Human Reproduction, Vol.24, No.4 pp. 815–819, 2009
Advanced Access publication on December 18, 2008 doi:10.1093/humrep/den460

human reproduction

ORIGINAL ARTICLE *Fertility control*

Increased access to emergency contraception: why it may fail

Laura Baecher[1,3], Mark A. Weaver[2], and Elizabeth G. Raymond[2]

[1]Department of Obstetrics and Gynecology, University of North Carolina at Chapel Hill, 101 Manning Drive, CB #7570, Chapel Hill, NC 27514, USA [2]Family Health International, PO Box 13950, Research Triangle Park, NC 27709, USA

[3]Correspondence address. Department of Obstetrics and Gynecology, University of North Carolina at Chapel Hill, 101 Manning Drive, CB #7570, Chapel Hill, NC 27514, USA. E-mail: lbaecher@hotmail.com

BACKGROUND: To explore why increased access to emergency contraception (EC) failed to reduce pregnancies in a recent randomized controlled trial.

METHODS: We used multivariable logistic regression to identify risk factors for unintended pregnancy using data from a trial involving sexually active women ($n = 1490$, aged 14–24 years) randomly assigned to either increased access or standard access to EC. We used predictive modeling to generate estimated pregnancy risk scores for each participant. We then examined EC use among women at low or high baseline risk of pregnancy.

RESULTS: Gravidity, recent history of unprotected sex (within 14 days of enrollment to study) and lower aversion to pregnancy predicted unintended pregnancy. Women in the increased access group were more likely than women in the standard access group to use EC repeatedly. This difference was significantly stronger ($P = 0.03$) among low risk women than high risk women [Relative risk (RR) 10.0, 95% confidence interval (CI) 6.5–15.4 and RR 5.5, 95% CI 3.8–7.9, respectively].

CONCLUSIONS: Increased access to EC had a greater impact on women who were at lower baseline risk of pregnancy. This may explain in part why increased access to EC has had no measurable benefit in clinical trials.

Key words: emergency contraception / unintended pregnancy / risk

Introduction

Emergency contraception (EC) was introduced in the early 1990s as an effective method of post-coital contraception. Levonorgestrel EC has been well established as an efficacious method of preventing pregnancy (Task Force on Postovulatory Methods of Fertility Regulation, 1998). Widespread access to EC was expected to substantially decrease the incidence of unintended pregnancy in the USA; however, this has not been realized (Trussell *et al.*, 1992; Finer and Henshaw, 2006). Multiple studies have failed to demonstrate a difference in unintended pregnancy rates between women provided with an advanced supply of EC and women who could obtain it only when needed (Lo *et al.*, 2004; Hu *et al.*, 2005; Raymond *et al.*, 2006; Walsh and Frezieres, 2006). Yet, failure of advance provision occurs despite a reported increase in use and more prompt use of levonorgestrel EC after unprotected coitus. This paradox has mitigated earlier enthusiasm regarding the public health importance of EC (Glasier, 2006).

The explanation for this failure remains elusive. We hypothesize that underlying risk of unintended pregnancy may influence response to an intervention of increased access to EC. That is, with increased access to EC, women at lower baseline risk of unintended pregnancy may use EC differently than women at higher risk.

To investigate this question, we used data from a recent trial of an intervention designed to optimize access to EC. The intervention of increased access to EC proved successful in increasing EC use; the mean number of uses per woman was 5.6 times higher in the intervention group than in the control group (Raymond *et al.*, 2006). Despite this increased frequency of EC use, the incidence of unintended pregnancy was similar between groups (Raymond *et al.*, 2006). For our analysis, we used predictive modeling to characterize each participant's baseline risk of unintended pregnancy as either high or low. We then evaluated whether the effect of the intervention on EC use differed between these two risk groups.

Materials and Methods

The trial was conducted between October 2002 and June 2005 at clinical sites in Nevada and North Carolina. CONSORT guidelines were adhered to in the design and reporting of the original study

(Moher et al., 2001). The protocol for this secondary analysis was approved by the institutional review board at the University of North Carolina at Chapel Hill.

