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Review article

Prevention and management of nausea and vomiting with emergency contraception: a systematic review☆

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Abstract

Background: Nausea and vomiting are side effects of emergency contraception pill (ECP) use. Different ECP regimens and the use of antinausea drugs may prevent these side effects.
Methods: We conducted two searches to identify data pertaining to the prevention of nausea and vomiting with ECP use and management of emesis with ECP use. Both searches queried the PubMed and Cochrane databases for peer-reviewed articles, in any language, published on January 1966–February 2012. Types of ECP included in our searches were levonorgestrel (LNG), Yuzpe regimens or ulipristal acetate (UA). Our search strategy for data on management of emesis with ECP use also included the gray literature. The gray literature includes materials such as reports, patent claims, prescribing information and package labels that are not published commercially.
Results: Eleven articles met the inclusion criteria. Split dose or two doses of LNG caused less nausea than UA and standard two-dose Yuzpe regimen in one study. Four studies demonstrated no difference between split-dose versus single-dose LNG. In two trials, meclizine and metoclopramide, given before Yuzpe ECPs, reduced nausea, but only meclizine reduced vomiting.
Conclusion: The evidence does not support routine use of antiemetics with ECP use. Data to guide management of emesis with ECP are limited to expert opinion and package labeling.

Keywords: Nausea; Emesis; Emergency contraception; Postcoital contraception

1. Introduction

Health care providers have several kinds of emergency contraception pills (ECPs) to choose from. ECP formulations and regimens available in the United States (US) include LNG pills, combined estrogen and progestin pills (Yuzpe method) or the newly marketed selective progesterone receptor modulator, UA [1,2]. Availability in different parts of the US, effectiveness and side effect profiles are known to vary among the available ECP options. Nausea and vomiting are common side effects reported with ECP use [3–5]. It is not known how emesis may impact the effectiveness of ECP.

The World Health Organization's Selected Practice Recommendations for Contraceptive Use provides guidance on the prevention of nausea and vomiting, which includes preferentially using LNG rather than the Yuzpe method and to not use antiemetics routinely [5]. We conducted a systematic review in preparation for a meeting of family planning experts convened by the Centers for Disease Control and Prevention in October 2011 to help inform the development of guidance for the forthcoming US Selected Practice Recommendations for Contraceptive Use. The objective of this systematic review is to identify evidence about how best to prevent or manage nausea and vomiting associated with ECP use, with either a particular pill formulation or regimen or with the use of antinausea medications.

2. Materials and methods

We searched PubMed and Cochrane databases for all peer-reviewed articles published between January 1966 and February 2012, in any language, relating to the use of Yuzpe regimen, LNG and UA as ECP. Search terms included

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emergency contraception, *morning after pill*, *emergency hormonal contraception*, *Plan B*, *post coital contraception*, *Yuzpe*, *levonorgestrel*, *ulipristal acetate nausea*, *nausea/prevention and control*. The search for articles concerning management of nausea and vomiting in women taking ECPs was conducted between the same dates and included the grey literature. The gray literature includes materials such as reports, patent claims, prescribing information and package labels that are not published commercially. Reference lists from articles identified by the search, as well as key review articles, were hand searched to identify additional articles. We did not contact any experts in the field to obtain unpublished data. We specifically included studies that examined the use of antinausea drugs to prevent nausea when using ECP or that quantitatively compared different ECP formulations and regimens with data on the side effects of nausea and vomiting. Other inclusion criteria were that all drug regimens for ECP must be available in the US (LNG single or split doses, UA and Yuzpe method). We excluded noncomparative studies.

All study authors participated in summarizing and systematically assessing the evidence through the use of standard abstract forms. The quality of each individual piece of evidence was assessed using the US Preventive Services Task Force grading system [6]. We assessed heterogeneity by examining the characteristics of the participants included in this study. We did not estimate summary measures due to the heterogeneity of the studies.

3. Results

The search strategy in PubMed identified 162 articles addressing nausea and vomiting prevention with various regimens of ECPs, as well as prophylactic antiemetic medication prior to using ECPs. After reviewing the titles and abstracts of these articles, and full articles when necessary, 11 articles met our inclusion criteria and are included in this review. The search strategy assessing management of vomiting during ECP use identified 1648 articles in the PubMed and Cochrane databases, of which zero met the inclusion criteria.

3.1. UA

Limited data exist with respect to UA and the prevention of nausea or vomiting (Table 1). A single randomized, double-blind placebo-controlled trial compared UA with split-dose LNG (.75 mg in two doses, given 12 h apart) within 72 h of unprotected intercourse (UPI) [7]. This trial was considered good in quality. The study enrolled 1672 women and examined efficacy and safety profiles. No statistically significant difference in emesis was found between the two groups (p=.6). However, the UA group experienced a higher rate of nausea than the LNG group (29% compared with 24%, p=.03). This study did not clearly describe how information about nausea or vomiting was collected.

3.2. Single-dose LNG versus split-dose LNG

Four trials, all considered good in quality, compared the use of a single-dose LNG (1.5 mg) to split-dose LNG to determine differences in side effects and efficacy (Table 2) [8–11]. Three of these trials administered ECPs to participants within 120 h of UPI [9–11], whereas one provided ECPs within 72 h [8]. When compared to the standard split-dose LNG, study participants in the single-dose LNG group reported similar rates of nausea and/or vomiting in all trials.

A double-blind randomized, placebo-controlled trial compared efficacy and safety of single dose LNG with a split-dose of LNG [11]. A total of 3022 women were enrolled from seven family planning clinics in Nigeria. Follow up was scheduled 1 week after the next expected menses, and 93% of subjects were retained. Information on side effects was collected with participant diaries. No significant difference in nausea or vomiting was reported between groups. In the split-dose group, 22% of women reported nausea compared with 21.7% in the single-dose group (p=.67). With regards to emesis, 8.7% of women in the split-dose group reported vomiting and 9.1% in the single-dose group (p=.64).

A double-blind, controlled trial randomized 2071 women to a single dose of 1.5-mg LNG or split-dose LNG within 120 h of UPI [10]. Data on side effects were collected with participant diaries. At the follow-up visit, 97% of participants were available. No significant difference in nausea or vomiting was noted between groups. In the split-dose group,

Table 1
Comparative studies examining UA

Author	Study	Population (*n*)	Exposure	Results	Strengths	Weaknesses	Quality
Creinin et al., 2006 [7]	RCT Follow up 5–7 days after next menses US	1672 women Women took pills within 72 h of UPI	UA 50 mg as a single dose Split-dose LNG 0.75 mg repeated 12 h later	Nausea Single-dose UA: 29% Split-dose LNG:24% p=.03 Vomiting Single-dose UA: 0.25% Split-dose LNG: 0.26% p=.60	Randomized, blinded	Method of side effect collection not described	Level I Good