

*Original Article***Comparison of efficiency and some complications of HD and levonorgestrel tablets as an emergency contraceptive method**

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Abstract

Background: This study aimed to define and compare the efficiency and complication between HD and levonorgestrel tablets as an emergency contraceptive method.

Methods: In this double blind clinical trial, the subjects included 68 women aged 15-45 years with regular menstruation cycles referred to Isfahan health centers within the first 72 hours after their unprotected coitus between May to Sep 2006. The subjects were selected by convenient sampling and randomly divided into two groups: one taking HD tablets and the other levonorgestrel. The data were collected by 3 questionnaires including demographic, productivity, coitus characteristics, efficiency and some complications such as nausea, vomiting, headache, dizziness and analytic statistical tests ran through SPSS software.

Results: Levonorgestrel had 100% efficiency in contraception (the difference was significant between two groups). There was no significant difference between changes in menstruation cycle and headache but there were differences considering nausea, vomiting and the times of vomiting within 24 hours after taking the second dose of the tablets; but it wasn't significant during the last six hours. Generally, in group of levonorgestrel side effects such as spotting, high amount or severe menstrual bleeding, occurrence and the times of vomiting, nausea severity, headache and dizziness were all witnessed less.

Discussion: Consumption of 0.75 mg levonorgestrel twice as an emergency contraceptive method has higher efficiency in prevention of unwanted pregnancies and lower side effects compared to HD tablets. It is suggested to plan and take necessary actions to produce and distribute these tablets as an emergency contraceptive method in Iran.

Key words: Emergency contraceptive methods, levonorgestrel, Yuzpe.

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If the population growth continues with the present rate, the world population in 2050 will overflow 90 billion people.¹ Increased rate of population growth is a major obstacle to social, economic and cultural developments, and affects numerous fields such as social welfare, employment, enjoyment of national net revenue, health and hygiene, treatment services, nutrition, education and etc.² Therefore through proposing various and new approaches in connection with family planning, many of such

problems can be controlled.³ Family planning can prevent over 25-30 percent of morbidity and mortality due to pregnancy⁴ and also prevent occurrence of unwanted pregnancies by the number of 450'000 cases per day.³ Although unwanted pregnancy occur due to various factors, its major reason is lack of using contraception means, failure of contraceptive procedures, and lack of continues use of contraception means.⁵

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Therefore in cases that child bearing is not intended and intercourse is done carelessly or without using contraceptives, or contraception method has failed, an emergency contraception procedure should be executed, as soon as possible.¹ Using emergency contraception means can decrease millions of abortions at global level, -two thirds of which performed in unhealthy conditions-⁶ and prevent occurrence of 1.7 million unwanted pregnancies in USA.⁷ So by using the emergency means, the risk of pregnancy decreases from 10-30% to 1%.⁸ Emergency contraception method is used following sexual intercourses without using reliable contraceptive means or in suspicious unwanted pregnancies following sexual intercourse. Using the emergency contraception means is effective up to 72 hours post unprotected sexual intercourse.⁶ Common emergency procedures include the usage of contraceptive pills, only progesterone pills (containing 75 Ml levonorgestrel) mifepristone, only estrogen, and cupric IUD.⁹ In Iran, available emergency contraceptive is HD pills which can decrease the risk of pregnancy up to 75%.⁷

The major problem in using HD pills is their side effects -nausea and vomiting-,¹⁰ which leads women toward not using them again.¹¹ Therefore, it is necessary that we think of new means of emergency contraception with less side effects and more efficiency. The procedure of using levonorgestrel is known as a golden standard in hormonal emergency procedures.¹² In preventing pregnancies this method is effective up to 97-99%.¹³ In a study conducted by WHO in 1998, occurrence of pregnancy in the group using Yuzpe regimen was 3.2% and in those consuming levonorgestrel was 1.1% which in this group such side effects as nausea, vomiting, vertigo and tiredness were significantly less witnessed.¹⁴ Since variability of emergency contraception means leads to increased usage of these methods and considering the fact that women are the major members of a family, assisting them in the field of family planning is a crucial step to improve their family quality and social life.¹⁵ Regarding the importance of population control and numerous

problems that caused by unwanted pregnancies, national research seem necessary to find newer emergency procedures, with less side effects and more effectiveness. Considering the side effects and effectiveness of HD tablets, international researches that indicate women with different nationalities, ethnics and races experience various symptoms and side effects,¹⁶ consumption of levonorgestrel (0.75 mg) which is more effective than HD pills and has less side effects, and that so far in Iran, no research has been conducted on this contraception mean, the researcher decided to conduct a study to determine effectiveness and some of the side effects (changes of the menstrual cycle, occurrence and number of vomits, severing of nausea, headache, and vertigo) in two emergency contraception methods which mentioned before (consumption of HD and levonorgestrel tablets) and compare them with each other. With hopes that this study will lead to more variable methods, decrease the number of unwanted pregnancies and increase the health of mother and child in the society.