A full description of the methods has been published (Raymond et al., 2006). Briefly, 1490 sexually active women aged 14–24 years who did not desire pregnancy for at least 1 year were enrolled. Women who planned to use longer acting contraceptive methods and women who had been pregnant within the past 6 weeks or were breast feeding were excluded. Demographic, behavioral and psychosocial information were collected from each participant at enrollment. Psychosocial questions addressed perceptions of pregnancy, sexually transmitted infection and various contraception methods. The full battery of psychosocial questions and details regarding the factor analysis methods are presented elsewhere (Weaver et al., 2008). Participants were then randomized to receive either increased access or standard access to EC. Participants in both groups were advised to take a single dose of 1.5 mg levonorgestrel as soon as possible after unprotected intercourse. Standard access group participants were informed how to obtain EC from the study site at the usual cost if needed. Increased access group participants were provided with two free packages of EC pills at enrollment, and free replacement packages were provided for each reported use of EC. Participants in both groups were asked to report each use of EC to the study site. Participants were followed in the clinic at 6 and 12 months after enrollment. Pregnancy tests were obtained at those times. Follow-up was equally high in both groups; 95% of participants in the increased access group and 94% of participants in the standard access group had a final contact at 365 days or later after enrollment (Raymond et al., 2006).

All analyses were performed on an intention-to-treat basis. Fifteen of the 1490 participants provided incomplete or inconsistent data on baseline variables used in the analysis. Of these 15, we included 10 in the analysis using derived variables and excluded the other 5 (1 in the increased access group and 4 in the standard access group) from the analysis, given inadequate information to derive unknown variables.

We selected 20 baseline variables that were potential predictors of unintended pregnancy. These variables are listed in Table I and include four psychosocial factors ('perceived efficacy of contraception', 'aversion to pregnancy', 'access to contraception' and 'stigma') derived in a prior exploratory factor analysis of the psychosocial questions (Weaver et al., 2008). A predictive logistic regression model was fit to estimate which set of these baseline variables predicted pregnancy during the trial. We used the standard access group only to develop the model in order to eliminate any effect of the intervention. The initial model included all potential predictors, and was reduced by sequential elimination of variables. Variables were removed from the model based on likelihood ratio tests if their significance level was >0.05. Randomization in the original study had been stratified by location (Nevada versus North Carolina); thus, location was included in every model. We assessed the reliability of our final model using the area under a receiver operating characteristic (ROC) curve and the Hosmer–Lemeshow goodness-of-fit test. To assess the consistency of our final variable selection, we used a repeated stepwise elimination procedure on 500 bootstrap samples. Using the final model, we predicted pregnancy risk for all participants in both intervention groups. Lastly, we stratified participants into high risk and low risk of unintended pregnancy using a ROC curve-derived cutoff that jointly optimized sensitivity and specificity of risk classification.

Table I Participant baseline characteristics by risk group

	Low risk of pregnancy, $n = 958$	High risk of pregnancy, $n = 527$
Advanced EC provision group	478 (50%)	267 (51%)
Nevada study site*	481 (50%)	416 (79%)
Age (years)	19.2 (2.6)	20.0 (2.6)
Hispanic ethnicity	89 (9%)	107 (20%)
Non-white race	192 (20%)	125 (24%)
Married	15 (2%)	61 (12%)
Graduated high school	627 (65%)	358 (68%)
Binge alcohol use past month†	352 (37%)	192 (36%)
Smoker	209 (22%)	195 (37%)
Number of previous pregnancies*	1.0 (0.2)	1.7 (1.0)
Prior abortion	63 (7%)	153 (29%)
Effective contraceptive use‡	558 (58%)	161 (31%)
Multiple partners past 6 months	357 (37%)	221 (42%)
STIs over past year	53 (6%)	35 (7%)
Prior EC use	304 (32%)	155 (29%)
Unprotected sex past 14 days*	43 (4%)	335 (64%)
Psychosocial factors§		
Efficacy of contraception	0.71 (0.14)	0.63 (0.14)
Aversion to pregnancy*	0.83 (0.18)	0.59 (0.28)
Access to contraception	0.82 (0.19)	0.78 (0.21)
Stigma	0.47 (0.21)	0.43 (0.23)

