Misoprostol compared with the Combination of Misoprostol and Letrozole on Induced Abortion

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Abstract

Background: Prostaglandins are the most common drugs used to induce abortion in the first and second trimesters of pregnancy. This study aims to compare the effects of misoprostol with the combination of misoprostol and letrozole on the success rate of induced abortion

Methods: This study is a prospective observational study on 200 women referred for therapeutic abortion to Ali Ibn Aboutaleb Hospital, Zahedan, Iran, in 2020-2021. Patients were randomly divided into two groups. The case group received combination therapy with misoprostol and letrozole, and the control group received just misoprostol. Data analysis was performed by SPSS software, version 24.

Results: In this study, 200 women who had been referred for therapeutic abortion were evaluated. There was no significant difference between the success rates of induced abortion in both groups as it was 78% in the case group (who received misoprostol + letrozole) and 71% in the control group (who received misoprostol). However, the patients in the case group (misoprostol + letrozole) experienced shorter durations from induction to abortion (P=0.029), shorter lengths of stay in hospital (P=<0.001), and less need to curettage (P=0.017) compared with the control group.

Conclusions: Even though the success rates of abortion were not significantly different in the case and control groups, it has been found that women who received the combination therapy with misoprostol and letrozole experienced shorter lengths of stay in hospital, shorter durations between induction and abortion, and less need to curettage.

Keywords: Abortion; Misoprostol; Letrozole

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Background

Abortion is defined as the deliberate termination of pregnancy before the embryo reaches the 20th week of gestation or 500 grams weight (1,2). It is estimated that approximately 40 million abortions are globally taking place every year, including legal and illegal abortions, which results in a 3.5% abortion rate (3). Termination of pregnancy is performed in case of severe or fatal fetal anomalies, severe maternal diseases, and fetal death. Induced abortion is legal in Iran under certain circumstances, including maternal life-threatening complications, fetal thalassemia major, fatal fetal anomalies, and some fetal chromosomal abnormalities before the spirit is given to the fetus (16th-17th weeks GA) (4). Surgical methods and procedures of induced abortion include dilatation and curettage (D&C), dilatation and evacuation (D&E), aspiration with vacuum, etc. Induction of abortion can be complicated and results in cervical rupture, uterine perforation, or injury to the abdominal viscera, even if it has been performed by an experienced surgeon. Medical abortion is an alternative method that has been widely used in the last 30 years ago due to lower costs, fewer complications, and appropriate responses compared to surgical methods (5). Prostaglandins are the most common drugs used to induce abortion in the first and second trimesters of pregnancy. Misoprostol is a prostaglandin E1 analogue prescribed for the prevention and treatment of gastric ulcers and duodenum for those who regularly use NSAIDs (4, 5). It has been also used for labor induction, the readiness of the cervix, postpartum hemorrhage’s control, and induction of abortion (6). Unlike other prostaglandins, Misoprostol selectively affects the uterus and cervix and has no adverse effect on the bronchus and blood vessels (7, 8). Letrozole is a non-stromal aromatase inhibitor used to treat estrogen-dependent breast cancer. Estrogen is effective for the continuation of pregnancy and is produced from the conversion of androgens by the activity of the aromatase enzyme. Letrozole reversibly and competitively bonds to the
hem of the cytochrome P450 and inhibits the aromatase enzyme to produce estrogen (7). While aromatase inhibitors directly inhibit estrogen biosynthesis and consequently, increase secretion of Follicle-stimulating hormone (FSH) from hypognatins, they do not have anti-estrogen side effects on the uterine mucosa and the cervix. Third-generation aromatase inhibitors, including letrozole, have strong and reversible effects. The other advantage of aromatase inhibitors, letrozole as well, is the lack of anti-estrogen effects which prevents endometrial morphological interference and cervix mucosa. Aromatase inhibitors have no androgenic, progestogenic, and estrogenic effects. Accordingly, it seems that aromatase inhibitors, such as letrozole, can open a new door in obstetrics and gynecology science and be a considerable treatment choice. (8). Considering the importance of therapeutic abortion and the inconsistent results of studies on the effects of misoprostol and letrozole on the induced abortion success rate, we aimed to compare abortions induced by misoprostol with abortions induced by the combination of misoprostol and letrozole.

