

# Vaginal bleeding following the use of a single dose of 1.5mg levonorgestrel (LNG) for emergency contraception

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## Summary

**Introduction:** Recent studies have shown that a single dose of 1.5 mg levonorgestrel is an effective and safe emergency contraceptive but detailed information on its menstrual side effects is lacking. This study assessed the vaginal bleeding patterns in healthy women who used the medication for emergency contraception.

**Study design:** A prospective observational study of 544 women who sought emergency contraception and volunteered to use a single dose of 1.5mg. levonorgestrel. They were assessed for bleeding patterns, pregnancies and side effects. **Results:** The pregnancy rate was 0.7% (95% CI, 0.0-1.4). Early or timely return of menses occurred in 69% of the women while in 21% menses was late by more than a week. Normal vaginal bleeding occurred in 57% of the women while others had intermenstrual bleeding/spotting, premenstrual bleeding /spotting or menorrhagia. Non-menstrual side effects include nausea, vomiting, dizziness, headache, breast tenderness and low abdominal pain. All side effects were well tolerated by the women.

**Conclusion:** A single dose of 1.5mg LNG when used for emergency contraception is safe and reliable but is associated with menstrual disturbances that may be of concern to a small number of users.

**Keywords:** Emergency contraception, Levonorgestrel, Vaginal bleeding, Menstrual changes.

## Résumé

**Introduction:** Des études récentes avaient démontré qu'une seule dose de 1,5mg levonorgestrel est une contraception d'urgence très efficace et sans danger mais des informations approfondies sur sa réaction secondaire en matière du cycle menstruel manquent. L'objet de cette étude est d'évaluer la tendance du saignement vaginal chez des femmes en bonne santé qui utilisaient des drogues pour une contraception d'urgence.

**Plan d'étude:-** Il s'agit d'une étude par observation en perspective de 544 femmes qui se sont présentées pour une contraception d'urgence et s'étaient portées volontaire pour utiliser une seule dose de 1,5mg levonorgestrel. On les avait évalué tout en notant tendance de saignement, grossesses et réactions secondaires.

**Résultats:-** Le taux de la grossesse était 0,7%(95% CI,0,0-1,4). Le retour en avance ou juste à temps des menstrues est arrivé en 69% des femmes tandis que chez 21 % des cas des menstrues étaient tardées pour plus d'une semaine. Saignement vaginal normal est arrivé chez 57% des femmes tandis que des autres avaient un saignement intermenstruel/spotting, vomissements, étourdissement, maux de tête,

tendreté du sein et douleur abdominale en bas. Toutes les réactions secondaires ont été bien tolérées par les femmes.

**Conclusion:-** Une seule dose de 1,5mgLNG quand administrée pour une contraception d'urgence est sans danger, et fiable mais est associée aux douleurs menstruelles qui pourrait être une affaire qui concerne un petit nombre de utilisatrices.

## Introduction

Emergency contraception (EC) denotes a contraceptive method to be used in emergency situations<sup>(1)</sup>. It is important that emergency contraceptives are available immediately to women who need them for their benefits to be realized. The two readily available emergency contraceptives in Nigeria, the Yuzpe regime (combined estrogen and progestin pills) and levonorgestrel (LNG) pills, contain mega doses of hormones in regular contraceptive pills and produce more severe side effects than the regular pills<sup>(2,3)</sup>. They are usually given in two doses 12 hours apart within 72 hours of unprotected sexual intercourse during the fertile period. Reports have shown that LNG pills are more effective than Yuzpe regime but cause a delay in the return of menses and bleeding problems<sup>(2,4)</sup>. Two recent studies suggest that a single-dose of 1.5 mg. LNG is as effective as the usual regimen of two-doses of 0.75 mg. LNG.<sup>(5,6)</sup> This single-dose regimen will seem appropriate for those who are likely to abscond after initial visit to the clinic or can not take the second dose. However, there is yet little information on this regimen in literature. This report assesses the vaginal bleeding pattern in women who have taken a single dose of 1.5 mg. LNG for emergency contraception.