Data represented *n* (%) for dichotomous variables and mean (SD) for continuous variables.
EC: emergency contraception, STI: sexually transmitted infection.
*Variables included in final predictive model.
†Defined as consuming more than five drinks in 1 day during the past month.
‡ Defined as any reported use of oral contraceptive pills, intrauterine device, contraceptive injections, patch, vaginal ring or vasectomy in the past month.
§Psychosocial factor scores are based on a continuous scale from 0 to 1, with higher scores indicating stronger response; for example, higher 'aversion to pregnancy' values represent greater aversion to pregnancy.

We then used a Mantel–Haenzel test of homogeneity to examine the association between randomization group and EC use in the year after enrollment, stratified by pregnancy risk, to see whether baseline pregnancy risk modified this association. We excluded all EC uses that occurred within the first day of enrollment from the analysis since participants often cited obtaining EC as the reason for their initial clinic visit and therefore many of those EC uses likely would have occurred in the absence of the intervention. This exclusion eliminated 128/2057 EC uses in the increased access group and 103/366 uses in the standard access group. We considered two measures of EC use over the 1 year of follow-up: ever use (0 versus ≥ 1 use) and multiple use (<2 versus ≥ 2 uses) during the study. We used a Cox proportional hazards model, stratified by location, to evaluate the association between baseline risk, intervention group and their interaction on time to pregnancy. We performed our analyses using Stata 10.0 software (StataCorp, College Station, TX, USA).

Results

A total of 740 women in the standard access group was used to develop the predictive model for pregnancy risk. Three baseline variables were significantly predictive of unintended pregnancy: number of previous pregnancies, history of unprotected sex within 14 days prior to study enrollment and the psychosocial factor 'aversion to pregnancy'. Our predictive model fit the data well (Hosmer–Lemeshow goodness-of-fit, $P = 0.23$; area under the ROC curve = 0.761). Of the 260 standard access group participants stratified as high risk, 50 (19%) had an unintended pregnancy during the follow-up year. In contrast, of the 480 participants stratified as low risk, 20 (4%) had an unintended pregnancy during the study. The distributions of risk scores in the increased access and standard access groups were similar, reflecting the randomization of the original study (Fig. 1). Of the 1485 participants in the analysis, 527 (35%) were designated as high risk (Table I).

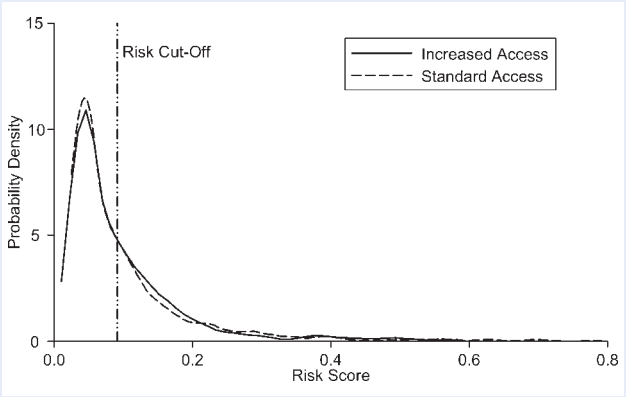

Figure 1 Risk score distribution by access group, with receiver operating characteristic curve-derived risk cutoff.

