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Emergency Contraceptive Use as a Marker of Future Risky Sex, Pregnancy and Sexually Transmitted Infection

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Abstract

Objective—To examine whether emergency contraceptive use predicts future sex at risk for pregnancy, pregnancy, or sexually transmitted infection among young women.

Study Design—A secondary analysis of control group participants (n=718) from a recent trial of advanced provision of emergency contraception.

Results—We found no association between use of emergency contraception and either pregnancy or infection. Recent use predicted decreased occurrence of subsequent sex at risk for pregnancy among women with a history of sexually transmitted infection (Relative Risk [RR], 0.39; 95% Confidence Interval [CI], 0.15, 0.97), while ever having used predicted increased occurrence among women who either were highly effective method users (RR, 1.45; 95% CI, 1.05, 2.01) or had no history of sexually transmitted infection (RR, 1.31; 95% CI, 1.04-1.65).

Conclusions—Information about prior emergency contraceptive use was not a useful predictor of subsequent pregnancy, infection, or sex at risk for pregnancy among these young women.

Keywords

Adolescent; Postcoital contraception; Pregnancy; Reproductive health care; Sexually transmitted infections

Introduction

In 2006, at least 45% of all pregnancies in adolescent and young adult women in the United States were unplanned.¹ This same group of women also had the highest rate of gonorrhea (606 – 648 cases per 100,000) and a higher rate of Chlamydia infections than older women.² Adolescent and young adult women are characteristically less consistent users of contraception,³ perceive higher barriers to accessing reproductive care, and are more likely to report having either sporadic sex or sex that is initiated under the influence of alcohol,⁴ especially when first becoming sexually active.⁵ Postcoital emergency contraception pills (ECPs) are a safe and

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effective compensatory method to prevent pregnancy following unprotected intercourse and are increasingly available to this group of women.

Accessing ECPs is evidence of difficulty using contraception effectively. One study of US ECP users reported that 16% had multiple unprotected sex acts since their last period.⁶ The most common reasons cited for requesting ECPs are failure to use any contraceptive method, condom breakage, and missed oral contraceptive pills.⁷⁻¹² Women who use ECPs also differ from their peers at the time they seek ECPs with respect to established risk factors for adverse reproductive outcomes. Studies in different settings find ECP users are of younger ages, are unmarried, tend to use condoms as the primary contraceptive method, have had a higher number of sexual partners,¹³ live in urban areas and had initiated sex at younger ages.¹⁴

But few published studies have actually documented that sexual risk behaviors are more common among ECP users than among nonusers subsequent to the coital act that prompted ECP use. Stewart et al. found no significant differences in pregnancy or STI diagnoses between adolescent ECP users and non-users over two years. However, follow-up was incomplete for much of the cohort who may have sought care outside of the study's clinic site.¹⁵ Studies in Europe have found a history of ECP use to be associated with current chlamydial infection,^{14, 16} higher subsequent pregnancy rates¹⁷ and subsequent unwanted pregnancies resulting in termination.¹⁸

A better understanding of whether or not ECP use is an indicator of increased risk for later adverse behaviors and events would be useful to inform the development of customized preventive counseling guidelines and interventions. To examine this issue, we analyzed data from the control arm of a recent randomized trial of advance provision of ECPs. This arm of the study was essentially observational; the study procedures were designed to minimize interference by the study in women's access to or use of ECPs or in their subsequent behaviors. We hypothesize that adolescent and young adult women who use ECPs are at higher risk than non-users for sex at risk for pregnancy, unintended pregnancy and sexually transmitted infection over a one year follow-up period.

