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# Concentration of depot medroxyprogesterone acetate and pain scores in adolescents: a randomized clinical trial

Albert G. Thomas[a,*], Sandra Klihr-Beall[b], Lorena Siqueira[b], Iris Horing[a], Jun Zhang[c]

[a]*Department of Obstetrics, Gynecology, and Reproductive Science, Mount Sinai School of Medicine, New York, NY 10029, USA*
[b]*Department of Adolescent Medicine, Adolescent Health Center, Mount Sinai School of Medicine, New York, NY 10029, USA*
[c]*Department of Community Medicine, Mount Sinai School of Medicine, New York, NY 10029, USA*

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**Abstract**

A prospective, single-blinded, randomized trial was initiated to determine whether injection site pain differed in adolescents receiving two concentrations of 150 mg of depot medroxyprogesterone acetate (DMPA). Ninety-five adolescents seeking injectable contraception were randomized to receive 150 mg of DMPA as follows: a deltoid injection of 1.0 mL from a single-unit-dose vial containing 150 mg/mL or 0.38 mL from a multidose vial containing 400 mg/mL of DMPA. A visual analogue scale was measured at each visit and cumulatively compared between the groups. Continuation rates were tabulated. The report of pain for the multidose vial group was significantly higher than for the unit-dose vial group ($p < .003$). The dropout rates for both groups were high at 1 year and were not statistically different (multidose group = 64% and unit-dose group = 77%). Twenty percent of the subjects in the multidose group vs. 22% in the unit-dose group discontinued due to bleeding irregularities. The concentrated form of DMPA led to greater pain at the injection site than did the less concentrated form, but this did not lead to higher discontinuation rates among adolescents.


*Keywords:* Adolescents; Injectable contraception; Depot medroxyprogesterone acetate; DMPA; Pain scores; Cost savings; Bioavailability; Randomized clinical trial

## 1. Introduction

Ample evidence describing depot medroxyprogesterone acetate (DMPA) as a safe, reliable contraceptive for women led to its eventual approval by U.S. Food and Drug Administration (FDA) in 1992 [1]. The only other long-term progestin contraceptive approved prior to this time was the subdermal levonorgestrel implant. The lack of progestin choices during the 1980s led to the formation of the Mount Sinai "DEPO Clinic" in 1984. This service within our family planning clinic became well known in the East Harlem community as a place where women could receive this exceptionally effective contraceptive. Clients desiring a DMPA injection were given an extensive counseling session about the "off-label" use of this drug as a long-acting contraceptive, after which they signed a specially designed consent form, documenting the use of DMPA. A concentrated solution (400 mg/mL) of DMPA was already approved by the FDA for the treatment of metastatic endometrial or renal carcinoma and was used in the Mount Sinai Family Planning Clinic for contraception at the dose of 150 mg/0.38 mL, administered by intramuscular deltoid injection. Suitable candidates, with a negative urine pregnancy test, were given their initial DMPA injection within 7 days of the beginning of a normal menses.

Anecdotal reports based on our nursing staff purported that DMPA injections were somewhat painful, but this observation was counterbalanced by the unique contraceptive role served by this progestin-only formulation. The purpose of this study, based at the Mount Sinai Adolescent Health Center, was to compare pain scores and continuation rates between two teen groups. One received 0.38 mL from a multidose 400-mg/mL vial and the other received 1.0 mL from a unit-dose 150-mg/mL vial.

## 2. Materials and methods

### 2.1. Subjects

Ninety-five consecutive adolescent clients, who chose DMPA as a contraception option, were recruited from the

* Corresponding author. Tel.: +1 212 241 3614; fax: +1 212 241 3833.
*E-mail address:* albert.thomas@mssm.edu (A.G. Thomas).

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Table 1
Demographics

| | Unit-dose group ($n=40$) | Multidose group ($n=55$) | p |
|---|---|---|---|
| Age (mean±SD) | 18±1.8 | 17±2.1 | ns |
| BMI (mean±SD) ($kg/m^2$) | 26.6±5.6 | 23.6±5.6 | ns |
| Race (%) | | | |
| Hispanic | 59 | 64 | ns |
| Black | 41 | 36 | |
| Nulliparous (%) | 55 | 61 | ns |
| Parous (%) | 45 | 39 | |

Adolescent Health Center between August 9, 1995, and July 31, 1997. Appropriate candidates received anticipatory counseling regarding potential benefits and risks, especially the associated menstrual changes that can occur with DMPA. Written consent was obtained for this study, which was approved by the Mount Sinai Medical Center Institutional Review Board (IRB).

