Comparison between Intravenous and Intramuscular Administration of Prostaglandin E₂ on Management of Missed Abortion

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Abstract

Background: To compare the efficacy of two routes of prostaglandin E₂ administration (Intravenous and Intramuscular) for treatment of missed abortion this study was conducted. Regarding the pilot cases of missed abortion admitted for termination of pregnancy intravenous administration of PGE₂ that had higher efficacy compare to intramuscular route, investigators designed this study.

Methods: In a randomized clinical trial, 50 women with confirmed missed abortion received 250-500 µg prostaglandins E₂ either intravenously or intramuscularly. Evacuation time set from drug injection to complete emptying of uterus. Complete uterine evacuation was defined as emptying of uterus from pregnancy materials without the need for surgical intervention and partial evacuation defined as incomplete emptying of uterus that need further surgical management. Data were analyzed using SPSS, version 13. All the data extracted with a checklist and compare by descriptive statistics and X² and t-tests.

Results: There was no statistically difference between the results of two administration routes. The mean of evacuation time in intravenous administration routes was significantly lower in compare to intramuscular administration routes (P< 0.5). There was no statistically significant difference in the demographic data in two groups.

Conclusions: There was no preference between two administration routes except for evacuation time that occurred more rapidly in intravenous administration of PG E₂.

Keywords: Missed abortion, Prostaglandin e₂, intramuscular administration, Intravenous administration, Iran

Introduction

Missed abortion also named early pregnancy failure occurs in 15-20% of all pregnancies (1) and defined as a nonviable pregnancy that retained in the uterus without spontaneous passage for at least 8 weeks since the demise (2). Traditionally, it is treated with surgical dilatation and curettage but waiting for spontaneous abortion or medically inducing abortion are alternative procedures. For a long time, dilation and curettage has been a standard of care for early pregnancy failure. Complications associated with surgery are infrequent but can be serious and uterine adhesions, perforation, cervical tears, intra-abdominal trauma, hemorrhage, post-procedural infection, incomplete evacuation and aesthetic complication can occur in this context (3-4). Expectant management has 96%
success rate in cases of incomplete miscarriage. However, in missed abortions, the complete expulsion rate by the end of the third week is in the range of 60% (5).

In recent decades, medical abortion was introduced successfully. It has some advantages like patients’ preference, the avoidance of general anesthesia and surgical intervention and its lesser cost. The disadvantages of medical abortion in the first trimester are a longer duration of and significantly higher volume of bleeding compared with that following surgical termination (6).

Prostaglandin analogues constitute the cornerstone of medical treatment for missed abortion. In studies evaluating medical treatment of missed abortion, success rates ranging between 25 and 94% are reported (7-8). These studies are difficult to compare, as differences in inclusion criteria, definitions of success, dosing intervals and routes of administration can be found. However, despite so many studies, a wide variety of prostaglandin regimens have been used, with varying routes of administration. The present study was conducted among women to compare intravenous and intramuscular administration routes of prostaglandin E2 in the management of missed abortion.

**Methods**

In a randomized clinical trial, 50 women presenting with a confirmed missed abortion (non-viable pregnancy) aged less than 20 weeks of gestation, enrolled in the trial based on investigator observation and this formula:

$$N = \left( \frac{Z_{1-\alpha} + Z_{1-\beta}}{2} \right)^2 \times \left( \frac{p_1 - p_2}{p_1 - p_2} \right)^2$$

$$P_1 - p_2 = 20\% \quad \alpha = 5\% \quad \beta = 20\% \quad N = 25$$

The Ethical Committee of the Hamadan University of Medical Science approved the study protocol, and informed consent was obtained from all participating patients. Patients were divided randomly in two groups equally, the first group received prostaglandin E2 intramuscularly (Prostaglandin, Sherkat-sahami-darou, Tehran, Iran) and the second group received it intravenously (Dinoprostone, Sherkat-sahami-darou, Tehran, Iran). Patients were blinded for their chosen protocol. This trail took place at Fatemiyeh referral University Hospital, in Hamedan, west of Iran in 2006. First trimester missed abortion was defined as ultrasound evidence of an intact gestational sac, no evidence of fetal cardiac activity (after 6 weeks LMP), a closed cervical os, and a history of no or minimal bleeding (9). Otherwise healthy patients with confirmed diagnosis of missed abortion that had no contraindications to prostaglandin E2 and had no history of herbal or chemical drug use for abortion, were included in this trail. Patients were excluded if had massive bleeding and dilated cervix with forceful contraction or severe drug side effect occurred. Complete uterine evacuation was defined as emptying of uterus from pregnancy materials without the need for surgical intervention and partial evacuation defined as incomplete emptying of uterus that need further surgical management.