Materials and Methods

This study is a prospective observational study on 200 women referred for therapeutic abortion to Ali Ibn Aboutaleb Hospital, Zahedan, Iran, in 2020. Inclusion criteria were 1: gestational age ≤8 weeks, and 2: indicating therapeutic abortion. Potential participants were excluded if they had the history of 1: cesarean section, 2: adrenal disease, 3: kidney or liver disease, and 4: sensitivity to prostaglandins. Patients were randomly divided into two groups. The case group received 5 mg letrozole (Abraham Pharmaceutical Company) every 8 hours (a total dose of 15mg/day) for two consecutive days (day one and day two). A letrozole placebo was given to the control group on day one and day three. On the third day morning, all participants were admitted to the Obstetrics and Gynecology Unit and received 800 mcg (4 vaginal tablets, 200 mcg) misoprostol (Cytotec Pfizer) every eight hours in a 24-hour cycle.
The tablets were placed in the posterior fornix. During the third day, all the side effects, including fever, sweating, fatigue, nausea, vomiting, abdominal pain, and bleeding, have been recorded as well as the time of tissue excretion. On the fourth day (the second day of hospitalization), a gynecologist performed transvaginal sonography on patients with vaginal discharge. The patients have been considered as having a complete abortion and discharged if 1) no pregnancy residuals were reported, or 2) had endometrial thickness ≤15 mm in sonography.

Another 800-microgram dose of vaginal misoprostol was given to the rest of the patients in both groups, who 1) had not have any vaginal discharge, 2) had have a pregnancy survival report in sonography, or 3) had have endometrial thickness ≥15 mm in sonography. All the remained patients underwent transvaginal sonography on the fifth day (the third day of hospitalization). They were discharged with the diagnosis of complete abortion if 1) no pregnancy residuals were reported, or 2) reported endometrial thickness was under 15 mm. Finally D&C was performed for the remaining patients who had pregnancy survival or endometrial thickness ≥ 15 mm. All participants in this study received written and oral informed consent and this project was approved by the Ethics Committee of Zahedan University of Medical Sciences on 01/11/2020 (Code of Ethics: IR. ZAUMS. REC.1399.337). Data analysis was performed by SPSS software, version 24, using Chi-Square and Independent T-test tests.

Table 1: Misoprostol Group compared with the Combination of Misoprostol and Letrozole Group.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Variants</th>
<th>Misoprostol group</th>
<th>Misoprostol and Letrozole group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Year ± SD*)</td>
<td>28 ± 5</td>
<td>29 ± 4</td>
<td>0.439</td>
<td></td>
</tr>
<tr>
<td>Success rate of abortion (Percent)</td>
<td>%71</td>
<td>%78</td>
<td>0.256</td>
<td></td>
</tr>
<tr>
<td>Duration from induction to abortion (Hour ± SD)</td>
<td>14.4 ± 4.6</td>
<td>12.6 ± 5.3</td>
<td>0.029</td>
<td></td>
</tr>
<tr>
<td>Length of stay (Day ± SD)</td>
<td>1.05 ± 0.35</td>
<td>0.85 ± 0.35</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Need for curettage (Percent)</td>
<td>%29</td>
<td>%15</td>
<td>0.017</td>
<td></td>
</tr>
<tr>
<td>Bleeding amount (ml** ± SD)</td>
<td>173 ± 81</td>
<td>179 ± 88</td>
<td>0.589</td>
<td></td>
</tr>
<tr>
<td>The frequency of side effects (Percent)</td>
<td>%27</td>
<td>%30</td>
<td>0.638</td>
<td></td>
</tr>
</tbody>
</table>

*SD = Standard Deviation  **ml = milliliter.