Upjohn Pharmaceuticals provided a limited free supply of unit-dose DMPA. This restricted our sample size to 100 subjects with a ratio of unit dose vs. multidose of 2:3. This randomization scheme would yield approximately 40 subjects in the unit-dose group and 60 in the multidose group. Our experience suggested that the multidose group DMPA was likely to be more painful than the unit-dose group. Assuming that the incidence of severe pain in the unit-dose group was 5%, our sample size would have 70% power to detect a minimal relative risk of 4.

Randomization was accomplished through the use of computer-generated random numbers. The assignment for each subject was sealed in an opaque envelope and opened after the participant had agreed to be enrolled and signed the informed consent. The nurses giving the injection were aware of the dose and concentration. However, subjects were blinded to dose and concentration. The nursing staff completed a demographics/clinical information sheet on each subject at each visit. Each subject received either the unit-dose (150 mg/mL) or the concentrated multidose (150 mg/0.38 mL) formulation injected into the deltoid muscle of the arm with a 20-gauge, 1.5-in. needle utilizing a 1-mL tuberculin syringe. After the injection, subjects were asked to complete a visual analogue pain assessment about DMPA [2]. Subjects were asked to complete questionnaires initially and at each three monthly injection visit.

Table 2
Visual analogue pain scores

| Pain score | Unit-dose group (%) | Multidose group (%) | p |
|---|---|---|---|
| 0 | 44 | 7 | .003 |
| 1 | 28 | 24 | .003 |
| 2 | 15 | 26 | .003 |
| 3 | 10 | 16 | .003 |
| 4 | 3 | 15 | .003 |
| 5 | 0 | 11 | .003 |

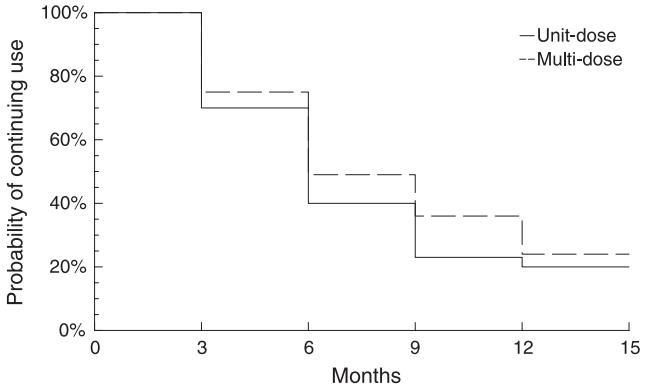


Fig. 1. Probability of continuing use.

### 2.2. Statistical analysis

Data were entered into a database created in EPIINFO (CDC, 1994) and then transported to the Statistical Analysis System (SAS, 1997) for analysis. We first compared the characteristics of the subjects in the two treatment groups at entry. The $\chi^2$ test was used for categorical variables and the Student $t$ test for continuous variables. We then compared the pain scores and reasons for discontinuation using the $\chi^2$ test. Log-rank testing was employed to examine whether the two treatment groups had similar continuation rates.

## 3. Results

Ninety-five adolescents seeking DMPA contraception and who gave written informed consent were randomized to either the multidose (400 mg/mL) or unit-dose (150 mg/mL) group. Forty adolescents were included in the unit-dose group and 55 in the multidose group. Subject characteristics are presented in Table 1. The demographics recorded were similar for each group. Pain scores were significantly greater in the multidose group than those in the unit-dose group (Table 2). Forty-four percent of the subjects in the unit-dose group vs. only 7% in the multidose group reported pain scores of 0 (no pain). Eleven percent of the subjects in the multidose group vs. 0% in the unit-dose group reported the injection as the "worst pain ever experienced" ($p<.003$). Fig. 1 illustrates the probability of continuing use, based on survival analysis, throughout the 12-month follow-up period. There were no significant differences in these probabilities (log-rank test $p=.42$). The probabilities were 20% and 27%, respectively, for the unit-dose and multidose groups. The major reason reported for discontinuation was bleeding and spotting. Failure to return to clinic was high: 59% for the unit-dose group and 63% for the multidose group. No pregnancies were noted during this study.

## 4. Discussion

In an effort to expand the contraceptive choices for our clients receiving care at the Mount Sinai Family