## Subjects and methods

Six hundred healthy women between 15 and 45 years of age who have had unprotected sexual intercourse and requested emergency contraception were counseled to use a single-dose of 1.5 mg LNG pills. The pills were given to those with regular menstrual cycles of 21-35 days if they gave informed written consent, had unprotected sexual intercourse within 72 hours of presenting in the clinic during the fertile period and were available for follow up. Pregnant women and those with contraindications to the use of hormonal contraceptives were excluded. The women took the pills in the presence of an observer and were advised to abstain from sexual intercourse until their next menstruation. Each woman was asked to keep record of all bleeding events in a menstrual calendar. Those who vomited within 4 hours of taking the pills had the medication repeated. Follow up was continued for at least 42 days or until the end of menstruation either in the clinic or at home for clinic defaulters. The ovulation date for each woman was calculated by subtracting

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14 days from the expected date of her next period, which was calculated from the mean cycle length of her three previous menstrual cycle. A delay of five or more days was taken as a significant delay in the onset of next menses.

**Analysis**

Bleeding and spotting events were assessed for 42 days following the drug intake. Bleeding was defined as bloody vaginal discharge that requires protection while spotting was any bloody vaginal discharge that does not require protection. Menorrhagia refers to heavy vaginal bleeding with more than minimal clots. Prolonged bleeding or spotting refers to bleeding/spotting episode lasting 10 or more days. All entries were made into a computer using EPI-Info version 6.02 (CDC/WHO, Atlanta, Georgia). Events are presented in frequency tables, means, standard errors and ranges.

**Result**

Analysis of events was made on 544 women who completed the study. Twenty three did not meet the criteria for inclusion while four women were totally lost to follow up and were withdrawn from final analysis. Additional 29 women did not provide enough information to be assessed for vaginal bleeding patterns and side effects.

Age, parity and time of coitus to treatment distribution of the women were shown in Table 1. The mean age of the women was 26.6 ± 7.2 (SE) years. The mean body mass index of the women was 25.8 ± 3.7 (SE) kg./m<sup>2</sup>. The mean cycle length was 28.5 ± 2.7 (SE) days. About 35% (200) had used EC in the past.

**Table 1 Selected sociodemographic characteristics of the 577 women recruited.**

Characteristics	Number of women (%)
<b>Age (years):</b>	
15- 19	112 (19.4)
20-24	146 (25.3)
25-29	162 (28.1)
30-34	97 (16.8)
35-39	45 (7.8)
40-45	15 (2.6)
<b>Parity:</b>	
0	237 (41.1)
1-2	312 (54.0)
3-4	28 (4.9)
<b>Interval between treatment day and ovulation day:</b>	
> 1 day before ovulation.	281 (48.7)
Ovulation day ± 1 day.	187 (32.4)
> 1 day after ovulation	109 (18.9)

Four pregnancies occurred giving a pregnancy rate of 0.7% (95%CI, 0.0-1.4). Table 2 shows the frequency of the vaginal bleeding events that occurred during the study among the 544 women that provided enough information to be assessed for vaginal bleeding patterns and side effects. It shows also the frequency of vaginal bleeding events in the 577 women who took the medication (the intention-to-treat

**Table 2 Change in vaginal bleeding and menstrual dates in the women characteristics.**

Characteristics	Percentage of women	
	ITT population (n = 577)	Women with adequage information (n = 544)
<b>*Vaginal bleeding</b>		
a) Intermenstrual bleeding/spotting	25.6	27.2
b) Premenstrual bleeding/spotting	9.4	9.9
c) Prolonged bleeding/spotting	3.0	3.1
d) Menorrhagia	11.3	15.6
e.) Normal	53.9	57.2
<b>Change in the onset of next menstrual cycle</b>		
>7 days earlier	19.8	21.0
7 -4 days earlier	15.1	16.0
Between 3 days earlier and 3 days later	30.3	32.1
4 - 7 days later	9.4	9.9
>7 days later	19.8**	21.0**

