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Original research article

Randomized clinical trial of self versus clinical administration of subcutaneous depot medroxyprogesterone acetate☆,☆☆

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Abstract

Objectives: To evaluate feasibility, acceptability, continuation, and trough serum levels following self-administration of subcutaneous (sc) depot medroxyprogesterone acetate (DMPA).
Study design: Women presenting to a family planning clinic to initiate, restart or continue DMPA were offered study entry. Participants were randomized in a 2:1 ratio to self- or clinician administered sc DMPA 104 mg. Those randomized to self-administration were taught to self-inject and were supervised in performing the initial injection; they received printed instructions and a supply of contraceptive injections for home use. Participants randomized to clinician administration received usual care. Continued DMPA use was assessed by self-report and trough medroxyprogesterone acetate levels at 6 and 12 months.
Results: Two hundred fifty women were invited to participate, and 137 (55%) enrolled. Of these, 91 were allocated to self-administration, and 90/91 were able to correctly self-administer sc DMPA. Eighty-seven percent completed follow-up. DMPA use at 1 year was 71% for the self-administration group and 63% for the clinic group (p=0.47). Uninterrupted DMPA use was 47% and 48% for the self and clinic administration groups at 1 year (p=0.70), respectively. Serum analyses confirmed similar mean DMPA levels in both groups and therapeutic trough levels in all participants.
Conclusions: Sixty-three percent of women approached were interested in trying self-administration of DMPA, even in the context of a randomized trial, and nearly all eligible for enrollment were successful at doing so. Self-administration and clinic administration resulted in similar continuation rates and similar DMPA serum levels. Self-administration of sc DMPA is feasible and may be an attractive alternative for many women.
Implications: Self-administration of sc DMPA is a feasible and attractive option for many women. Benefits include increased control over contraceptive measures and less time spent on contracepting behaviors. Globally, self-administration has the potential to revolutionize contraceptive uptake by increasing the number of women with access to DMPA.

Keywords: Contraception; Injectable; Depot medroxyprogesterone acetate; Self-administration

1. Introduction

Many women are at high risk of becoming unintentionally pregnant each year because of a gap in contraceptive use [1]. The shorter effective timeframe and need for continued provider intervention sets depot medroxyprogesterone acetate (DMPA) apart from other longer acting contraceptives. Many women discontinue DMPA secondary to unpredictable bleeding, and difficulty in access is also a problem with only 27–53% of women continuing at 1 year [1–4]. The advent of a subcutaneous (sc) formulation of DMPA can alleviate the need to return to clinic for subsequent injections and makes administration outside of the clinical setting possible. While this formulation is not currently labeled for self-administration in the US, many

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subcutaneously delivered medications including enoxaparin, heparin, insulin, and gonadotropins frequently are self-administered. In addition, pilot studies evaluating self-administration of injectable contraceptives showed favorable results with both patient willingness and ability to self-inject [5–8].

2. Materials and methods

This clinical trial compared continuation of DMPA between women randomized to self-administration or clinic administration of sc DMPA. Participant-related activities were conducted between 2010 and 2011 in New York City. The Columbia University Institutional Review Board approved this study, and all patients gave informed consent. Eligible women were aged 18 or greater, seeking DMPA for contraception, and available for follow up for 1 year. We excluded women with medical contraindications to the use of DMPA based on the World Health Organization Medical Eligibility Criteria, enrolling only women in Category 1 or 2 [9]. We also specifically excluded women with a suspected or confirmed pregnancy or desire for pregnancy within 1 year. Procedures for enrollment, instruction, and observation for DMPA self-administration were successfully piloted with the first five eligible participants.

We stratified participants based on never, current, or past use of DMPA and randomized them to self or clinic administration. The sequence for the 2:1 (self vs. clinic administration) treatment allocation was determined using a computerized random-number generator in blocks of six. An investigator not involved with participant contact generated the allocation schedule, which was concealed until after informed consent. Group assignments for each stratum were placed in sequentially numbered opaque envelopes. After informed consent and screening were completed, the next envelope in the sequence was opened, and participants were enrolled by the study coordinator.

All enrolled participants answered a baseline questionnaire to assess demographic and reproductive characteristics, past contraceptive practices, and future pregnancy plans. Participants initiated DMPA on the day of the enrollment visit, including continuing users, women within Days 1–5 of the menstrual cycle, and all others, who received sc DMPA per Quickstart protocol [10]. Those randomized to the self-administration arm were taught to self-inject by the study coordinator using modified illustrations from *Instructions for the use of depo-subQ provera 104* [11]. The participant performed the initial injection in the abdomen or thigh under supervision, and if deemed acceptable, was given prepackaged sc DMPA (Depo-subQ Provera 104®, Pfizer, NY, USA) containing a prefilled syringe and needle to use at home, along with alcohol pads, a bandage, a urine pregnancy test, and a DMPA calendar giving dates for the next injection. Participants beyond Day 1–5 of the menstrual cycle at enrollment were instructed to use the urine pregnancy test in 3 weeks; the research coordinator contacted each of these women to ensure that the pregnancy test was taken and that the result was negative [12]. Participants received instructions on how to restart DMPA outside of the usual 14 week dosing window under the Quickstart protocol if temporary discontinuation occurred during the study. Each participant received a sharps disposal canister and instructions in safe needle disposal.

All participants received appointments for revisits at 6 and 12 months, scheduled immediately prior to the anticipated date of the third and fifth contraceptive injections. Participants randomized to clinic administration received routine appointments for their next injections, and clinic charts were reviewed to verify administration of DMPA. At 6 months, those in the self-administration group were reevaluated for ability to self-inject, and received additional prepackaged sc DMPA for home administration. At the 12-month exit interview participants responded to questions regarding continuation, satisfaction and administration. At both the 6 and 12 month visits, we collected a blood specimen to measure medroxyprogesterone acetate (MPA) levels. There were no additional costs to the participants for sc DMPA use; however, participants were compensated up to US$120 for complete study participation.

Specimens were centrifuged, and aliquots were stored at −80°C until analysis. MPA was measured in serum by an in-house developed Ultra Performance Liquid Chromatography Tandem Mass Spectrometry (UPLC-MSMS) assay using an Acquity UPLC and a Xevo TQ-S Mass Spectrometer (Waters, Milford, MA, USA). In short, 20 uL of 10-ng/mL D8-Progesterone (internal standard) in ethanol was added to 250 uL of serum, followed by a liquid/liquid extraction using 1-chlorobutane. MPA was detected at a mass to charge transition 387.2 → 285.1 and D8-Progesterone at 323.3 → 100.1. Samples were quantified using a calibration line which was run on a daily basis together with quality controls. The assay is linear between 25 and 8000 pg/mL with a lower limit of quantification <25 pg/mL. Interday precision was 9.1% at 118 pg/mL and 2.6% at 1021 pg/mL.

Enrollment of 132 women was planned a priori to have 80% power to detect a 30% or greater difference in continuation rates between the groups. With a two-sided α=0.05, β=0.80, and accounting for a predicted 20% dropout rate, enrolling 132 subjects in a 2:1 intervention to control ratio would suffice. We compared categorical and continuous variables using χ^2, Fisher's Exact Test, Student *t* test, or Wilcoxon–Mann–Whitney test, as appropriate. Spearman rank correlation was used to compare DMPA levels at 6 and 12 months. Statistical analyses were performed using SAS statistical package v.9.3 (SAS Institute, Cary, NC, USA).

3. Results

Fig. 1 shows the flow of participants through this trial. Two hundred fifty women were screened, and 63% were