

Risk of Pregnancy Among Women Seeking Emergency Contraceptives From Pharmacists in British Columbia

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Abstract

Objective: Recent revision of the method used to estimate risk of pregnancy among women requesting medication for emergency contraception (EC) suggests that the effectiveness of EC may be lower than is generally believed. We undertook a population-based study to estimate the risk of pregnancy among women requesting EC from pharmacists in British Columbia under conditions of routine care.

Methods: We obtained data on time since unprotected intercourse and medication provided for women in British Columbia requesting EC from January 1, 2001 to December 31, 2002.

Results: More women obtained levonorgestrel (60.7%) than the Yuzpe regimen (39.3%) for EC, and of those reporting contraceptive failure, 90% requested EC because of condom failure. Overall, the estimated risk of pregnancy among the 11 795 women who obtained EC was 4.12 % (95% confidence interval 3.77–4.49).

Conclusion: Under routine conditions, the population-based predicted risk of pregnancy is lower than has previously been estimated. This suggests that the relative reduction in pregnancies achieved with EC is lower than is currently assumed by clinicians and patients.

Résumé

Objectif : La révision récente de la méthode utilisée pour estimer le risque de grossesse chez les femmes qui demandent une contraception d'urgence (CU) semble indiquer que celle-ci pourrait être moins efficace que ce que l'on croyait. Nous signalons les résultats avérés menés par une étude visant l'obtention d'une estimation en population générale du risque de grossesse chez les femmes qui adressent une demande de CU, auprès des pharmaciens de la Colombie-Britannique, dans le cadre des soins habituels.

Méthodes : Nous avons obtenu des données (couvrant la période allant du 1^{er} janvier 2001 au 31 décembre 2002) sur le délai depuis les relations sexuelles non protégées et sur les médicaments offerts aux femmes de la Colombie-Britannique demandant une CU.

Key Words: Emergency contraception, pregnancy, effectiveness, Yuzpe, levonorgestrel

Competing Interests: None declared.

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Résultats : Le lévonorgestrel (60,7 %) a été offert à un plus grand nombre de femmes que le schéma Yuzpe (39,3 %) aux fins de la CU; de plus, 90 % des femmes qui signalaient un échec de la contraception déposaient une demande de CU en raison d'un échec du condom. Globalement, l'estimation du risque de grossesse chez les 11 795 femmes qui ont obtenu une CU était de 4,12 % (intervalle de confiance à 95 %, 3,77–4,49).

Conclusion : Dans des conditions habituelles, l'estimation en population générale du risque de grossesse est inférieure à ce qui avait été auparavant estimé. Cela laisse entendre que la baisse relative du nombre de grossesses attribuable à la CU est inférieure à ce qui est actuellement présumé par les cliniciens et les patientes.

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INTRODUCTION

Emergency contraception (EC) is believed to be effective in reducing the risk of pregnancy following unprotected intercourse.¹ In clinical trials, different regimens can be compared with respect to pregnancy (EC failure) rates, but it is not ethical to conduct placebo-controlled trials to determine the efficacy of different EC regimens. As a result, the effectiveness of EC regimens must be estimated from a comparison of the observed pregnancy rate with the expected rate. Prior to 1998, the expected pregnancy rate among women seeking EC in clinical trials was based upon the number of women treated who had intercourse on a given cycle day, using data derived from studies of the probability of conception on each cycle day.² This method of calculation is referred to hereafter as the traditional method.

The two most commonly used methods of EC are the Yuzpe and levonorgestrel regimens.¹ The Yuzpe regimen comprises ingestion of 100 µg of ethinyl estradiol and 1.0 mg of dl-norgestrel on two occasions 12 hours apart; the levonorgestrel regimen (marketed in Canada as Plan B) comprises ingestion of either 1.5 mg of levonorgestrel as a single dose, or 0.75 mg levonorgestrel on two occasions