Methods

The present study is a clinical, three stage, double-blind multivariate trial. The research population is composed of all the 15-45 years old women who referred to Isfahan health and treatment centers from 21.04.2006 till 21.08.2006 for receiving contraceptives. Easy sampling was used in which 68 individuals were randomly and systematically categorized into two groups. Criteria for being admitted to the research were that the individuals should be in the group of 15-45 years old, having unprotected sexual intercourse, their husbands using either condom or interrupted contraception method, having no prohibition in executing hormonal contraception procedures, having regular menstrual cycles with average length of 28-30 days, having no condition such as breast feeding, myoma and etc that leads to disordered menstrual cycle, having no emergency contraception means before, having no self-medication, using no tablets that decreases the effect of contraceptive pills and having unprotected sexual inter-

course in last 72 hours. Conditions such as digestive and mental disorders, migraine, depression, unknown vaginal hemorrhage were amongst criteria for not admitting the subjects to the study. Data collection tool used in this research included a three section questionnaire, one form related to demographic specifications of menstruation and intercourse, another one about the number of vomits, intensity of nausea, headache and vertigo and the last one about effectiveness of pills and modifications of the menstrual cycle. To assess scientific validity of forms, the content validity method was used. Scientific validity of tests were achieved by conducting β HCG tests in a laboratory under supervision of a technician and for measuring intensity of side effects the visual assessment ruler was used¹⁷. This ruler is standard so that the degree of side effect with scale of more than 7 was considered as intensive, with scale of more than 3.5 and less or equal to 7 as medium, with scale of less or equal to 3.5 as mild and with scale of zero as without complication. The women that referred to the health-treatment centers were selected randomly. This included those who needed emergency procedures. After considering the criteria for being accepted in the study or not, they were randomly categorized in two groups of HD and levonorgestrel consumers. Each group received an envelope that in group A included a placebo and a levonorgestrel tablet and in group B included 2 HD pills. Pills existing in each envelope were consumed at an interval of 12 hours and the first dose of pills was consumed during a period of 72 hours following unprotected intercourse. At admission time, questionnaires were completed through interviews. Then forms for studying the complications and modifications of the menstrual cycle were given to selected centers and they were instructed how to complete the forms. Since consumption of HD pills leads to temporary side effects, such as vomiting, nausea, headache and vertigo, and that the complication do not last over 24 hours, and also according to a new study mean half-life of oral

levonorgestrel is 24.4 hours, in this study those complications that followed consumption of the last dose of pills and modifications of the menstrual cycle at the end of the first and third weeks after consumption of emergency pills were studied. If there was a delay over one week in menstruation time from the expected time, to exclude the possibility of pregnancy, BHCG test was performed. To analyze data, the descriptive statistical (frequency distribution and drawing diagrams and tables) and inductive methods (χ^2 , Man-Whitney, and paired-t) were executed via SPSS software.

Results

The results of the study showed that 95.6 % of the studied subjects in both groups were married and 4.4% were single and that 61.8 % of them were housewives. Mean age in the group taking HD pills was 30.27 years and that of the levonorgestrel consuming group was 27.5 years and in both group mean number of children was 2 and mean menstrual cycle was 28.06 days and these features indicate the similarity of specifications between both groups.

Also, our findings indicated that occurrence of pregnancy in taking HD pills has been 5.9% and in those taking levonorgestrel has been zero percent. From the viewpoint of efficacy there was a significant statistical difference ($P = 0.04$) between two groups (table 1).

However, based on χ^2 test, there was no significant difference between the two groups in the time of next menstruation after consuming pills (table 1).

Based on χ^2 test, considering the menstruation length, in the HD consuming group there was a significant difference ($P = 0.011$) between the period before consuming HD pills and after it, while in the levonorgestrel consuming group, this difference was not significant ($P = 0.61$).

Based on Man-Whitney test, there was no significant difference between the two consumer groups regarding the amount of menstrual hemorrhage after taking pills (table 2).

Table 1: Frequency distribution of studied subjects, regarding efficacy of HD and levonorgestrel pills as an emergency contraception method

Group	Taking HD pills		Taking levonorgestrel pills		Total	
	No.	%	No.	%	No.	%
Pregnancy						
Did not occur	32	94.1	34	100	66	97.1
Occurred	2	5.9	0	0	2	2.9
Total	34	100	34	100	68	100

Table 2. Frequency distribution of studied subjects according to the amount of menstrual hemorrhage after taking pills in both groups

Group	HD pills consumers		levonorgestrel pills consumers		Total	
	No.	%	No.	%	No.	%
Amount of hemorrhage						
Intensive	3	9.4	3	8.9	6	9
Moderate	23	71.9	28	82.3	51	77.2
Stain	6	18.8	3	8.8	9	13.6
Total	32	100	34	100	66	100

Based on Man-Whitney test, in all the times the difference between the two groups considering the intensity of nausea was significant and the obtained P from the first to the sixth hour was 0.14, 0.002, 0.003, 0.001, 0.02, and 0.02, respectively. Also in all the times, except for the sixth period of six hours, the difference between the two groups considering vertigo was significant and the P obtained from this period was 0.02, 0.01, 0.006, 0.0005, 0.03, and 0.1, respectively, while there was no significant difference considering headache between the two groups, and the obtained P from the first to sixth hour was 0.1, 0.13, 0.1, 0.19, 0.27, and 0.16, respectively. Based on Man Whitney the difference between the two groups considering vomiting was significant ($P = 0.002$).

