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Health Approach in the control of Irregular Bleeding due to Depomedroxy Progesterone Acetate

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Abstract

Background: The main cause of discontinuing the use of depomedroxy progesterone acetate (DMPA) is irregular bleeding. This study compared placebo with two kinds of combined oral contraceptive pills including low dose (LDOCP) and high dose (HDOCP) on control of abnormal uterine bleeding in DMPA users.

Methods: Ninety DMPA users complaining of bleeding were studied in a triple blind randomized clinical trial. Bleeding days were observed for 4 mo. Analysis of results was done by SPSS for Windows.

Results: Age, education, and bleeding days in prior month were similar in all three groups. The bleeding in all three groups were reduced in the first, second, third and fourth months of the study comparing to the month before it. Although time factor was effective in all groups, considering combination of two factors, time and treatment methods including all visits, there was no significant change in duration of the 4 mo. However, significant changes were recorded in the first month in treatment group comparison with placebo.

Conclusion: Time is the main factor in reduction of irregular bleeding of DMPA users. Two kinds of OCP have important effects in quicker reduction or stoppage of bleeding, although not continuous in the following months.

Keywords: *Depo medroxy progesterone acetate, contraception, oral contraceptive, irregular bleeding*

Introduction

The history of contraception is long; however, the voluntary control of fertility is even more important in modern society. Effective control of reproduction is essential for woman's ability to accomplish her individual goals. From a larger perspective, the rapid growth of the human population in this century threatens the survival of all (1).

It has been proved that some contraceptive methods are more effective than others are.

In the group of injectable hormonal contraceptives, depo medroxy progesterone acetate (DMPA) with a dosage of 150 mg every 3 mo is highly effective, producing pregnancy rates of about 0.3 per 100 women per year. Probably because of the high blood levels of the progestin, efficacy appears not to be reduced by administration of other drugs and is not dependent on the patient's weight. DMPA appears to have many benefits. Decreases in anemia, pelvic inflammatory disease, ectopic pregnancy, and endometrial cancer have been reported (1).

The advantage of injected progestins includes a contraceptive effectiveness comparable with or better than combined oral contraceptives, long lasting action with injections required only 4 to 6 times a year, and minimal impairment of lactation (2).

In a study in the USA it was demonstrated that DMPA was associated with a high incidence of breakthrough bleeding (BTB) during the first 6 mo of use which often leads to discontinuation (3).

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Seventy percent of women continue using DMPA at the end of first year (1). Disruption of menstrual cycle and bleeding at irregular intervals is one of the main causes of discontinuing the use of DMPA (4). The most common cause of discontinuation was the side effects including abnormal uterine bleeding and weight gain (5).

Although irregular bleeding is not dangerous, many of the users withdraw from this method due to this issue (6). Health statistics in Hamadan Province in 1997 indicated that 7% of non-pregnant married women in reproductive age used DMPA (7).

In Iranian Moslem women who are adamant to praying five times per day and not being able to do so while they have bleeding, are more sensitive to this problem. DMPA is a contraceptive method without the need for individual to have constant daily motivation and discipline and it has been proved for more popular in rural areas of Iran.

Regarding to encourage this safe and relatively cheap contraceptive method, abnormal bleeding should be a subject of concern.

It is stated that the management strategies for women with abnormal uterine bleeding who are using progestin-only contraceptive methods include counseling and reassurance, as well as the administration of supplemental estrogen and/or an non steroidal anti inflammatory drug during bleeding episodes (8).

In our health treatment organization, referral of patients is limited to the level of general practitioners. In this way, gynecologists are not present in current referral system. DMPA users complaining of bleeding cannot be managed in the free health system. It is more important in villages, where DMPA is available free of charge, the side effects are not dealt with due to lack of specialist. If we can introduce an effective and practical method within our health system, it will be a giant step forward in our medical practice. Oral contraceptive pill, which can be recommended by a low-level medical health provider, is one way to treat and control abnormal uterine bleeding in DMPA users.

This survey was conducted to compare placebo with two kinds of oral contraceptive pills including low dose (LDOCP) and high dose (HDOCP) in control of abnormal uterine bleeding in DMPA users.

