ASSESSMENT OF TWO EMERGENCY CONTRACEPTIVE REGIMENS IN IRAN: LEVONORGESTREL VERSUS THE YUZPE

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ABSTRACT
Objective: The purpose of this study was to compare the efficacy and tolerability of two emergency contraception (EC) methods, levonorgestrel versus the Yuzpe.

Methods: In a prospective, randomized, comparative study, we included 122 healthy volunteers who in the observed cycle had had only one act of unprotected intercourse within 72h of treatment. They were randomly allocated in levonorgestrol group (n=62) and Yuzpe (n=60). The levonorgestrel regimen consisted of two pills: 0.75 mg levonorgestrel, taken twice in the 12-h interval within 72h after unprotected intercourse. The Yuzpe method included two HD contraceptive pills taken as another regimen. Data were collected by questionnaire at first and 3 weeks later. The differences were compared with X2 & Fisher exact tests.

Results: There were no significant differences between two groups in any of the observed parameters. The levonorgestrel regimen was found superior to Yuzpe because it’s more effectiveness (respectively 100% vs 91%, p=0.026) and fewer side effects.

Conclusion: The study showed more effectiveness and safety of the levonorgestrel regimen as emergency contraception. Thus we recommend levonorgestrel as an alternative EC method instead of the Yuzpe regimen in Iran or other developing countries in order to decrease unwanted pregnancy.

Key words: Yuzpe, Levonorgestrel, emergency contraception

INTRODUCTION
Emergency contraception (EC) as a means to prevent unwanted pregnancies in special situations such as condom accidents, sexual abuse, and unprotected intercourse occurring around mid cycle, when there is a high probability of pregnancy. It is estimated that wider use of EC would greatly reduce the number of unwanted pregnancies and the number of abortions resulting from them. The most widely used emergency contraception (EP) methods in the world are the Yuzpe regimen (combined estrogen-progestin contraceptive pills) and the levonorgestrel (LNG) regimen (progestin only). The Yuzpe regimen was developed in 1980 and later compared to the LNG regimen in clinical trials. In the large randomized trial to date, the LNG regimen has been shown to be more effective and associated with fewer side effects than Yuzpe regimen. The Yuzpe method of emergency contraception involves taking two doses of combined estrogen/progestin pills, with each dose containing 100µg of ethinyl estradiol and 500µg of levonorgestrel. The first dose is taken within 72h of unprotected coitus and the other is taken 12h later. The total regimen is therefore 200µg of ethinyl estradiol and 1 mg of levonorgestrel. But levonorgestrel 0.75 mg is marked as two pills taken within 72h of unprotected intercourse and the other is taken 12h later. The most frequent women’s complaint was nausea and vomiting. Vomiting occurs in about 5.6% of women taking the LNG regimen compared to about 18.8% for the Yuzpe regimen.

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The management of vomiting shortly after taking EC is not well defined. Ho and Kwan had fewer side effects and better efficacy with levonorgestrel compared to the Yuzpe method. Several clinical studies have shown that combined emergency contraception pills (ECP) can inhibit or delay ovulation. Some studies have shown histologic or biochemical alterations in the endometrium after treatment with the regimen, leading to the suggestion that EPCs may act by impairing endometrial receptivity to implantation of a fertilized egg. Additional possible mechanisms include dysfunctional ovulation; interference with corpus luteum function; thickening of the cervical mucus resulting in trapping of sperm; alterations in the tubal transport of sperm, egg or embryo; and direct inhibition of fertilization. No clinical data exist regarding the last three of these possibilities. The aim of this study was to compare the effectiveness between the Yuzpe and levonorgestrel regimens of EC in order to introduce safer and more effective method.