12 hours apart.¹ Of the two clinical trials that have been conducted comparing these regimens, the first found no difference in pregnancy rate.³ In the second, a multinational World Health Organization (WHO) study, 1998 women were randomized to either the Yuzpe or the levonorgestrel regimen. The observed pregnancy rates were 3.2% and 1.1%, respectively (relative risk [RR] 0.36 for pregnancy after the levonorgestrel regimen compared with the Yuzpe method; 95% confidence interval [CI] 0.18–0.70).⁴ On the basis of the traditional method, the effectiveness of the regimens was estimated to be 57% for the Yuzpe regimen and 85% for the Plan B regimen. Among the 1157 women who were considered “correct users” of EC by self-report, the effectiveness was 76% for the Yuzpe regimen and 89% for the levonorgestrel regimen. This latter result is usually referred to when the effectiveness of these two regimens for EC is discussed. Recently, Wilcox et al. suggested that the traditional method of estimating risk of pregnancy may overestimate the expected pregnancy rate and, therefore, the effectiveness of EC.⁵ With the traditional method, the day of ovulation was estimated by subtracting 14 days from a woman’s usual cycle length; the risk of pregnancy was then estimated by the proximity of the day of unprotected intercourse to the expected day of ovulation. This method could be applied only to women with regular cycles, and this has been an inclusion criterion for many EC studies. Wilcox et al. proposed a new approach (hereafter referred to as the revised method) based on the fact that women do not know when they ovulate, but they do know when they begin to menstruate. They derived empirical estimates of the probability of pregnancy for each day of a woman’s menstrual cycle, allowing an estimate of the risk of pregnancy after unprotected intercourse according to the cycle day on which intercourse occurred.⁵ To date, there have been no population-based studies evaluating the risk of pregnancy using the revised method among women seeking EC.

In December 2000, in the province of British Columbia, pharmacists were authorized to provide EC (the Yuzpe regimen or levonorgestrel) to women without a physician’s prescription. We subsequently conducted a population-based study of EC provision by pharmacists and physicians in British Columbia during 2001 and 2002.⁶ On the basis of information obtained from women seeking EC from a pharmacist, we were able to estimate the risk of pregnancy, using the revised method, in women who received either the Yuzpe or levonorgestrel regimen.

METHODS

In December 2000, the Province of British Columbia enacted legislation granting authority to specifically trained, certified pharmacists to provide women with post-coital (emergency) contraceptives containing ethinyl estradiol

50 µg in combination with dl-norgestrel 0.50 mg (for the Yuzpe regimen), or levonorgestrel 0.75 mg (Plan B, Paladin Laboratories Inc., Montreal), without a physician’s prescription. Under this authority, pharmacists were required to conduct a brief, structured interview with the patient, providing information on the effectiveness, side effects, and costs of the Yuzpe and levonorgestrel regimens. Pharmacists were authorized to provide EC for immediate or future use. On a written consent for EC treatment form, women provided information about their age, whether EC was for immediate or future use, time since unprotected intercourse, time since the beginning of the last menstrual cycle and reason for requesting EC. On the consent form, pharmacists documented the date and time of dispensing and the medication provided. We obtained de-identified copies of written consents for EC treatment from the College of Pharmacists of British Columbia for the period from January 1, 2001, to December 31, 2002, and these accounted for 96.1% of all ECs provided by pharmacists during that period.⁶ The expected number of pregnancies in the Yuzpe and levonorgestrel cohorts was estimated from the reported time between the onset of the last menstrual cycle and the occurrence of unprotected intercourse, using the daily risk of pregnancy for all women (i.e., without consideration of whether they had regular or irregular cycles) based on the revised method.⁵ The risk of pregnancy in each group and overall was based on the number of pregnancies expected for women obtaining EC on a given day of the menstrual cycle as a proportion of the entire cohort. This study was approved by the Clinical Research Ethics Board of the University of British Columbia.

