trials have evaluated the association between weight gain and DMPA in Navajo women. We aimed to clarify whether DMPA is associated with weight gain in Navajo women and to quantify the magnitude of weight gain. A cohort of 172 Navajo women who had used DMPA continuously for one or 2 years comprised the study group. A cohort of 134 Navajo women who used a non-progestin method or no method over 1 or 2 years comprised the comparison group. Initial weight, one-year weight and 2-year weights were recorded for all patients. Study subjects gained a mean of 6 pounds over one year and 11 pounds over 2 years relative to the comparison group ( $p < 0.001$ ) after controlling for possible confounding variables including age, parity and initial weight. Use of DMPA is associated with significant weight gain in Navajo women. This weight gain is greater than that reported in previous uncontrolled studies in non-Navajo populations. This information should be utilized in counseling Navajo women about the side effects of DMPA. © 2000 Elsevier Science Inc. All rights reserved.

*Keywords:* Depo-Provera; Navajo; Weight

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### 1. Introduction

Depo-medroxyprogesterone acetate (DMPA) was approved by the FDA for use as a contraceptive in 1992 and has become an increasingly popular form of reversible contraception. The National Survey of Family Growth reported in 1995 that 3% of women used DMPA [1] contraception. Recent reports indicate that DMPA use has become particularly prevalent among adolescents [2,3]. The trend of increasing utilization of DMPA for contraception has also been observed among Navajo women. Data from the Navajo Area Supply Service Center, which is the pharmaceutical distribution center for all Navajo Indian Health hospitals and clinics, reflect this increased usage: 491 doses of DMPA were distributed in 1993 compared with 16,308 in 1997.

Weight gain associated with the use of DMPA has been reported in several studies involving women of different ethnic and racial backgrounds [4,5]. The DMPA package insert describes an average weight gain of 5.4 and 8.1

pounds over 1 and 2 years, respectively. Anecdotal reports by many Indian Health Service providers raised concerns that Navajo women were gaining more weight while on DMPA than anticipated. Review of the literature demonstrated that previous studies lacked comparison groups to identify whether possible confounders such as age, parity, and initial weight might have had an effect on reported weight gains.

The specific aim of the study was to compare the change in weight over time in a group of Navajo women using DMPA relative to a comparison group of Navajo women who were using other forms of contraception or no contraception. The study was designed to evaluate weight change in two groups: women who received DMPA immediately postpartum, accounting for almost half of all new DMPA starts, and women who received DMPA remote from pregnancy.

### 2. Materials and methods

This retrospective chart review was authorized by the Indian Health Service Institutional Review Board with sup-

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port from appropriate tribal entities. Women included in the study received care at one of three Indian Health Service facilities serving the Navajo population: Northern Navajo Medical Center, Gallup Indian Medical Center, and Tuba City Medical Center. All three hospitals kept logbooks of all DMPA injections given for contraception. Study subjects were identified from the logbooks and all charts of patients who received their first injection of DMPA from 12/2/92 to 6/26/95 at these institutions were reviewed. Members of the Navajo tribe, between the ages of 18 and 40 at the time of the first DMPA injection, who completed at least five consecutive injections at intervals of 10–14 weeks, and who had weights recorded at 1-year and/or 2-year intervals, were included. Women with incomplete records or history of diabetes or thyroid disease were excluded.

Eligible women were divided into two groups. “Interval” subjects were those at least 20 weeks beyond an antecedent pregnancy of at least 20 weeks gestation when they received their first dose of DMPA. “Postpartum” subjects were those who received their first DMPA injection at 5–8 weeks after delivery of a singleton pregnancy of at least 20 weeks gestation. Patients were excluded from the “postpartum” group if they had pre-eclampsia or multiple gestation with the index pregnancy.