Among both high and low risk women, increased access to EC increased use compared with standard access (Table II). Baseline pregnancy risk did not significantly affect the association between increased access to EC and ever use of this method ($P = 0.48$, Table III). In the high risk group, increased access participants were 2.6 times as likely to ever use EC as the standard access group, with a similar increased likelihood [relative risk (RR) = 2.9] among the low risk group. However, baseline pregnancy risk did significantly modify the association between the intervention groups and repeated use of EC ($P = 0.03$, Table III). High risk women in the increased access group were 5.5 times as likely to use EC repeatedly as high risk women in the standard access group; low risk women in the increased access group were 10.0 times as likely to use EC repeatedly as low risk women in the standard access group.

The relative hazard of unintended pregnancy between randomization groups was not significantly modified by baseline risk (Cox proportional hazard, $P = 0.81$). Among low risk women, those provided with increased access to EC became pregnant at 0.89 times the rate of those with standard access [95% confidence interval (CI) 0.47–1.69], with 18 and 20 pregnancies, respectively. Among high risk women,

Table II Total number of EC uses by access and risk group*

	Increased access, $n = 745$			Standard access, $n = 740$		
	n	Total EC uses	Mean EC uses	*n*	Total EC uses	Mean EC uses
High risk	267	823	3.08	260	124	0.48
Low risk	478	1103	2.31	480	136	0.28

*Excluding EC uses occurring within the first day of enrollment.

Table III Ever and repeated use of EC by risk and access group

	Increased access		Standard access		RR (95% CI)*
	n	%	*n*	%	
High risk					
Total	267		260		
Ever use	198	74	74	28	2.6 (2.1–3.2)
Repeated use	157	59	28	11	5.5 (3.8–7.9)
Low risk					
Total	478		480		
Ever use	301	63	105	22	2.9 (2.4–3.5)
Repeated use	209	44	21	4	10.0 (6.5–15.4)

RR: relative risk, CI: confidence interval.
*Mantel–Haenzel tests of homogeneity comparing risk ratios for high risk and low risk participants: *P*-value = 0.48 for ever use, *P*-value = 0.03 for repeated use.

those provided with increased access became pregnant at 0.98 times the rate of those with standard access (95% CI 0.66–1.45), with 49 and 50 pregnancies, respectively.

No follow-up pregnancy data were collected for 49 of the 1485 participants in this analysis. Women missing pregnancy status differed significantly in pregnancy risk compared with women with known pregnancy status. Of the 22 women missing pregnancy information among the increased access group, 15 (68%) were classified as high risk. Of the 27 women missing pregnancy status among the standard access group, 11 (41%) were classified as high risk.

Discussion

In our trial, women at low and high baseline risk of pregnancy responded differently to an intervention designed to optimize access to EC. The intervention resulted in increased EC use among both risk groups, but the increase in repeated use was significantly greater in low risk women than in high risk women. Indeed, women at low baseline risk were 10 times more likely to use EC repeatedly if they received increased access than if they were in the standard access group. In contrast, the effect of the intervention on repeated EC use was only half as great among women who had a high baseline pregnancy risk.

This finding is noteworthy because women at low risk for pregnancy are arguably the subgroup least in need of a pregnancy reduction intervention. In our analysis, even the 10-fold increase in repeated EC use produced by the intervention did not result in a significant decrease in the probability of unintended pregnancy among low risk women. This differential effect of the intervention by pregnancy risk—specifically, its relatively poorer success in increasing EC use in the highest risk women—may partially account for its failure to produce a decrease in pregnancy incidence in the full trial population.

Why might the intervention have been more effective in increasing EC use in women at low risk of pregnancy? Our analysis found that low risk participants were substantially more averse to pregnancy at study enrollment, and accordingly, they were more likely to be using highly effective contraceptives and less likely to have recently had unprotected sex. Such women assigned to the increased access group may have continued this predisposition toward protective behaviors by taking advantage of the opportunity to increase their EC use. In contrast, high risk women randomized to the increased access group may have been less primed to make use of EC even when it was readily available.

