Effectiveness of Misoprostol in the Management of Intra-Uterine Foetal Death

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Abstract
Background: Misoprostol – a prostaglandin E₁ analogue is effective in the induction of labour in the 2nd and 3rd trimester pregnancies. There is paucity of information in the use of misoprostol for labour induction in our setting.

Method: Non-randomized clinical trial.

Results: Thirty-four consecutive patients with real time ultrasonographically confirmed intrauterine fetal demise from 14 weeks gestation were recruited into the study. Twelve patients had oral administration while 22 were given misoprostol via the vaginal route. The mean age and parity of these patients were 26.7 ± 6.8 years and 3.2 ± 3.3 respectively. The mean uterine size at induction was 24.5 ± 8.2 weeks. Mean onset of painful uterine contractions was 5.02 ± 5.2 hours (Range 0.5 – 22 hours) while the mean induction – delivery interval was 14.6 ± 10.4 hours (Range 3-46 hours). The success rate of induction was 100% within 48 hours. Induction – delivery interval was not dependent on uterine size/Gestational age. Side effects encountered were minor namely nausea and vomiting. There were more side effects on oral administration.

Conclusion: Misoprostol is effective in the termination of 2nd and 3rd trimester pregnancies associated with intrauterine fetal demise. Studies are needed to compare the efficacy of misoprostol with oxytocin in the induction of labour with live fetuses in our setting.

Key words: Misoprostol, labour, induction, pregnancy, side effects

Rapport
Introduction : Le Misoprostol un prostaglandin E₁ analogue est efficace dans le déclenchement dans le 2ème et 3ème trimestres des grossesses. Il y a une pénurie de l’information dans l’utilisation de misoprostol pour le déclenchement dans notre milieu.

Méthode : Procès clinique non-randomisé

Résultats : Trente-quatre patients consécutifs avec le décès de fetal intratérinaire confirmé à travers un vrai ultrasonographie à partir de 14 semaines de la gestation ont été récruités pour cette étude. Douze patients avaient eu une administration orale tandis que 22 ont été donnés misoprostol à travers la voie vaginale. L’âge moyen et parité des patients étaient 26,7 ± 6,8 ans et 3,2 ± 3,3 respectivement. La taille moyenne de l’utérine pendant le déclenchement était 24,5 ± 8,2 semaines. Moyen du commencement de la douleur de la contraction d’utérine était (5,02 ± 5,2 heures (groupe 0,5 – 22 heures) tandis que moyen de déclenchement – accouchement interval était 14,6 ± 10,4 heures. (Tranche 3 – 46 heures). Le taux du succès du déclenchement était 100% en moins de 48 heures. Déclenchement - accouchement interval n’était pas dépendant sur la taille utérine/l’âge gestational. Réactions secondaire éprouvées étaient peu à savoir : la nausée et vomissements. Il y avait plus de réactions secondaires sur l’administration orale.

Conclusion : Le Misoprostol est très efficace dans la termination de 2ème et 3ème trimestres des grossesses ayant rapport avec le décès de fetal intratérinaire. On a besoin des études pour comparer l’efficacité de misoprostol avec oxytocin dans le déclenchement avec des foetus vivant dans notre milieu.

Mots clés : Misoprostol, accouchement, déclenchement, grossess, réactions secondaire
Introduction

Misoprostol is a prostaglandin E\textsubscript{1} analogue used for the prevention and treatment of gastric and duodenal ulcers induced by non-steroidal anti-inflammatory drugs. Although misoprostol is not approved by the United State Food and Drug Administration for use in pregnancy, it is an important drug for women’s reproductive health.\textsuperscript{1} Research findings in the last 5 years have revealed misoprostol to be effective in the induction of labour in the second and third trimester pregnancies.\textsuperscript{1,9} Misoprostol is also effective in the early termination of pregnancies (≤ nine weeks) when used in combination with mifepristone or as a single agent,\textsuperscript{10} and holds promise for other indications including cervical priming,\textsuperscript{11} treatment/prevention of postpartum haemorrhage\textsuperscript{12,13} and management of spontaneous abortion.\textsuperscript{10}

The advantage of using misoprostol for induction of labour and abortion over conventional oxytocics is overwhelming. Firstly it is a stable analogue of prostaglandin E\textsubscript{1} and thus less subjected to strict storage rules – an obvious advantage in tropical climate. Secondly, it is cheap and widely available and thirdly, in addition to intravaginal administration, it can be taken orally. These advantages make misoprostol a favorable agent in our environment where conventional prostaglandin E\textsubscript{2} is not only scarce but prohibitively expensive. Furthermore oxytocin, which is the only agent readily available and within reach of many patients is not very effective in termination of midtrimester pregnancies.

There is paucity of information regarding the value of misoprostol in the induction of labour in our setting. Reports from Uganda,\textsuperscript{9} South-Africa\textsuperscript{6} and Egypt have shown misoprostol to be effective in the induction of labour and termination of 2\textsuperscript{nd} trimester pregnancies. The effectiveness of misoprostol in management of foetal death and induction of labour in term pregnancies have been reported.\textsuperscript{14,15}

The aim of this study was to investigate the effectiveness of misoprostol in the induction of labour and abortion in 2\textsuperscript{nd} and 3\textsuperscript{rd} trimester pregnancies associated with intrauterine foetal death.

