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ORIGINAL ARTICLE

Efficacy and Safety of Misoprostol in Induction of Labour in a Nigerian Tertiary Hospital

L'efficacité et la sûreté de Misoprostol dans l'Induction de Travail dans un Hôpital Tertiaire Nigérian.

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ABSTRACT

BACKGROUND: **Misoprostol – a stable prostaglandin E1 analogue– is effective and safe in the induction of labour. There is paucity of information about the use of misoprostol for labour induction in Nigeria.**

OBJECTIVE: **To evaluate the efficacy of misoprostol in the induction of labour in the third trimester.**

METHODS. **Consecutive patients for induction of labour were randomized into misoprostol or oxytocin study groups. The misoprostol group received intravaginal 50μg 6- hourly to a maximum of four doses. Those in the oxytocin group received a maximum of 48 iu/min. Outcome measures included induction-delivery interval, mode of delivery, Apgar score, perinatal death and maternal complications.**

RESULTS: **Sixty-two patients were recruited into the study-34 received misoprostol while 28 received oxytocin. The modal gestational age and Bishop score prior at induction were >36 weeks and 5-7 respectively. Hypertension in pregnancy was the commonest indication for induction of labour followed by prolonged pregnancy. The overall induction-delivery interval was 12.2 ± 5.2 hours; Misoprostol v oxytocin, mean(range): 12.1(7–27) vs 12.3(4–27) hours, p = 0.88). There were no significant differences in the mean Apgar score and perinatal mortality rate in the two study groups. There were two cases of primary postpartum haemorrhage in the oxytocin group but none in the misoprostol group. One case of ruptured uterus was encountered in the misoprostol group. No case of maternal mortality was recorded. Four patients in the misoprostol group had minor side effects mainly nausea and vomiting.**

CONCLUSION: **The efficacy of misoprostol in the induction of third trimester labour is comparable to oxytocin. The risk of ruptured uterus associated with misoprostol appears higher than that of oxytocin in the induction of labour. Further studies are needed to verify this observation in our setting.WAJM 2007; 26(3): 213 – 216.**

Keywords: **Pregnancy, induction of labour, misoprostol, oxytocin**

RESUME

Contexte: *Misoprostol – un prostaglandin stable E1 analogue est efficace et sûr dans l'induction de travail. Il y a le manque d'information de l'usage de misoprostol pour l'induction travailliste dans Nigéria.*

Objectif : *Pour évaluer l'efficacité de misoprostol dans l'induction de travail dans le troisième trimestre.*

Méthodes: *Les malades consécutifs pour l'induction de travail ont été répartis au hasard dans misoprostol ou les groupes d'étude d'oxytocine. Le groupe de misoprostol a reçu intravaginal 50mg 6-horaire à au maximum quatre doses. Ceux-là dans le groupe d'oxytocine a reçu au maximum 48 iu/minimum. L'issue mesure uncluded l'intervalle d'induction-livraison, le mode de livraison, le score d'Apgar, la mort périnatal et complications. maternel.*

Résultats : *Les malades de soixante-deux ont été recrutés dans l'étude-34 misoprostol reçu pendant que 28 oxytocine reçue. L'âge de gestational de nodal et le score d'Evêque préalables à l'induction étaient >36 semaines et 5-7 respectivement. L'hypertension dans la grossesse était l'indication la plus commune pour l'induction de travail suivi par la grossesse prolongée. L'intervalle général d'induction-livraison était 12,2 ± 5,2 heures ; l'oxytocine de v de Misoprostol, mean(range) : 12.1(7-27) vs 12. contre 12.3(4-27) hours, p heures, p=0.88). . Il n'y avait pas de différences significatives dans le score d'Apgar moyen et le taux de mortalité périnatal dans les deux groupes d'étude. Il y avait deux cas d'hémorragie postpartum primaire dans le groupe d'oxytocine mais aucun dans le groupe de misoprostol. Un cas d'utérus rompu a été rencontré dans le groupe de misoprostol. Aucun cas de mortalité maternelle a été enregistré. Quatre malades dans le groupe de misoprostol ont eu des effets secondaires la mineurs principalement nausée et le vomissement.*

Conclusion: *L'efficacité de misoprostol dans l'induction de troisième travail de trimestre est comparable à l'oxytocine. Le risque d'utérus rompu a associé avec misoprostol apparaît plus haut que cela d'oxytocine dans l'induction de travail. Plus les études sont eu besoin de vérifier cette observation dans notre cadre. WAJM 2007; 26(3): 213 – 216.*

Mots clés: Pregnancy, l'induction de travail, misoprostol, l'oxytocine

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Abbreviations: USB, United States dollar; WHO, World Health Organisation.

INTRODUCTION

Misoprostol is a prostaglandin E_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 US Food and Drug Administration for use in pregnancy, it is an important drug for women's reproductive health.[1] Research findings within the last ten years have revealed misoprostol to be effective in the induction of labour in the second and third trimester pregnancies.[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,[10] and holds promise for other indications including cervical priming,[11] treatment/ prevention of postpartum haemorrhage [12,13] and management of spontaneous abortion.[10] The advantage of using misoprostol for induction of labour or abortion over conventional oxytocics is overwhelming. Firstly it is a very stable analogue of prostaglandin E_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, sublingually and rectally. These advantages make misoprostol a favorable agent in our environment(sub-Saharan Africa) where conventional prostaglandin E_2 is not only scarce but prohibitively expensive. Furthermore, oxytocin (syntocinon) the only agent widely available and relatively within reach of many patients is not very effective in termination of midtrimester pregnancies and thus frustrating.