Methods

A detailed description of the study has previously been provided.¹⁹ Briefly, the original study was conducted between October 2002 and June 2005 in Nevada and North Carolina, and was approved by the institutional review boards of University of California at San Francisco and Family Health International. The study enrolled sexually active women aged 14-24 years who had no desire for pregnancy in the next year. Major exclusion criteria were current or planned use of a long-term contraceptive method (e.g. depo-medroxyprogesterone acetate, tubal sterilization), pregnancy within the past six weeks and current breastfeeding. The study gathered demographic and behavioral data, including ECP use from each participant through a self-administered computerized questionnaire at enrollment and two return visits scheduled at 6 and 12 months thereafter. Clinic records were reviewed to validate women's self-reported use of ECPs obtained from the study clinic. At study visits, women submitted self-collected vaginal and urine specimens. If a subject could not attend a follow-up visit, she was asked to perform a home pregnancy test and mail a vaginal specimen to the study. Vaginal specimens were analyzed by polymerase chain reaction for gonorrhea, chlamydial infection and trichomoniasis (Roche Diagnostic Corporation, Indianapolis, IN). Participants were randomly assigned to either an increased access group, in which women received two free packs of ECPs at enrollment with unlimited free re-supply throughout the study, or to a standard access group. This secondary analysis is restricted to the cohort of women randomized to the standard access group with any follow-up data (n=718). At enrollment participants in this group were counseled to obtain and take ECPs as a single dose of 1.5 mg levonorgestrel as soon as possible after

unprotected intercourse and to notify the study site; however, the study provided neither unsolicited counseling about contraception nor any financial support towards the procurement of ECPs.

We defined two time-dependent variables to characterize ECP use and modeled each separately. We classified a participant as “not a recent user” until her first use of ECPs after enrollment, and subsequently as a “recent user.” We classified a participant as a “never-user” if she had not used ECPs before the study up until her first use during the study, and otherwise as an “ever-user.” This second variable combines information on pre- and post-enrollment ECP usage and serves to characterize a woman's long-term exposure profile.

We considered three outcomes in these analyses: sex at risk for pregnancy, time-to-pregnancy and time-to-STI. We defined the first outcome as reported sexual intercourse in the 14 days prior to a scheduled follow-up interview that puts the participant at a presumably non-negligible risk for pregnancy. This included acts of vaginal intercourse performed without any contraception and acts for which condoms or oral contraceptives were not used effectively (e.g. an active oral contraceptive pill was missed or a condom broke during intercourse). Women whose first use of ECPs was in the 14-day pre-interview period were not considered “recent users” in this analysis so as to ensure that exposure to ECPs occurred prior to the reported outcome. We compared the probability of sex at risk for pregnancy by ECP use using a log-binomial model with generalized estimating equation methods and an unstructured working correlation matrix to account for the repeated measurements from each subject.

Study personnel assigned an estimated date of conception to each incident pregnancy based on last menstrual period or ultrasound when available. If a subject first used ECPs between 11 days prior to the date of conception to eight days after this date, we considered the pregnancy to be an emergency contraception failure¹⁹ and did not count her as exposed. This reassignment assured that all pregnancies in the analysis resulted from sex acts that followed the ECP use considered to be the exposure. One pregnancy was reassigned based on this criterion. We defined time-to-pregnancy as the period from enrollment until either the estimated date of conception or censoring at the last date of study contact, with each women contributing a maximum of 365 days of observation. We estimated hazard ratios of pregnancy according to ECP use by Cox proportional hazards regression after verifying the proportional hazards assumption.

We similarly estimated hazard ratios of in-study STIs by ECP use. In this analysis, women began contributing person-time from enrollment if STI negative at enrollment or from the date of effective STI treatment if positive at enrollment and ceased to contribute follow-up time at the first date at which a specimen was collected that tested positive for any study STI or at the lesser of time to their last negative sample collection date or 365 days.

In all adjusted analyses, we considered the following covariates, coded dichotomously unless otherwise noted, based on the available literature: age at enrollment (ordinal), lifetime number of sexual partners (ordinal), history of pregnancy, history of STI, history of consuming 5 or more drinks at a time, and any Black race reported from among the list of all self-reported races. Additionally, for the analysis of sex at risk for pregnancy, we considered use of a highly effective contraceptive method defined as self-reported use of intrauterine device, sterilization or any hormonal contraceptive method other the ECPs as a dichotomous time-varying covariate assessed at the time of response. Prior to fitting the model, we assessed each covariate as a potential effect measure modifier, noting all covariates with a Mantel-Haenszel test of homogeneity p-value less than 0.15. Our initial full model included interactions between all so-noted effect modifiers and exposure as well as terms for all potential confounders. We employed a backwards elimination strategy, removing one model term at a time beginning with

the one with the least significant p-value, to arrive at a final model in which all confounders and modifiers were significant at $p=0.05$. The design variable for location (North Carolina or Nevada) was forced into all models and visit number was included in all analyses of sex at risk for pregnancy. All analyses were conducted in SAS version 9.1.3 (SAS Institute Inc., Cary, NC).