Results

In this study, 200 women who had been referred to Ali Ibn Abitaleb Hospital in Zahedan for therapeutic abortion were evaluated. The mean age of the patients was 28±5 years, which was not significantly different between the two groups (P=0.43) (Table 1). In this study, the success rate of complete abortion was 78% in the case group (who received misoprostol + letrozole) and 71% in the control group (who received misoprostol) and was not significantly different between the two groups. (P=0.256). The patients in the case group (misoprostol + letrozole) experienced a shorter duration from induction to abortion compared with the control group (P=0.029). In the case group, the mean length of stay in hospital was also significantly shorter (P=<0.001). Besides, the less need for curettage among the patients who received misoprostol + letrozole was significant (P=0.017). However, there was no significant
between the side effects in both groups (P=0.63) (Table 1).

Discussion

In this study, the success rate of abortion and the rate of side effects were not significantly different between the two groups. The main results were shorter lengths of stay, shorter duration from induction to abortion, and less need for curettage in the case group other studies on the effectiveness of misoprostol and misoprostol + letrozole in induced abortion have shown inconsistent results. Zahra Rezaei et al. performed a study on 214 pregnant women in the first trimester of pregnancy and compared the effect of misoprostol with misoprostol + letrozole in induced abortion. It was finally shown that misoprostol is as effective as its combination with letrozole (9).

In a study conducted by Ezatollah Haj Seyyed Javaid et al. on 70 women who were candidates for legal abortion in the first trimester, the success rate of abortion was significantly higher in women who received misoprostol + letrozole compared with those who received just misoprostol. However, bleeding, cervix opening time, duration between induction and abortion, and complications were not different between the groups (10). In another study conducted by Forough Javanmanesh et al., the effectiveness of these two medical treatments has been compared among 46 pregnant women with gestational age < 20 weeks. The results indicated that the combination of misoprostol and letrozole significantly resulted in a higher abortion success rate (P=0.0001) (11). A study by Behroozi Lak et al. showed that women who received misoprostol + letrozole not only had a higher success rate of abortion compared to those who just received misoprostol but also had a shorter length of stay in hospital and less need for curettage (12). Vivian Chi Yan Lee et al. also performed the same study on 168 pregnant women and found that the combination of misoprostol and letrozole was more effective than therapy with misoprostol in induced abortion. Moreover, vomiting, as a side effect of treatments, was lower in those who received the combination therapy (13). In another study conducted by Zahra Allameh et al. in 2016, the successful rate of abortion induced with misoprostol + letrozole was 80%, while it was 75% for misoprostol, and no significant difference was detected (14). In study by Mohammed AL-taie et al on 128 women complete abortion rate was 93.2% in misoprostol with letrozole group and in 68.7% in the misoprostol group and pretreatment with letrozole plus Misoprostol was more effective for prompting abortion in the first trimester of pregnancy without increasing side effect compared to misoprostol alone (15).

In another study conducted by Mohammed Hussein Moustafa et al on 85 women use of letrozole pretreatment followed by misoprostol for induction of abortion in the first trimester is associated with higher complete abortion rate than misoprostol only (16). In study by Afifi et al on 200 women Misoprostol alone group has a significantly high duration of vaginal bleeding and incomplete abortion in comparison with misoprostol with Letrozole group (17). This inconsistency in the results of different studies can be the consequence of different demographic characteristics of cases under investigation, different dosages of medications in the studies, and performing the treatments on populations with different gestational ages.

Conclusion

Finally, the results of this study showed that the success rates of abortion were not significantly different in the case and control groups. However, it has been found that women who received the combination therapy with misoprostol and letrozole experienced shorter lengths of stay in hospital, the shorter time duration between induction and abortion, and less need to curettage. Therefore, prescribing misoprostol and letrozole for induced abortion is more beneficial than induction with misoprostol in pregnant women.
References