The comparison group were also members of the Navajo tribe, were between the ages of 18 and 40, had weights recorded at 1-year and/or 2-year intervals, and did not have diabetes or thyroid disease. Comparison subjects were also divided into 2 groups. The “interval” comparison group consisted of women at least 20 weeks beyond an antecedent pregnancy when their first weight was recorded and was generated from a convenience sample of a list of women provided by our cytology reference laboratory. The list provided the names of women who had received at least two consecutive yearly Pap smears, were Navajo, and were in the appropriate age group. The list helped us to identify women who had weights recorded approximately a year apart. The charts of these women were reviewed for eligibility and the comparison group was selected from those who met the above criteria. The “postpartum” comparison

Table 1  
Demographics

	Study patients (mean ± SD)	Comparison patients (mean ± SD)	p value
Interval group (n = 115)		(n = 94)	
Age (years)	25.1 ± 6.4	29.1 ± 6.1	0.001
Parity	1.6 ± 1.7	2.2 ± 1.8	0.008
Height (inches)	63.5 ± 2.4	63.3 ± 2.2	NS
Initial weight (pounds)	154.7 ± 34.1	155.7 ± 27.3	NS
Postpartum group (n = 57)		(n = 40)	
Age (years)	22.9 ± 5.8	27.8 ± 5.6	0.001
Parity	1.8 ± 1.2	3.1 ± 1.8	0.001
Height (inches)	63.0 ± 2.3	63.1 ± 1.8	NS
initial weight (pounds)	144.6 ± 28.8	163.8 ± 30.9	0.003

Table 2  
Weight gain (pounds), interval group

	Study patients (mean ± SD)	Comparison patients (mean ± SD)	p value
One year	9.3 ± 11.0 (n = 115)	3.1 ± 7.2 (n = 94)	<0.001
Two years	15.8 ± 13.2 (n = 35)	4.0 ± 9.4 (n = 64)	<0.001

group consisted of women whose first weight was recorded at 5–8 weeks after singleton delivery. These women were identified from delivery logbooks. The next consecutive delivery after a “postpartum” subject who met the eligibility criteria was selected as a comparison subject.

The following information was abstracted from all charts: age, parity, height, initial weight, weight at one year and weight at 2 years. Additionally, method of contraception, if any, was abstracted from the charts of controls. Data was analyzed using SAS. When differences in demographic factors were found between the groups, those factors were used as covariates in ANCOVA analysis.

### 3. Results

A combined total of 306 DMPA and comparison subjects were analyzed. In the “interval” category, 115 DMPA and 94 comparison subjects were analyzed. In the “postpartum” category, there were 57 DMPA subjects and 40 comparison subjects. The two groups of DMPA users—interval and postpartum—were found to be different with respect to demographic factors. Demographic information for the DMPA and comparison groups is presented in Table 1. Because of demographic differences, these factors were used as covariates in analysis of covariance (ANCOVA) and age, parity and initial weight were adjusted for in analyzing weight gains over time in the two groups.

Results for weight change over 1 and 2 years are presented in Tables 2 and 3. Table 2 illustrates weight changes in the interval group. The mean difference in weight gain in the DMPA users over one year was 6.2 pounds ( $p < 0.001$ ) and over 2 years was 11.8 pounds ( $p < 0.001$ ). These differences persisted after adjusting for age, parity, and initial weight (ANCOVA,  $p < 0.01$  for both groups).

Table 3 illustrates weight changes in the postpartum

Table 3  
Mean weight gain (pounds), postpartum group

	Study patients (mean ± SD)	Comparison patients (mean ± SD)	p value
One year	7.0 ± 9.8 (n = 57)	1.3 ± 10.1 (n = 40)	0.008
Two years	14.2 ± 12.8 (n = 29)	3.6 ± 11.1 (n = 20)	0.004

group. The mean difference in weight gain in the DMPA subjects over one year was 5.8 pounds ( $p = 0.004$ ) and over two years was 10.6 pounds ( $p = 0.004$ ). The statistical significance of these findings was also maintained after adjusting for age, parity and initial weight (ANCOVA,  $p \leq 0.01$  for both groups).

#### 4. Discussion

The present study adds to the literature examining weight change in association with DMPA use. Our results indicate that DMPA use is strongly associated with weight gain in Navajo women. Other studies have suggested but not established this relationship.

Several cross-sectional studies dating from the 1980s indicate that women using DMPA weigh more than those not receiving hormonal contraception [5–7]. In these studies, women on DMPA weighed from 1.3–7.4 kg more than non-users.