Results

This cohort represents a sexually experienced group of adolescents and young adults (Table 1). Before enrollment, participants had a median of 5 male sexual partners over their lifetime. Although 84% planned at enrollment to use oral contraceptive pills (OCPs), only two-thirds reported using this or any other highly effective contraceptive method for at least part of the month prior to either their six or 12-month follow-up visits.

Participants completed the first follow-up visit at a median of 182 days after enrollment (range 146-643 days), and the second visit at a median of 376 days (range 303 – 524). Most (174/227) in-study ECP use occurred prior to the first follow-up visit (Table 2). Eighty-six percent of the women enrolled in the standard access arm of the original trial completed both follow-up visits. Among these women, use of ECPs during the study was associated with not currently using a highly effective contraceptive method ($p<0.0001$).

Approximately one third of respondents reported sexual activity that would place them at risk for pregnancy in the two weeks prior to each follow-up visit (Table 3). In unadjusted analyses using GEE and including design variables, recent ECP use was not significantly associated with increased probability of sex at risk for pregnancy (Relative Risk [RR], 1.21; 95% Confidence Interval [CI], 0.99-1.46), whereas ever-use of ECPs was weakly associated (RR, 1.25; 95% CI, 1.03-1.50). In multivariable analyses, we found a significant interaction between recent ECP use and history of STI ($p=0.03$), such that recent ECP use was more strongly associated with sex at risk for pregnancy among women with no history of STI than among women who had such a history (Table 4). Indeed, among women with a previous STI diagnosis, recent ECP users were only 39% as likely to report sex at risk for pregnancy at follow-up compared to non-users. We found a corresponding significant interaction between ever use of ECPs and history of STIs ($p=0.05$). Similarly, we found that ever use of ECPs was more strongly associated with sex at risk for pregnancy among women who were using a highly effective contraceptive method in the month prior to the sex act than among women who were not ($p=0.03$).

A total of 70 first pregnancies occurred during follow-up, producing an overall incidence rate (IR) of 10.5 pregnancies per 100 woman-years. Twenty-nine pregnancies (42%) occurred to women who had ever previously used ECPs and 15 of those (52%) used ECPs for the first time during the study period. Bivariable analysis provided no evidence of an association between recent ECP use and time-to-pregnancy (Hazard Ratio [HR], 0.85; 95% CI, 0.48-1.52) or ever ECP use and time-to-pregnancy (HR, 0.85; 95% CI, 0.53-1.37). Even after adjustment for location and history of pregnancy, we found no evidence of an association with recent ECP use (HR, 0.70; 95% CI 0.39- 1.25) or ever ECP use (HR, 0.74; 95% CI 0.46-1.20).

Fifty-three incident cases of chlamydial infection, trichomoniasis or gonorrhea were diagnosed and laboratory confirmed in the study with a mean follow-up of 360 days per woman (IR, 7.6 cases per 100 woman-years). Twenty-four ECP users were diagnosed with STIs, of whom 15 (63%) used ECPs during the study period. Bivariable analysis showed no evidence of an association between recent ECP use and time-to-STI diagnosis (HR, 1.09; 95% CI, 0.60-1.99) or ever ECP use and time-to-STI diagnosis (HR, 0.91; 95% CI, 0.54-1.6). After adjusting for

location, the modeled associations for both recent ECP use (HR, 1.19; 95% CI, 0.64, 2.20) and ever ECP use (HR, 0.94; 95% CI 0.54, 1.61) remained non-significant.

Comment

Contrary to our hypothesis, these data provide no evidence of differences between ECP users and non-users with respect to their time-to-pregnancy or STI diagnosis, and for the majority of our study population, there was no evident difference between sex at risk for pregnancy among ECP users and non-users. These findings suggest that neither lifetime history of ECP use nor recent ECP use would serve as a useful clinical marker of increased pregnancy or STI risk.