Materials and Methods

Thirty-four consecutive patients with ultrasonographically confirmed intrauterine fetal death from 14 weeks and above were recruited into the study from Ahmadu Bello University Teaching Hospital Zaria (14 patients) and Federal Medical Center, Azare (20 patients) between September 2002 and March 2003. Patients with scared uterus and those with previous anaplyactoid reaction to prostaglandins were excluded from the study. Biologic data were noted and coagulation profile was done for all patients. The following protocol was used:

i. Fundal height from 14 to 20 weeks: 400μg of misoprostol (orally or vaginally depending on patient preference) were given 12 hourly to a maximum of 4 doses. The vaginal administration was deposited in the posterior fornix.

ii. Fundal height 20 to 26 weeks: 200μg 12 hourly, maximum of 4 doses.

iii. Fundal height ≥28 weeks: 50μg of misoprostol six hourly to a maximum of 4 doses.

It should be noted that in all the patients, once painful uterine contractions were achieved, no further dose of misoprostol was given. The timing of initial dose of misoprostol, onset of painful uterine contraction and expulsion/delivery were recorded. The induction expulsion/delivery interval was calculated. Side effects due to the drug and complications were noted. Ancillary treatment if needed was offered and the clinical suspicion of the cause of fetal demise was recorded. The data was analyzed using SPSS 10.0 statistical software.

Results

The mean age of the 34 patients was 26.7 ± 6.8 years with range 15-45 years. Mean parity was 3.2 ± 3.3 years (Range 0-14). Uterine size ranged from 14 to 36 weeks with a mean of 24.5 ± 8.2 weeks and the onset of uterine painful contractions ranged from 0.5 to 22 hours with a mean of 5.02 ± 5.3 hours.

The mean induction – delivery interval was 14.6 ± 10.4 hours with a range of 3 to 46 hours. Table 1 showed uterine size and the induction – delivery interval. The induction delivery interval was not dependent on the gestational age.

Table 2 shows side effects of misoprostol versus route of administration. Side effects are nausea and vomiting. These side effects are more common with oral administration compared to vaginal route. There was one case of retained placenta and products of conception respectively. The retained placenta was removed manually and manual vacuum aspiration was done for the retained products of conception.

Table 3 showed the etiologies (on clinical grounds only) and frequencies of fetal death. Although in majority of the cases, the cause was unknown, hypertensive crises and malaria were important causes. Others here included two cases of haemoglobinopathies (sickle cell anemia), one case each of lobar pneumonia and severe anaemia.

<table>
<thead>
<tr>
<th>Uterine size (weeks)</th>
<th>No.</th>
<th>Mean induction-delivery interval (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>14-20</td>
<td>17</td>
<td>15.1 ± 10.5</td>
</tr>
<tr>
<td>22-28</td>
<td>8</td>
<td>9.2 ± 6.9</td>
</tr>
<tr>
<td>≥28</td>
<td>9</td>
<td>18.5 ± 11.5</td>
</tr>
<tr>
<td>Total</td>
<td>34</td>
<td>14.6 ± 10.4</td>
</tr>
</tbody>
</table>

p = 0.85 (Student t-test) and 0.181 (one way ANOVA)
Table 2: Route of administration and side effects of misoprostol

<table>
<thead>
<tr>
<th>Route of administration</th>
<th>Side effects</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>None</td>
<td>Nausea</td>
</tr>
<tr>
<td>Oral</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Intravaginal</td>
<td>18</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>24</td>
<td>5</td>
</tr>
</tbody>
</table>

p = 0.005 (Pearson Chi-square test)

Table 3: Causes of foetal death in patients given misoprostol

<table>
<thead>
<tr>
<th>Causes</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unknown</td>
<td>16 (47.1)</td>
</tr>
<tr>
<td>Hypertensive disorders in pregnancy</td>
<td>9 (26.5)</td>
</tr>
<tr>
<td>Malaria in pregnancy</td>
<td>4 (11.8)</td>
</tr>
<tr>
<td>Urinary tract infection pregnancy</td>
<td>1 (2.9)</td>
</tr>
<tr>
<td>Others</td>
<td>4 (11.8)</td>
</tr>
<tr>
<td>Total</td>
<td>34 (100.0)</td>
</tr>
</tbody>
</table>

Discussion

The success rate of 100% within 48 hours of induction in this study is similar to findings of other workers. Nakintu in Uganda recorded a success rate of 100% while Fawole and colleagues documented 93% success rate. Also our mean induction – delivery interval of 14.6 hours is comparable to that reported from Ibadan (Nigeria) of 17.5 hours and Kampala of 14.7 hours. Our mean onset of painful uterine contractions of 5.02 ± 5.3 hours is similar to that of Fawole and colleagues of 5.0 ± 8.4 hours. The observation in our study (Table I) that the delivery – induction interval was not dependent on gestational age is consistent with earlier reports.

Nausea and vomiting were the only side effects recorded in this study and is in line with findings of other workers. However, our side effects rate of 14.7% were higher than that reported by Fawole of 7.1%. It should be noted that although the side effects of misoprostol in our study were minor, there were significantly more common when misoprostol is administered orally compared with the vaginal route (p <0.05). This suggests that intravaginal administration may be the route of choice.

It can be concluded that misoprostol is effective and safe in the induction of labour-abortion in the 2nd and 3rd trimester pregnancies associated with fetal demise in our setting. Studies are needed to document the efficacy of misoprostol in the induction of labour with live fetuses in our environment.

References