In 1973, Schwallie [8] reported results of a prospective cohort trial conducted in Michigan using over 3000 “private” and “clinic” patients receiving DMPA: mean weight gain over one year of use was 5.4 pounds and 8.1 pounds over 2 years. Overall, at one year, 69% of women had gained weight, 25% had lost weight and 6% had experienced no change in weight. In 1980, Mukherjia [5] studied 138 women using DMPA and found a mean weight gain of 4 kg in the first year and 2 kg in the second year of use. A 1986 World Health Organization [6] trial followed 1216 women in developing countries randomized to different doses of DMPA. At one year, average weight gain in both groups was 1.48 kg. Although these studies strongly suggest that DMPA is associated with weight gain, none of them included a comparison group. The lack of a comparison group raises the concern that the documented weight gains may have been attributable to confounding factors. Only 2 prior reports of weight change in women using DMPA include a comparison group. In 1995, Mainwaring [9] performed a prospective cohort study of 71 Caucasian women choosing either Norplant, DMPA or the progestin-only contraceptive pill. These women were observed over a one-year period with no significant differences between pre- and post-treatment weight. Moore [10] retrospectively reviewed weight change over a one year period in 150 progestin-only contraceptors: 50 DMPA users, 50 Norplant users and 50 progestin-only contraceptive pill users. The study group consisted of women whose ethnicity was not specified, attending a rural Medicaid-funded Obstetrics and Gynecology clinic. Although a trend toward more weight gain in DMPA users was noted, no significant increase in weight occurred in any of the groups.

Our study demonstrates large increases in weight associated with DMPA use both at years 1 and 2, confirming the anecdotal concerns expressed by Indian Health Service providers. The strength of this study lies in its inclusion of a

comparison group of women not using DMPA. Interestingly, we found that the comparison groups also gained a considerable amount of weight: 2.5 pounds on average at one year and 3.9 pounds on average at 2 years. The extent of weight gain attributable to DMPA alone is substantial. When this amount is added to the amount gained by the comparison groups, the total amount is even more noteworthy. Previous uncontrolled reports studied other populations in which it is unknown whether women not on DMPA gain weight over time to the same extent as Navajo women. However, assuming there is a net baseline of increase in weight over time, previous studies may have overestimated the extent of weight gain attributable to DMPA alone.

Recent reports highlight the relatively high discontinuation rates of DMPA. Abnormal bleeding and weight gain are cited as the two most common reasons for discontinuation [11]. In a population-based study from Australia, Paul [12] found that only 53% of women contraceptors initiating DMPA used the method for a year or more, with menstrual disturbances and weight gain cited as the most common causes of discontinuation. Unfortunately, we were unable to retrieve data related to discontinuation from our population. Although weight gain is a primary reason for discontinuation, its impact may be lessened by anticipatory counseling. Lei [13] reported on the importance of thorough and structured pre-treatment counseling regarding side effects in a population of Chinese women using DMPA. Continuation rates improved dramatically with such counseling.

Finally, this study suggests metabolic differences between the Navajo population and other populations previously studied in that hormones may exert different effects on different racial and ethnic populations. Native Americans are known to have high rates of Type II diabetes that is frequently associated with obesity. The significant increases in weight gain in Navajo women associated with DMPA may have negative health implications.

Two limitations of this study should be noted. The comparison groups differed from the study groups in some demographic variables. Women in the comparison group more frequently used the intrauterine device or tubal ligation contraception and, therefore, were older and of higher parity. However, the statistical significance of the differences in weight change was maintained after controlling for these parameters. The comparison group did include some users of combination oral contraceptive pills that could be a potential confounder for weight change. We doubt that this significantly altered the results, however, since reports suggest little effect on weight change by oral contraceptives [14,15].

Our findings have important implications for the use of DMPA contraception in Navajo and other women. Although the conclusion that DMPA is associated with weight may only strictly be applied to Navajo women, the findings of the present report confirm those of previous cross-sectional studies in other populations. The agreement between these reports suggests that weight gain may, in fact, be

associated with DMPA in other populations. Providers should be aware of the potential for significant weight gain in their patients and review their medical histories carefully. Educational materials and contraception counseling regarding DMPA for Navajo women should include information regarding weight gain. Such counseling will allow women to make a more informed choice regarding their contraceptive method. In addition, counseling may decrease method discontinuation. Finally, our data underscore the need for studies that take into account racial and ethnic differences in ascertaining side effects of hormonal contraception.

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