RESULTS

The results in the Table show that women who obtained levonorgestrel were slightly older and requested EC sooner after unprotected intercourse than those who received the Yuzpe regimen. Most women were requesting EC because of failure of birth control, which was due to breakage of condoms in about 90% of documented cases in both groups. On the basis of the time since onset of the last menstrual bleed, the mean risk of pregnancy was slightly higher among women who received levonorgestrel, although there was considerable overlap of the 95% confidence intervals. When the data for all women are combined, the mean risk of pregnancy is estimated to be 4.12% (95% CI 3.77–4.49). This risk of pregnancy is substantially lower than that estimated in studies comparing the effectiveness of the levonorgestrel and Yuzpe regimens.^{3,4}

The Figure shows that women in both groups were requesting EC during the period of highest probability of

Characteristics and risk of conception among women who received the Yuzpe and levonorgestrel regimens

	EC regimen provided	
	Levonorgestrel (n = 7160)	Yuzpe (n = 4635)
Age	26.0 (\pm 7.5)	24.6 (\pm 7.3)
Time (hours) since unprotected intercourse*	24.5 (\pm 19.0)	26.6 (\pm 18.7)
Time (days) in cycle*	15.8 (\pm 7.5)	15.9 (\pm 7.8)
Reason for EC:		
No birth control used	43.8%	43.7%
Failure of birth control method	56.2%	56.3%
Condom failure [†]	92.0%	90.0%
Other types of failure [†]	8.0%	10.0%
Mean estimated risk of pregnancy (95% confidence intervals)	4.16 (3.71–4.65)	4.02 (3.48–4.63)

*Continuous data presented as mean \pm standard deviation for all women who noted the first day of their last menstrual cycle on the consent for treatment form.

[†]Based on data available from 2997 women receiving the levonorgestrel regimen and 1646 receiving the Yuzpe regimen.

pregnancy, although a substantial proportion of women requested EC either early or late in their cycle.

