The Effect of Combined Pills in Abnormal Uterine Bleeding Due to Norplant

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Abstract

Objective: Comparison of two kinds of combined oral contraceptive pills (low and high dose) in control of abnormal uterine bleeding due to norplant.

Study Design: Norplant users complaining of abnormal uterine bleeding visited in health care services of Hamadan University, took part in a triple blind randomized clinical trial. Regarding inclusion criteria, 100 women in three random groups took LDOCP (N=33), HDOCP (N=33) and placebo similarly. Patients were monthly followed up with regard to abnormal bleeding until four months. Drugs were decoded after data gathering. Data analysis was done using SPSS software with one-way and two-way variance analysis test at the significance level of 0.05.

Result: Age, education level, number of children, length of norplant usage and bleeding days per month in the month before the study were not significantly different in three groups.

Mean bleeding days in the first month in the placebo, LDOCP and HDOCP groups were 15.7, 9.4 and 8.2 days respectively (p=0.001). Mean bleeding days in the second, third and fourth months of the study were not significantly different in the three groups. Two variable variance analysis revealed time as a meaningful factor in mean bleeding days. However, treatment modality and interaction of time and treatment were not meaningful.

Conclusion: Time was the most effective factor in bleeding of norplant users. Contraceptive pills speed up bleeding reduction in the period of its prescription.

Key words: Norplant, Uterine Hemorrhage, Oral Contraception, Combined pills

Introduction

Rapid growth of population threatens the survival of human being in current century. With each woman expected to have no more than one or two children, most of the reproductive years are spent trying to avoid pregnancy. Norplant implants system is one of the most effective contraception methods including six silastic levonorgestrel containers that are implanted subdermaly. Thus, this effective contraception works for 90 months. Total pregnancy rate is 1% in five years.

Norplant induces endometrial atrophy and irregular menstrual bleeding from spotting to complete amenorrhea. Gradually irregular bleeding turns in to normal menstrual cycles.

A study in Hamadan province in 1997 revealed that 0.1% of non-pregnant married 15 to 49 year old women used Norplant. This population
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was 0.01% in rural and 0.1% in urban areas. In a study in Edinburgh patients were followed two years after norplant insertion. Bleeding was the main cause of the method withdrawal in 43% of cases.

In a survey in Indonesia the comparison of norplant and IUD users revealed less bleeding and less frequent menstruation and more amenorrhea in norplant users. In Brazil 50 women complaining of frequent and prolonged bleeding with norplant divided into three groups taking Ethinyl Estradiol (EE), combined oral contraceptive pill and placebo. OCPs lead to excellent results in bleeding reduction.

Another study was done in abnormal bleeding with norplant, ethinyl estradiol (50 microgram), oral contraceptive pills containing 50 microgram EE and 250 mcg levonorgestrel and placebo were prescribed. Combined OCPs was more effective than EE alone and EE more effective than placebo.

Muslim women are more sensitive to uterine bleeding due to their religious customs. Abnormal uterine bleeding might be treated by low dose estrogen, low dose levonorgestrel or bromphen.

In our country the majority of women in reproductive years are supervised by health providers and general physicians in primary health care system. Tertiary health care including gynaecologist are not free of charge for patients. So, norplant users complaining of abnormal bleeding should obligatory seek medical care out of health care system or withdraw the method. An effective treatment proposal practical for primary health care providers can solve the problem and reduce patient's cost and confusion. Oral contraceptive pills, permitted to be prescribed by health care providers are one of the abnormal bleeding treatment modalities in norplant users.

This study is designed to compare the effect of two kinds of oral contraceptive pills (LD and HD) with placebo in the reduction of norplant users' bleeding.

Study Design

In a triple blind randomized controlled clinical trial norplant users complaining of uterine hemorrhage who were visited in health care services in first half of 1999 in Hamadan Province took part in a study. Patients who planned to continue the method, suffered from more than 7 days bleeding in month, implanted norplant more than one month ago, and not under another hormonal treatment were studied with their written consent.

Patients prone to bleeding due to other reasons such as uterine myoma, coagulation disorder or using anticoagulant drugs and having contraindication to usage of estrogen containing drugs were excluded from the study. Thus 100 women were randomly studies in three groups including placebo (n=34), LDOC (n=33) and HDOC (n=33). Drugs were given in 20 similar capsules in a package containing a code. The drugs were unknown to the patients, drug givers and researchers. The drugs were decoded when the data were analyzed.

Number of children, education, bleeding days in the month before the study were recorded in questionnaires. A daily bleeding chart and necessary information were given to the patients who were asked to take a capsule daily even if a bleeding was stopped. They were scheduled for the next month appointment and were informed to call in case of occurring any problem. In the next visits they were given new bleeding charts. Whenever the charts were incompletely filled in or there were any problem, the researcher helped him. In missed patients, active follow up was done three times by phone or house call. Immigrants or completely missed patients were excluded from the study. Every patient was preplanned to be studied for 5 appointments in 4 months. If someone was missed after the second visit, here first month information would be used.

Data analysis was done using SPSS software. Variance analysis tests were used with the significance level of α=0.05. Box's test was used for the similarity of covariance matrices.