Materials and Methods

Ninety DMPA users complaining of bleeding were studied in a triple blind randomized clinical trial. All these women reported more than 7 days bleeding in a month. None of them were under other hormonal treatments. Everyone who was planning to change this method or had any contraindication to estrogen use or harboring any other kind of disease with bleeding tendency such as myoma and anticoagulant therapy was excluded from the study. They randomly were divided by groups of 30, 34 and 26 persons in placebo, LDOCP and HDOCP groups, respectively.

Women were receiving placebo, LDOCP (each tablet containing 30 mcg ethinyl estradiol and 150 mcg levonorgestrel) or HDOCP (each tablet containing 50 mcg ethinyl estradiol and 250 mcg levonorgestrel). The above drugs were prepared in a package of 20 similar shaped capsules with distinct codes. Women were requested to use one capsule every day regardless of their menstrual cycle. Individual information was written in a questionnaire by the researcher. Every woman knew that she should continue to take the capsules even when her bleeding had stopped. She was made responsible to be aware and note daily spotting or bleeding in a simple chart. Patients were visited every month (5 visits in 4 mo). In her second visit, she was questioned about drug use, bleeding withdrawal, problems from the chart and she was given a new chart and given a set up time for her next month's appointment. If the chart was lost or not correctly filled, the researcher was responsible to complete it. If there was a delay of five days for the appointment a phone call or a visit

to her home (minimum of three times) was made. If someone changed her contraceptive method, did not use capsules, or was not aware of her home address, the person was excluded from research. If some one avoided of DMPA re-injection after 3 mo or decided to use oral contraceptive pills for bleeding control or contraception, she was excluded from that time and was regarded as method withdrawal. However, her data was used for follow up and comparison in second or third month with other groups.

Data were analyzed by SPSS software. Univariate and multivariate analyses of variance tests were used.

Ethical and scientific design of the study was approved by research committee of Hamadan University.

Results

The mean age of women was 27.9, 29.3 and 29 years in placebo, LDOCP and HDOCP groups, respectively, indicating no significant difference (*P*= 0.648).

Three groups were similar in the standard education. Less than diploma level was 80%, 81.8%, and 84.6% in those mentioned groups, respectively.

Mean duration of DMPA usage was 4.6 mo. 70.5% of these women complaining of bleeding with DMPA use were new users, with first injection application less than 3 mo. Only 7.4% of them had their first injection applied more than 12 mo ago.

Mean bleeding days per month was 21.4, 22.3 and 21.8 in placebo, LDOCP and HDOCP groups, respectively. There was no significance difference (*P*= 0.831).

Mean duration of drug to stop bleeding was significantly reduced in LDOCP and HDOCP in comparison to placebo (*P*= 0.002) (Table 1).

Mean bleeding days in the first month study including the drug use days were significantly reduced during first month in LDOCP and HDOCP groups, in comparison to placebo group (*P*= 0.015) (Table 2).

There was no difference in mean of bleeding days in second, third and fourth month between the three groups (Fig. 1).

Mean bleeding days of three groups was separately compared between the month prior to the study, with the following first, second, third and fourth months again separately. In all groups, bleeding days of the month before the study was significantly more than each individual month after study including first, second, third and fourth (Fig. 1)

Time factor was an extremely important and effective factor in all groups (*P*= 0.000) (Table 3).

Using box's test considering combination of two factors, time and treatment methods regarding all visits revealed no significant change in overall bleeding pattern (*P*= 0.292) (Table 3). This test showed significant changes only in the first month between drugs and placebo.

Forty-one women from the original 90 (45.5%) withdrew from DMPA application in this study. The breakdown of this group was 56%, 39.4% and 36% in those groups, respectively.

Table 1: Comparison of mean duration of drug usage to stop bleeding in three groups of DMPA users

	Mean (day)	Maximum (day)	Minimum (day)
Placebo	16.2	30	0
LDOCP	7.2	30	0
HDOCP	7.7	30	0

Anova test (*P*=0.002)

Table 2: Comparison of Mean bleeding days in first month in three groups of DMPA users

	Mean (day)	Maximum (day)	Minimum (day)
Placebo	16.6	30	2
LDOCP	11.2	30	0
HDOCP	10.8	30	2

Anova test (*P*=0.015)

Table 3: Summary of combination effects of time and drug in different groups of DMPA users