Women then received 250 µg prostaglandin E2 intramuscularly or 500 µg intravenously. In intramuscular administration group, dosage repeated if we did not receive proper response after 4 h. In intravenous group 500 µg prostaglandin E2 was diluted by 500 ml normal saline 0.9% and transfused in 30 min (10, 11). Vital signs and symptoms were recorded every 30 min. Evacuation time was set from drug administration to complete emptying of uterus. The complete evacuation confirmed by ultrasonography in 24 h after the termination of pregnancy. Both sonographies were done by a same sinologist and one sonographic device in a case of medical management failure patients underwent dilation and curettage promptly. Patients with complete evacuation were discharged after 36 h without any medication but patients underwent Dilation and Curettage (D&C) received 200
mg doxycycline qid for 7 d after hospital discharge.
Data were analyzed using SPSS, Version 13. Non-parametric was used for correlation between classified variables, fisher exact test and chi-square tests, and t-tests were used for parametric data. Differences were considered statistically significant if \( P < 0.05 \).

**Results**
Fifty patients completed the trail successfully. The age range was 16 to 40 yr. 38% of the women were primiparous and 62% were reported as multiparous. As shown in Table 1, there was no statistically significant difference in the demographic data in two groups. There was no statistically difference between the results of two administration routes with chi square test. The mean of evacuation time were 17.91±11.39 and 9.65±7.91 h in intramuscular and intravenous administration routes, respectively (\( P = 0.010 \)). Table 2 shows patients characteristics and complications in both groups. Vomiting was not reported by any of the women participating in this study but dyspnea and diarrhea were reported by 3 patients.

**Table 1:** Demographic data in both intravenous (IV) and intramuscular (IM) administration groups

<table>
<thead>
<tr>
<th>Demographic Item</th>
<th>IV</th>
<th>IM</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age (Year) mean±SD</td>
<td>27.08±5.45</td>
<td>28.28±6.67</td>
<td>0.490*</td>
</tr>
<tr>
<td>Gestational age (Week) mean±SD</td>
<td>14.32±3.30</td>
<td>13.84±4.35</td>
<td>0.662*</td>
</tr>
<tr>
<td>Nulliparous</td>
<td>11(44)</td>
<td>8(32)</td>
<td></td>
</tr>
<tr>
<td>Multiparous</td>
<td>14(56)</td>
<td>17(68)</td>
<td>0.28**</td>
</tr>
</tbody>
</table>

*Student t-test, **fisher’s exact

<table>
<thead>
<tr>
<th>Medical Item</th>
<th>IV n (%)</th>
<th>IM n (%)</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active Bleeding</td>
<td>7 (28)</td>
<td>7 (28)</td>
<td>NS*</td>
</tr>
<tr>
<td>Uterus cramp</td>
<td>0 (0)</td>
<td>3 (12)</td>
<td>NS*</td>
</tr>
<tr>
<td>Complete evacuation</td>
<td>8 (32)</td>
<td>6 (24)</td>
<td></td>
</tr>
<tr>
<td>Partial evacuation</td>
<td>14 (56)</td>
<td>14 (56)</td>
<td>NS**</td>
</tr>
<tr>
<td>Failure of evacuation</td>
<td>3 (12)</td>
<td>5 (20)</td>
<td></td>
</tr>
<tr>
<td>Dilatation and curettage</td>
<td>8 (32)</td>
<td>6 (24)</td>
<td>NS*</td>
</tr>
<tr>
<td>Complication</td>
<td>2 (8)</td>
<td>1 (4)</td>
<td>NS*</td>
</tr>
<tr>
<td>Dosage</td>
<td>Single</td>
<td>Multiple</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5 (20)</td>
<td>7 (28)</td>
<td>NS*</td>
</tr>
<tr>
<td></td>
<td>20 (80)</td>
<td>18 (72)</td>
<td></td>
</tr>
</tbody>
</table>

NS= not significant, *Fisher’s exact test, **chi square test

**Discussion**
Nonsurgical treatment options are becoming increasingly popular among women needing to terminate a pregnancy and their physicians. Pregnant women are interested in noninvasive options to avoid complications that may adversely affect their fertility (3). In the presented study, there was no significant difference between intravenous and intramuscular administration routes. Also we could not find any significant difference between the two groups with respect to vaginal bleeding, side effect, surgical intervention need, uterus cramp, dosage of the drugs except for evacuation time.
Several clinical trials have evaluated the use of prostaglandin E₂ and other prostaglandins for the termination of early pregnancy failure and their administration routes (3-8). As mentioned by Ratnam several administration routes of prostaglandins are acceptable and have similar effectiveness (10). The most evaluate route of prostaglandin administration was evaluated in PG E₁ especially orally and vaginally (11). We faced with a paucity of data about the evaluation of administration routes for prostaglandin E₂ in published articles. Various routes of administration e.g. intravenous, intramuscular, intra-amniotic, extra-amniotic and vaginal for terminating pregnancies of varying gestations have been examined. Intravenous infusion causes severe side effects such as fever, vomiting and diarrhea (5-7). In this study we faced with limited number of complications (three patients). Some few studies evaluate IM route and vaginal application of PG E₂ (11) and another route of administration that administered sulprostone by extraamniotic instillation (12). In conclusions, there was no preference between two administration routes except for evacuation time that occurred more rapidly in intravenous administration of PG E₂.

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Reference