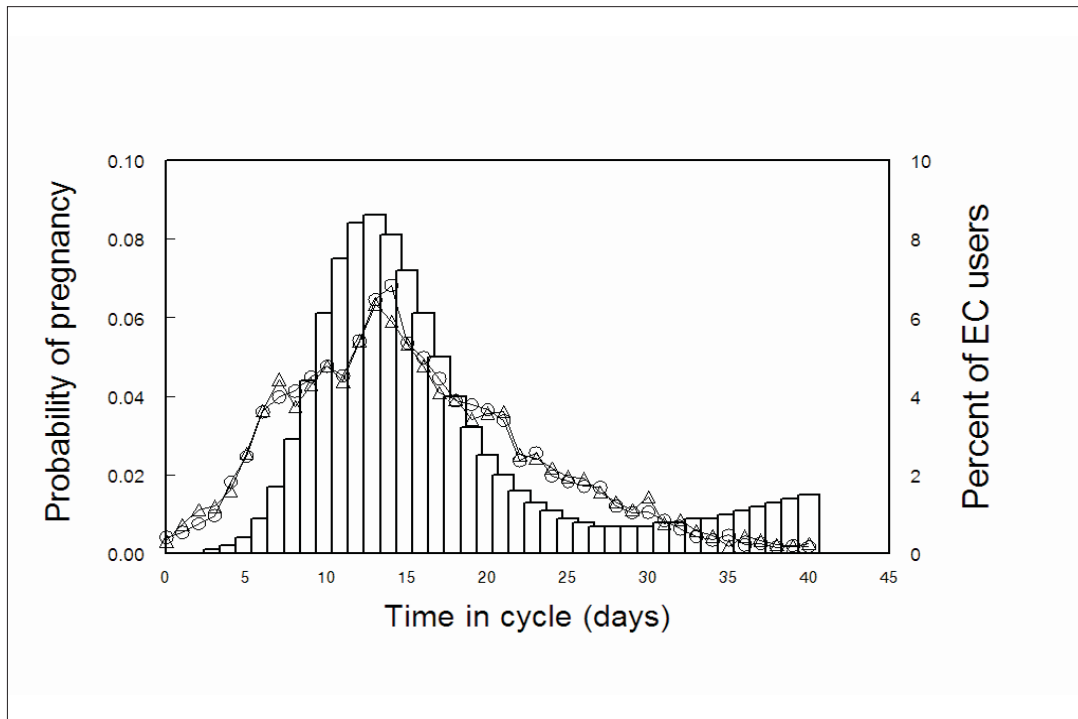
DISCUSSION

This is the first report of risk of pregnancy among a population-based cohort of women requesting EC from pharmacists under conditions of routine use. Overall, in the two groups combined, the estimated risk of pregnancy was 4.12%, which is markedly lower than that reported when effectiveness of EC has been estimated in clinical trials.^{2–5} The small observed difference (0.14%) in risk of pregnancy between women receiving levonorgestrel or the Yuzpe regimen (see Table) may have been due to chance or may indicate that women requesting levonorgestrel were attempting to offset what they perceived to be a higher pregnancy risk on the basis of the counselling they received from their pharmacists. Conversely, as women in the cohort choosing levonorgestrel were slightly older, it is possible that they were better able to pay the higher price for the regimen that is better tolerated and believed to be more effective. Our results also indicate that women who requested EC from their pharmacists typically did so during the period of highest risk of pregnancy during their menstrual cycle. However, substantial numbers of women requested EC either before day 10 or after day 20 of their cycle (see Figure). This may be a reasonable strategy, as it has been shown that the risk of pregnancy is not zero on any day after the first two days of the cycle.⁵

The authors of the WHO study⁴ used the traditional method to estimate the risk of pregnancy in women for whom the outcome was known, and they found the risk to be 7.7% and 7.4% among those randomized to the levonorgestrel and Yuzpe regimens, respectively. On the basis of the observed pregnancies (1% and 3.2% in the respective groups), the effectiveness of the levonorgestrel and Yuzpe regimens was therefore concluded to be 85% and 57%, respectively.⁴ Trussell et al. re-evaluated the risk, using the revised method, among WHO subjects who received the Yuzpe regimen.⁷ They estimated the risk of pregnancy to be 5.2%, and they thus re-calculated the effectiveness of the Yuzpe regimen to be 46.8%.

Participation in clinical trials of EC regimens usually involves strict entry criteria that can affect the risk of pregnancy among those enrolled relative to the general population.⁷ The Population Council trial involved three randomized groups of women (total enrolment, 2041) who received variants of the Yuzpe regimen.⁸ However, during the year-long recruitment period, data including cycle day were obtained from all women (20 437) requesting EC from the three participating clinics during the first year of the study. Using the revised method, Trussell et al. estimated the risk of pregnancy to be 5.4% among participants in the Population Council trial and 3.9% among all the women who requested EC from the clinics during the study period.⁷ The latter estimate of risk of pregnancy among all women is similar to that in the present cohort of women in British

Probability of pregnancy among women requesting EC from pharmacists in British Columbia



Bars represent the predicted probability of pregnancy on each day of the menstrual cycle.⁵ Open circles (Yuzpe cohort) and open triangles (levonorgestrel cohort) represent the women's self-reports of the day in the menstrual cycle on which unprotected intercourse occurred.

Columbia who obtained EC from pharmacists under conditions of routine care. Mikolajczk and Sanford have recently suggested that methods for estimating pregnancy risk that do not account for average cycle length and timing of ovulation in individual women will systematically overestimate the risk of pregnancy and therefore overestimate the effectiveness of EC.⁹ However, they argue that the revised method used in this study is better than previous ones if data about previous cycle length are not available.⁵

During the two-year period of the present study in British Columbia, 20 116 women obtained prescriptions for EC, of which 77% were for the Yuzpe regimen and 23% for levonorgestrel.⁶ Although these women may have requested EC from their physicians because they were unaware that pharmacists were authorized to provide it, in some cases they may have done so to avoid the counselling fee charged by pharmacists or to obtain coverage from government programs or reimbursement from third party payers. Thus, it is possible that our estimate of the risk of pregnancy in women who request EC from pharmacists is different from the risk in women who obtained prescriptions for EC from their physician. Further population-based studies are being conducted in British Columbia to

estimate the pregnancy rate in women who received EC from physicians or pharmacists. These will provide information about the effectiveness of EC and about whether and to what extent levonorgestrel is superior to the Yuzpe regimen.

CONCLUSION

If the estimates of risk of pregnancy from the present study and related studies are reasonably accurate, the effectiveness of EC among women in the general population may be markedly lower than is currently believed by professionals and advocates for wider EC use. In light of these observations, consideration should be given to revising the information on effectiveness that physicians, pharmacists and other health care professionals provide to women seeking EC.

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