Results

One hundred norplant users were studied in three groups including placebo (n=34), LDOC (n=33) and HDOC (n=33). Three groups were similar regarding mean age, number of children, and education (table 1).

Mean lengths of norplant usage at the beginning of the study were 8.4, 9.8 and 7.7 months in placebo, LDOC and HDOC groups revealing no significance difference. (P=0.424)

Eight three percent of the population has been using norplant for less than one year. Mean bleeding days in the month before the study showed
significance difference in three groups. (P=0.865) (Table 2). Mean intervals between drug intake and bleeding withdrawal were 12.4 (SD=9.3), 5 (SD=5.9) and 5.4 (SD=6.7) in placebo, LDOCP and HDHOCP groups. The difference between the groups was statistically significant (P=0.003). Mean bleeding days in the first study month were significantly different in the three groups (P=0.001). It was 9.4 and 8.2 days in LDOCP and HDHOCP while 15.7 days in placebo groups. (Table 2). Mean bleeding days in the second, third and fourth months were similar in all groups (Table 2). Bleeding reduction in the first month of the study was observed in all three groups in comparison to the month of the study was observed in all three groups in comparison to the month before the study. In every group, mean bleeding days of the second, third, and fourth months of the study were less than the month before the study. (Figure 1).

![Figure 1: Mean Bleeding Days According to Time in Three Groups](image)

Bivariable analysis of variance was done to reveal the difference between mean bleeding days according to the time and treatment groups. Box's test did not rule out the hypothesis of similarity between covariance matrices. (P=0.88).

Bivariable analysis of variance did not show two-way effect of time and treatment type (0.054). Time factor was significant in mean difference at the level of 0.0001 while treatment was not (P=0.3). Eight cases withdraw the method. The most common cause of the method withdrawal in 5 cases was bleeding.

**Discussion**

In the current study mean bleeding days in LDOCP and HDHOCP groups during the first month (while taking drugs) were less than placebo group. From the second to the fourth month of the study the mean bleeding days were similar in all the three groups. Mean bleeding days of the first month were significantly reduced in comparison to the month before the study. Although the mean bleeding days in all groups showed a deceleration pattern, were never less than mean bleeding days in the month before the study. Norplant bleeding is said to simulate normal menstrual pattern as time passes.

| Table: Demographic Characteristics of the Study Groups |
|---------------------------------|---------|---------|---------|
|                                 | LDOCP N=33 | HDHOCP N=33 | Placebo N=34 |
| Age (Year)                      | 23.9 (SD=2) | 24.1 (SD=1.4) | 22.8 (SD=1.5) |
| Number of children              | 1.5 (SD=0.3) | 1.6 (SD=0.7) | 1.4 (SD=0.5) |
| Length of Usage (months)        | 6.8 (SD=0.7) | 7.2 (SD=0.6) | 4.4 (SD=0.7) |
| Lower than High School Diploma  | 27 (81.8) | 28 (84.8) | 23 (67.6) |
| Higher Than High School Diploma | 6 (18.2) | 5 (15.2) | 11 (32.4) |

* One-way analysis of variance
** P>0.05 not meaningful

We found that times makes a significant difference between mean bleeding days in the month before the study compared to the next months. With respect to drug intake in the first month did not found treatment to be effective in the mean bleeding days in the three groups during the next months. (bivariable analysis of variance).

Only 17% of the study population has been using Norplant for more than one year. It confirms the effect of time in bleeding pattern of norplant users and also reduction of bleeding problems and medical referrals after the first year. So regarding to
significantly less mean interval between drug intake and bleeding withdrawal and less mean bleeding days in LDOCP and HDOCP groups in comparison to placebo in the month of drug intake (first month), we can consider OCP as an effective way to control bleeding in norplant users during OCP intake.

In the study of Brazil, positive therapeutic effects of OCP in comparison to placebo in the reduction of bleeding in norplant users was revealed. Another study showed OCP to be more effective than ethinyl estradiol, and ethinyl to be more effective than placebo in the control of norplant bleedings.

| Table 2: Mean Bleeding Days in the Followup of the Three Groups |
|------------------|--------------|--------------------------|
| Month           | LD (SD)      | HD (SD)                  | Placebo (SD) | Levela |
| Before          | 22 (3.5)     | 22.1 (4.7)               | 21.3 (5.4)   | P=0.805 |
| First           | 9.4 (6.5)    | 8.2 (5.9)                | 15.7 (5.4)   | P=0.003 |
| Second          | 8.7 (7.1)    | 11.8 (8.3)               | 17.8 (8.3)   | P=0.108 |
| Third           | 12.1 (7.1)   | 14.4 (8.3)               | 15.2 (8.6)   | P=0.644 |
| Fourth          | 19.2 (8.7)   | 12.4 (6.5)               | 14 (9.3)     | P=0.437 |

a Based on one way analysis of variance

Considering similar bleeding reduction in LDOCP and HDOCP in our study, LDOCP with less dosage is preferred.

In conclusion regarding to the role of time in the reduction of norplant bleeding, counselling and education are recommended before the implantations of norplant. On the other hand OCP can speed up bleeding reduction while taking it.

References