STUDY DESIGN
One hundred twenty four healthy women volunteered for randomized comparative study measuring the effectiveness of two EC regimens from September 2006 to June 2007. The protocol was approved by the Shahid Sadoughi University Ethics Board and written informed choice was obtained from all participants. The comparison was focused on two regimens of postcoital contraception (PCC): the Yuzpe regimen and LNG. In the levonorgestrel group and the Yuzpe regimen group, 62 women were randomly allocated in each group. Randomisation was performed by the randomisation schedules. Having only

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one act of unprotected intercourse within 72h of treatment in the observed cycle was study inclusion criteria. Reasons for exclusion included a history of irregular menstrual cycles, contraindications to hormonal contraception including impaired liver function, blood clotting disorders, family or personal history of venous thromboembolism or pulmonary embolism, intolerance to oral contraceptives and not to return for follow up visit. The levonorgestrel regimen consisted of two pills: 0.75 mg levonorgestrel taken twice in the 12h interval. The Yuzpe regimen consisted of two tables of ethynylestradiol 100µg and levonorgestrel 500µg, taken twice in the 12h interval as well.

Finally, the medical history was taken and general examination and a pregnancy test were performed. All women were keeping a diary of the menstrual period and side effects, coitus protection with condom after the PCC in the same cycle and were asked to return for a follow-up visit one week after the expected menstrual period. The pregnancy was confirmed by a positive pregnancy test.

RESULTS
Demographic characteristics for the five subjects studied on the Yuzpe regimen and LNG regimen are provided in Table 1. There were no significant differences between the groups in any of the observed parameters. Two women were excluded from the study because they were lost to follow-up. Pregnancy occurred in five patients (8.3%) in the Yuzpe regimen, but no pregnancy occurred in the LNG (p=0.026). In the Yuzpe group 60% of women and in the LNG group 62% of women reported normal and regular menses in the treatment cycle. But menstruation time was changed in 30% of women in the Yuzpe and 37% in the LNG group (Table 1). None of the observed women reported any change in the length or amount of bleeding. There was no vomiting and necessity for substitute pill intake in the levonorgestrel group. Nausea, vomiting, headache and weakness were statistically less frequent. Otherwise a higher frequency of these parameters was observed in the Yuzpe group (Table 2).

Table 1: Demographics for Subjects Studied on The Yuzpe Regimen and Levonorgestrel Regimen.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Yuzpe regimen (n=60)</th>
<th>Levonorgestrel mean(SD)</th>
<th>P_value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age (years)</td>
<td>29.1(±7)</td>
<td>26.3(±6)</td>
<td>0.33</td>
</tr>
<tr>
<td>Gravid</td>
<td>3.03(±2.2)</td>
<td>2.4(±2.1)</td>
<td>0.118</td>
</tr>
<tr>
<td>Parity</td>
<td>2.8(±2.23)</td>
<td>2.3(±2.13)</td>
<td>0.18</td>
</tr>
<tr>
<td>Menstruation time with PCC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal cycle vs. after treatment</td>
<td>36(60%)</td>
<td>39(62.09%)</td>
<td>0.945</td>
</tr>
<tr>
<td>Early menstruation</td>
<td>14(23.3%)</td>
<td>18(29.03%)</td>
<td></td>
</tr>
<tr>
<td>Late menstruation</td>
<td>5(6.6%)</td>
<td>5(8.06%)</td>
<td></td>
</tr>
<tr>
<td>Interval between coitus and PCC(h)</td>
<td>7.9(±8.01)</td>
<td>11.6(±13.3)</td>
<td>0.065</td>
</tr>
</tbody>
</table>

PCC: Post coital contraception;
SD: Standard deviation;
<sup>a</sup>: If P<sub>value</sub> was less than 0.05, there was significant difference between two parametr.

Table 2: Incidence of Complaints after Postcoital Intake of Each Regimen (%).

<table>
<thead>
<tr>
<th>Complications</th>
<th>Yuzpe Group (n=60)</th>
<th>LNG Group (n=62)</th>
<th>P_value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>68.3</td>
<td>6.5</td>
<td>0.000</td>
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<tr>
<td>Vomiting</td>
<td>25</td>
<td>0</td>
<td>0.000</td>
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<tr>
<td>Headache</td>
<td>21.7</td>
<td>0</td>
<td>0.000</td>
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<tr>
<td>Weakness</td>
<td>16.7</td>
<td>1.6</td>
<td>0.004</td>
</tr>
<tr>
<td>Hot flash</td>
<td>6.7</td>
<td>3.2</td>
<td>0.436</td>
</tr>
</tbody>
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REFERENCES