Source of Change	Sum. of squares	Degree of freedom	Average sum of squares	F	Level of significance
Between individuals: 1- effect of time on bleeding	5790.435	4	1447.60	23.483	0.000
2- effect of time and treatment method	598.975	8	74.872	1.215	0.292
Between groups: 3- effect of treatment method	43.779	2	21.890	1.120	0.887

Box's test reveals that the combination balance effect is running. (P=0.089) Mean monthly bleeding day's month

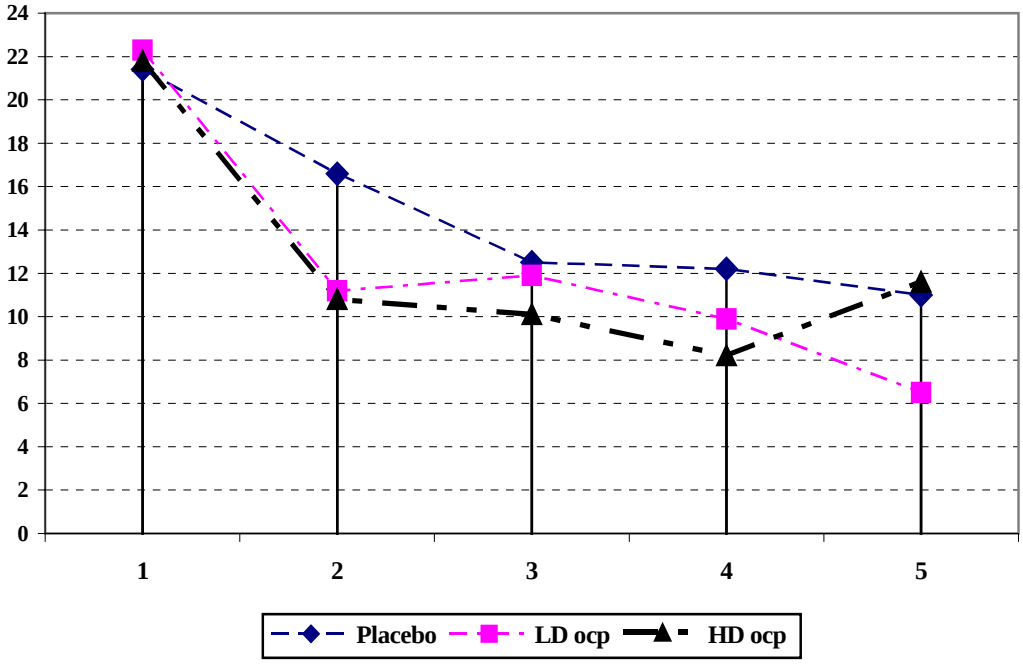

Fig. 1: Mean monthly bleeding days of three groups of DMPA users in follow up period

Discussion

Regarding natural history of irregular bleeding with DMPA, indicates amenorrhea in 50% of women by first year and 80% by third year (1).

In the majority of teenagers who used DMPA, amenorrhea took place. This amenorrhea was regarded as a positive effect (9). Most women can wait for amenorrhea without treatment if they know what to expect with time (10).

An important and revealing fact in our study is the significant change of bleeding pattern in comparison of the month prior to study and the first month of study in all groups even placebo group. It shows how important time scheduling is.

In a double-blinded placebo-controlled study in Thailand mefenamic acid in comparison to placebo was not effective in long-term control of bleeding during DMPA use (11).

Another study revealed that the endometrial stromal progesterone receptor score in DMPA users with amenorrhea was significantly higher than that of with bleeding (12).

It is suggested that persistent irregular bleeding can be treated by adding low-dose estrogen temporarily (1). In the view of hormonal control of DMPA bleeding it was demonstrated that OCP had excellent therapeutic effects (13).

In the present study, reduction of bleeding in first month was significantly more prominent in drug groups. Although this reduction showed only in the first month, this indicated the importance of LDOCP and HDOCP in rapid reduction or stoppage of bleeding with no persistent effects. After the first month we could not see the difference in three groups.

It seems that perhaps LDOCP and HDOCP with their rapid effects can encourage women to have more patience and wait in the hope that time will solve their problems.

In our Moslem society, these rapid effects can help women administrate their Islamic duties with prays.

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