Our findings contrast with the results of two studies reporting recent ECP use as a marker of chlamydial infection. One case-control study of young women reported ECP use in the previous year associated with an odds ratio (OR) of 2.5 (95% CI, 1.1- 5.9).²⁰ In an adjusted analysis that included older women, Verhoeven et al. also observed a positive association between ever having used ECPs and risk of current or future STI (OR, 1.68; 95% CI, 1.31-3.29).¹⁴ With respect to pregnancy, our findings concur with another US study, which used data retrospectively obtained by chart review at an urban hospital and reported that women prescribed ECPs were no more likely than women seen for routine care to have a documented pregnancy in the subsequent two years.¹⁵ However, in a study of 135 Swedish women, the reported pregnancy rate in the year after ECP use was four times the national average among women of similar ages.¹⁸ A case-control study from the UK also observed an association between ECP use and pregnancies ending in abortion, versus those carried to term.¹⁷

ECP use was associated with an increased risk of the intermediate outcome, sex at risk for pregnancy, among women using a highly effective contraceptive method and those without a history of STI at baseline. One possible explanation is that ECP use signals the beginning of a decline in contraceptive vigilance among women who had previously taken steps to avoid STIs and pregnancy (e.g., women who had used both condoms and a highly effective contraceptive method who transition to condoms alone). Consistent with this explanation, in a study of ECP users, 8% switched to a non-highly effective contraceptive method in the six months following ECP use,²¹ suggesting that for a small proportion of users of highly effective contraceptive methods, the time following ECP use may represent a crisis period in which health behaviors change. On the contrary, women who had previously experienced adverse reproductive health consequences when they failed to plan ahead may redouble their safe sex practices after unsafe behaviors are repeated, explaining the observed protective effect of ECP use among recent ECP users who once had an STI. More detailed information on the reasoning behind young women's contraceptive decision-making than was obtained by the parent study is necessary to fully understand these observed differences.

Our analysis has a number of advantages over past studies. ECP users and non-users came from a single population unlike the Swedish study which compared an exposed clinic population to the general population.¹⁸ Additionally, we observed a high number of pregnancies, which gave us more power to detect the presence of an association should one exist. Because we actively captured ECP usage, sexual risk behavior and outcome data prospectively, we minimize recall bias, and by achieving very complete follow-up we also minimize selection bias. Unlike prior cross-sectional studies, we have clear evidence of the timing of ECP use relative to our outcomes.

The power of our STI analysis is limited by the small number of diagnosed infections observed in this population. The corresponding effect measures are therefore imprecise and we could not stratify by specific diagnoses. Additionally, the parent study did not collect some

established, clinically relevant indicators of adolescent sexual risk, specifically socioeconomic status and age at first intercourse. If a poor woman's access to emergency contraception at a reduced cost through the clinic's sliding fee scale increased her reliance on this method and reduced her adherence to her primary method, failure to adjust for this in our analysis would overestimate the observed association. However other preventative health services would likely also be available at a reduced cost to these women, therefore we consider this limitation minor. Age at first intercourse may already adequately have been considered in this analysis by considering both lifetime number of male sex partners and current age as potential confounders. Ideally we would also have been able to collect data on our time varying covariate, current contraceptive method, at the time of exposure to ECPs. However, the original study collected this information at baseline, six- and 12-months. Therefore, we may miss contraceptive changes in those intervals and this confounder may be misclassified for some women.

Appropriately identifying young women at elevated risk for unintended pregnancy or STI is a necessary step towards prevention of these undesired outcomes. Health care providers and researchers have anecdotally noted higher risk behaviors among ECP users compared to their peers. Interventions such as packaging ECPs with coupons for hormonal contraceptive pills and providing long-lasting injected contraceptives on the day ECP is requested have been suggested to “bridge” these ECP users to safer reproductive behaviors.^{22, 23} Our findings do not support a model in which ECP users are at higher need of contraceptive bridging than their sexually active peers. However, we did find an alarming amount of sexual activity occurring without adequate pregnancy prevention. Equally troubling, in-study ECP use fell well below the two-week prevalence of sex at risk for pregnancy, from which we conclude that many women do not seek out ECPs after sex at risk for pregnancy even when they are aware post-coital options are available. Underutilization of ECPs and insufficient pregnancy and STI prevention activities suggest the reproductive needs of young women are not being met. Research and clinical efforts should focus on improved risk communication, explicit instruction on effective contraceptive use and improved identification of high risk adolescents prior to the initiation of sexual activity.