\* Some women had more than one type of vaginal bleeding

\*\* Include 4 women who got pregnant.

population). Normal vaginal bleeding occurred in 311 (57.2%) women. Bleeding/spotting in the first 7 days of treatment (intermenstrual bleeding/spotting) occurred in 148 (27.2%) women while bleeding/spotting thereafter till onset of menses (premenstrual bleeding/spotting) occurred in 54 (9.9%) women. Among these 202 women with early bleeding, 114 (21%) started their menses more than 7 days earlier than expected while 88 (16%) women had vaginal bleeding/spotting that were not menses. The patterns of the vaginal bleeding/spotting were unrelated to the women's age or previous use of emergency contraceptive pills.

Nonmenstrual events reported were nausea, vomiting, dizziness, headache, breast tenderness and low abdominal pain. Only 7.8% of the women recruited vomited and were given a repeat dose of the pills. In general, these side effects were well tolerated by the women.

**Discussion**

This study shows that a single dose of 1.5mg LNG pills is effective for emergency contraception with a pregnancy rate of 0.7%. This has been stated in our earlier report (5) and is similar to the findings by WHO in a multi-center international trial (7). The modes of action of LNG pills are still uncertain but experiments have indicated that LNG delays ovulation, prevents implantation and increases cervical hostility to sperm among other things (7,8). LNG has been shown to also attenuate or delay pre-ovulatory lutenizing hormone (LH) surge (7-10). LNG effect on ovarian function may be dependent on the dose administered, the number of doses given and the timing of administration in the menstrual cycle (11). Kesseru and co-workers (10) reported a decreased midcycle LH peak in women who took two or more doses of LNG pills after sexual

intercourse. These hormonal disturbances will logically affect hormonal interplay in the menstrual cycle and produce menstrual disturbances, a major use related adverse event that influences the acceptability of most contraceptives. Although such disturbances are more of a feature of regular progesterone only contraceptives<sup>(12)</sup>, the disturbances encountered in this study call for concern since most women will like to be able to predict the onset of vaginal bleeding and be adequately prepared for it. While early return of menses is reassuring, a delay in onset of menses can be worrying to women who are already concerned about the possibility of an unintended pregnancy. It is very reassuring from this study that more than half of the women had an early return of their menses and only 21 % had a delay for more than a week beyond the expected day of onset of menses. This is contrary to the effect of mifepristone which delays the onset of next menses for up to two weeks in a larger percentage of women<sup>(6)</sup>. This finding is an important counseling information to give to emergency contraceptive seekers. Such information should prevent unwarranted surgical procedures for phantom pregnancies with attendant complications.

Emergency contraceptives with sex steroid contains larger doses of the steroids than is contained in regular contraceptives, which is administered for a short period. Thus the immediate side effects experienced by ECP users are expected to be more exaggerated than those experienced by regular oral contraceptive pills users. Apart from the 7.8% of the women who vomited their LNG pills and had them re-administered, the side effects encountered in this study were well tolerated by the women despite the large dose of LNG. Reports have shown that occurrence of side effects is affected by many factors that include individual and regional variations<sup>(6,12)</sup>. A multinational trial by WHO showed that the incidence of side effects was unrelated to the number of LNG tablets taken and varied markedly between centers<sup>(12)</sup>. Therefore, it can be confidently concluded that a single dose of 1.5 mg. LNG is safe and reliable to be used for emergency contraception.

#### Acknowledgement

We are grateful to the study participants and the family planning nurses of Fertility Research Unit, U.C.H, Ibadan, Planned Parenthood Federation of Nigeria and Association of Family and Reproductive Health, Ibadan who contributed to the success of the study.

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