One other explanation for our findings is that the risk profile of participants may have changed because of the intervention. Recent analyses of these same data suggest that women identified as low risk based on enrollment data, who then received an advanced supply of EC, may have adopted risk behaviors more consistent with a high risk participant, secondary to increased reliance upon EC as a contraceptive method (Raymond and Weaver, 2008;Weaver *et al.*, 2008). Since EC use increased substantially with increased access among both risk groups without a concomitant decrease in pregnancy incidence, it remains feasible that women provided with an advanced supply of EC were using EC as a substitute for other more reliable methods. Under this hypothesis, the intervention may have had two independent and counteracting effects: increasing EC use among high risk women as well as increasing risk behaviors among initially low risk women.

Although follow-up was high, 49 of 1485 (3%) women were missing pregnancy information at the end of their study year, which may have contributed to a selection bias. Women missing pregnancy data among the increased access group tend to have been at high pregnancy risk. In contrast, those among the standard access group tend to have been at low risk. This difference may have led to overestimation of the benefit of the intervention in reducing unintended pregnancy in the original analysis.

If advance provision or other increased EC access interventions are to have a beneficial effect in reducing unintended pregnancy incidence, they must be targeted toward the women who most need them. Further research to elucidate reasons why women at high risk of pregnancy may be relatively unresponsive to efforts to improve their use of EC and test resolutions to this problem is critically needed.

Funding

Support for the original study was provided by Family Health International (FHI) with funds from the National Institute of Child Health and Human Development (NICHD) Grant Number 5 R01 HD39907-04. Plan B was donated to that trial by Barr Pharmaceuticals Inc., Pomona, NY. Support for the preparation of this article was provided by FHI with funds from the William and Flora Hewlett Foundation. The project was also supported by Award Number T32HD040672 from the National Institute of Child Health And Human Development. The content is solely the responsibility of the authors and does not necessarily represent the views of the National Institute of Child Health and Human Development, the National Institute of Health or FHI.

References

Finer LB, Henshaw SK. Disparities in rates of unintended pregnancy in the United States, 1994 and 2001. *Perspect Sex Reprod Health* 2006; **38**:90–96.

Glasier A. Emergency contraception. Is it worth all the fuss? *BMJ* 2006; **333**:560–561.

Hu X, Cheng L, Hua X, Glasier A. Advanced provision of emergency contraception to postnatal women in China makes no difference in abortion rates: a randomized controlled trial. *Contraception* 2005; **72**:111–116.

Lo SS, Fan SY, Ho PC, Glasier AF. Effect of advanced provision of emergency contraception on women's contraceptive behavior: a randomized controlled trial. *Hum Reprod* 2004;**19**:2404–2410.

Moher D, Schulz KF, Altman DG. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomised trials. *Lancet* 2001;**357**:1191–1194.

Raymond EG, Stewart F, Weaver M, Monteith C, Van Der Pol B. Impact of increased access to emergency contraceptive pills: a randomized controlled trial. *Obstet Gynecol* 2006;**108**:1098–1106.

Raymond EG, Weaver MA. Effect of an emergency contraception pill intervention on pregnancy risk behavior. *Contraception* 2008; **77**:333–336.

Task Force on Postovulatory Methods of Fertility Regulation. Randomized controlled trial of levonorgestrel versus the Yuzpe regimen of combined oral contraceptives for emergency contraception. *Lancet* 1998; **352**:428–433.

Trussell J, Stewart F, Guest F, Hatcher RA. Emergency contraceptive pills: a simple proposal to reduce unintended pregnancies. *Fam Plann Perspect* 1992;**24**:269–273.

Walsh TL, Frezieres RG. Patterns of emergency contraception use by age and ethnicity from a randomized trial comparing advance provision and information only. *Contraception* 2006;**74**:110–117.

Weaver MA, Raymond EG, Baecher L. Attitude and behavior effects in a randomized trial of increased access to emergency contraception. *Obstet Gynecol* 2008; (in press).

Submitted on October 5, 2008; resubmitted on November 17, 2008; accepted on November 24, 2008