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Table 1

Characteristics of 718 Women with Standard Access to Emergency Contraceptive Pills Contributing to Any Analysis

	n	%
Baseline		
Site		
North Carolina	285	40
Nevada	433	60
Age		
14-18	269	37
19-21	248	35
22-24	201	28
Planned to Use OCPs	602	84
Any Black Race Reported	75	10
High School Graduate	491	68
Married	37	5
> 5 Alcoholic Drinks at a Time in the Past Month	277	39
Previously Pregnant	178	25
Diagnosed with an STI in the Past Year		
No	631	88
Yes	39	5
Don't Remember	48	7
Lifetime Number of Male Sex Partners		
1-2	210	29
3-7	287	40
≥8	221	31
Ever Used ECPs		
No	503	70
Yes	213	30
Don't Remember	2	<1
Follow-up		
Used ECPs Between Enrollment and 6 months	174	24
Used ECPs Between Enrollment and 12 months	227	32
Using a Highly Effective Contraceptive Method ^a at First Follow-up Visit ^b	439	63
Using a Highly Effective Contraceptive Method ^a at Second Follow-up Visit ^c	405	64

OCPs, oral contraceptive pills; STI, sexually transmitted infection; ECPs, emergency contraceptive pills.

^aSelf-reported use of any hormonal contraceptive method other than ECPs, or intrauterine devices.^b699 women completed a first follow-up visit at approximately 6-months^c637 women completed a second follow-up visit at approximately 12-months

Table 2Description of ECP use prior to and during the study period in the analysis population (N=718)^a

	History of ECP use at baseline (N=212)		No history of ECP use at baseline (N=504)	
	n	%	n	%
First ECP Use in Study				
None	129	61	360	71
Before first follow-up visit	60	28	114	23
Between follow-up visits	23	11	30	6

ECP, emergency contraceptive pill

^aTwo women could not recall at baseline whether they had ever previously used ECPs.

Table 3
Sex at risk for pregnancy, pregnancy and STI diagnoses during the study.

Outcome	6 month visit ^a			12 month visit ^a		
	No. Analyzed	Yes	%	No. Analyzed	Yes	%
Sex at Risk for Pregnancy	699	226	32	637	208	33
Pregnancy	717	36	5	672	34	5
STI ^b	714	13	2	692	40	6

STI, sexually transmitted infection

^aFor sex at risk for pregnancy outcome, 6-month and 12-month refer to the first and second follow-up visit whenever they occurred; number analyzed refers to the number of women who appeared at that follow-up visit. For pregnancy and STI outcomes, all outcomes occurring in the 180 days post-enrollment are included in the 6-month, and between 181-365 days post-enrollment in the 12-month category. The total number analyzed reflects women contributing a minimum of 1 day of analysis (6 month) or 181 days of follow-up (12 month).

^bLaboratory-confirmed positive test results for chlamydial infection, gonorrhea or trichomoniasis after enrollment.

Table 4

Conditional effects of ECP use on the prevalence of risky sex in subpopulations based on significant interactions

Subpopulation	Recent ECP Use	History of ECP Use
	Relative Risk ^c (95% CI)	Relative Risk ^d (95% CI)
No History of STI ^a	1.09 (0.89, 1.32)	1.31 (1.04, 1.65)
History of STI ^a	0.39 (0.15, 0.97)	0.61 (0.29, 1.30)
Highly Effective Contraceptive Method ^b	----	1.45 (1.05, 2.01)
No Highly Effective Contraceptive Method ^b	----	0.95 (0.76, 1.17)

ECP, emergency contraceptive pill; STI, sexually transmitted infection; CI, confidence interval

^a In the year prior to enrollment according to self-report at enrollment visit.^b Most effective contraceptive method used in the month preceding the follow-up visit.^c Relative risk comparing those with recent ECP use to those without, adjusted for location, visit number, highly effective contraceptive method at follow-up and history of pregnancy at baseline.^d Relative risk comparing ever ECP users with never users, adjusted for location, visit number, the lifetime number of male sexual partners and history of pregnancy at baseline.