Discussion

Results of the present study showed that levonorgestrel has been a hundred percent effective in preventing unwanted pregnancies. Also, results of the research conducted by Kolarov et al (2004) indicated that consumption of levonorgestrel as an emergency contraception course is 98% effective in preventing unwanted pregnancies.¹⁸ Also Tanchev et al (2004) reported in their research that this method is one hundred percent effective.¹⁹ Although there was no significant statistical difference between the two groups considering changes in menstruation

cycle, results showed that the on-time occurrence of the next menstruation in the levonorgestrel consuming group was twice the HD consuming group. The research conducted by Hamoda et al (2003) on on-time occurrence of menstruation in the group taking levonorgestrel showed that in 70% of the subjects, the next menstruation post-consumption of this drug has been on-time and as predicted and in 8% menstruation has occurred later than expected time.²⁰ Another study on Yuzpe method showed that about 38% of HD pill consumers had their menstruation before the expected time and only 8% of them had menstruation delay.⁹ Results of these studies support the present research since the most studied subjects had their menstruation on-time or sooner than they expected and a few percent experienced delayed menstruation. Also the present results showed that the percentage of the witnessing stain in the HD consumers were twice as in levonorgestrel consumers. Also the results of Webb research (2004) showed that the witnessing of stain in Yuzpe method has been more than those of levonorgestrel.²¹ Interruption of exogenous progesterone and estrogen both lead to hemorrhage that the amount and period of it in different individuals is completely variable.⁷ On the other hand, irregular menstruation haemorrhage is the major problem of progesterone pill consumers.⁷ However, it can be concluded that

use of estrogen and progesterone hormones as an emergency contraception causes changes in the natural menstrual cycle due to interference with normal body hormones, which are unpredictable and vary from one individual to another.

Findings showed that intensity of nausea and number of vomits in the HD pill consumers has been more than those taking levonorgestrel. In a research conducted by WHO (1998), occurrence of nausea in the HD pill consumers had been 50.5% and in those taking levonorgestrel pills it had been 23.1%. Also occurrence of vomiting in the Yuzpe group had been 18.8% and in the levonorgestrel consumers had been 5.6%,¹⁴ it seems that the estrogen fraction of HD pills is effective in causing nausea and vomiting since generally nausea is related to estrogen fraction of pills.²² Also, findings showed that there is no significant statistical difference between the two groups considering headache occurrence. However, it is worth mentioning that the highest frequency of headache occurrence reported in both groups was mild, and the most frequency of intensive headache in the HD consumers was more than in the levonorgestrel consumers. In the research conducted by WHO (1988), percentage of headache occurrence in levonorgestrel pill consumers had been 16.8% and in HD pill consumers had been 20.2% that like the present research, the statistical difference between the two groups was not significant.¹⁴ Also, according to the research conducted by Ashok et al (2004), occurrence of headache in the Yuzpe method was 32.4%²³ while Okewole et al (2005) in their research reported that the headache due to consumption of 1.5mg levonorgestrel was 20%.²⁴ It can be concluded that consumption of high level of progesterone and sudden fall of estrogen and progesterone following their high level consumption as an emergency contraception has a major role in headache occurrence and that percentage of headache occurrence following sudden interruption of estrogen is higher than sudden interruption of progesterone and this is the reason why those subjects using Yuzpe method are proved to suffer more from headache. Findings showed that severity

of vertigo due to HD pill consumption as an emergency contraception method is more than levonorgestrel consumption and statistically the difference between the two groups was significant.

Results of the study conducted by WHO (1998) indicated that 16.7% of the subjects using Yuzpe method and 11.2% of those consuming levonorgestrel suffered from vertigo.¹⁸ In Tanchev et al study (2004), 6.8% of the subjects consuming levonorgestrel suffered from headache.¹⁹

According to the results of this study, effectiveness of levonorgestrel in preventing unwanted pregnancies is more than the Yuzpe method which shows superiority of levonorgestrel pills from this point of view. In addition, percentage of occurrence and severity of complications such as nausea and vertigo, and occurrence and number of vomiting was considerably less in the levonorgestrel pill consumers.

Also, occurrence and severity of headache in the levonorgestrel pill consumers was reported to be lower than HD pill consumers, though the difference between them was not significant. Results revealed that after using levonorgestrel pills as an emergency contraception method, probability of on-time occurrence of menstruation is more than after consuming HD pills and the percentage of the witnessing of stain in HD consumers was over twice time more than in levonorgestrel consumers which shows superiority of levonorgestrel from this point of view, too. Finally results of this study indicated that consumption of levonorgestrel pills as an emergency contraception method was effective and has fewer side effects. So it's offered to run more researches with more subjects all around the country and if the results would be favourable, increase the production of these pills in the country if possible and make packages containing two pills, special for emergency contraception that would be available at all the pharmacies and health and treatment centres all over the country and try to make it a substitute for HD pills as a contraception method.

Also, the authors declare that have no conflict of interest in this study and they have surveyed under the research ethics.

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