There is paucity of information regarding the value of misoprostol in the induction of labour in sub-Saharan Africa. Reports from Uganda,[9] South-Africa[6], Egypt[8], and Guinea[14]have shown misoprostol to be effective in the induction of labour and termination of 2nd trimester pregnancies. In Nigeria, Fawole and colleagues[15], Ezechi et al[16] and Loto et al[17] all from South-Western part of the country have demonstrated the value of misoprostol in the termination of second and third trimesters pregnancies.

The aim of this study was to investigate the efficacy and safety of misoprostol in the induction of third trimester labour in Federal Medical Center Azare- a tertiary care facility (in a semi-urban setting) which serves as a referral center to the whole of northern part of Bauchi State, in northern Nigeria.

SUBJECTS AND METHODS

This study was a randomised clinical trial comparing oxytocin to misoprostol in labour induction, conducted at the labour unit of Federal Medical Center Azare, Nigeria.

Sixty-two consecutive patients with medical indication of labour induction were randomized into misoprostol or oxytocin group using computer generated numbers and delivered by sealed envelopes.

Thirty- four patients received intravaginal misoprostol (deposited in the posterior fornix) 50µg six hourly to a maximum of four doses. No further dose of misoprostol was given once adequate uterine contractions were achieved (three contractions in 10 minutes each lasting for at least 40 seconds). The 28 patients randomized into oxytocin group were commenced with 2iu/min to maximum of 8iu/min using gravity fed infusion. Four of these patients had cervical ripening with foley's catheter prior to oxytocin infusion. Labour was monitored in the two groups using the WHO composite partograph with digital palpation of uterine contractions and intermittent auscultation of fetal heart with a pinard stethoscope. Outcome measures such as delivery-induction interval, mode of delivery, perinatal outcome and maternal complications were compared between the two groups.

The study period was from November 2005 to October 2006. Patients with scarred uterus and multiple gestation were excluded from the study. Only patients that consented were included into the study. Permission to undertake the study was obtained from the ethical committee of the institution.

RESULTS

Sixty-two patients were recruited into the study-34 received misoprostol while 28 were randomized into the oxytocin group. During the study period 1462 deliveries were conducted giving an induction rate of 4.2%. The overall mean age of the patients was 25.3 ± 7.7years (range 15-45 years). It was 26.1 ±8.0 years in the misoprostol group and 24.4 ±7.2 years in the oxytocin group(P value=0.365). The overall mean parity was 2.6 ± 2.9(range 0-12). It was 3.1± 3.2 and 2.03± 2.4 in the misoprostol and oxytocin groups respectively(p =0.168). The modes of the gestational age and Bishop score prior to induction were >36 weeks and 5-7 respectively (Table 1).

Hypertensive disorders in pregnancy (pre-eclampsia/eclampsia) were the commonest indication of induction of labour followed by prolonged pregnancy (Table 2). The overall mean induction-delivery interval was 12.2 ± 5.2 hours (range 4–27hrs) It was 12.1 hours in the misoprostol group(range 7-27hrs) and 12.3hrs in the oxytocin group(range 4–27hrs). The difference was not statistically significant(p value=0.88; 95% confidence interval –3.1-2.6). The correlation pvalues for gestational age and Bishop score versus induction-delivery interval were 0.12 and 0.02 respectively.

Table 1: Distribution of patients by gestational age and Bishop score

Variable	Number(%)
Gestational age (weeks)	
28 – 32	9 (14.5)
33 – 36	9 (14.5)
>36	44 (71.0)
Total	**62 (100)**
Bishop score	
<5	12 (19.4)
5 – 7	29 (46.8)
>7	21 (33.9)
Total	**62 (100)**

Table 2: Frequency of Indications for Labour Induction.

Indication	Number (%)
Pre-eclampsia/Eclampsia	25 (40.3)
Prolonged pregnancy	15 (24.2)
Intrauterine fetal death	11 (17.7)
Premature Rupture of membranes	8 (17.7)
Non-Hypertensive medical disease in pregnancy	2 (3.2)
Intrauterine growth restriction	1 (1.6)
Total	**62 (100)**

The mode of delivery between the study groups is shown in Table 3. The Gresarean section rate was 0.34% in the misoprostol group and 0.27% in the oxytocin group (P value= 0.599). The combined mean Apgar Score was 7.5 ± 2.4. It was 7.1 ± 2.6 and 7.9 ± 2.3 respectively in the misoprostol and oxytocin groups (p=0.28, 95% confidence interval –2.1-0.63). There were three stillborns in the misoprostol group (stillborn rate of 48/1000) while in the oxytocin group, two stillborns were encountered giving a still born rate of 32/1000. The difference in the stillborn rate was not statistically significant(X^2 =0.142, df=2, P value=0.706).

Table 3: Comparison of Mode of Delivery of Misoprostol vs Oxytocin groups

Mode of Delivery	Study group		Total
	Misoprostol	Oxytocin	
Spontaneous vaginal delivery	25	19	44
Instrumental delivery	3	5	8
Caesarean Section	5	4	9
Total	33	28	61

Chi-Square = 1.026, df =4, P-value = 0.599; The case of ruptured uterus was not included.

Table 4: Maternal Complications in the study groups

Complication	Study group		Total
	Misoprostol	Oxytocin	
None	33	25	58
Primary postpartum Haemorrhage	-	2	2
Ruptured uterus	1	-	1
Perineal laceration	-	1	1
Total	**34**	**28**	**62**

There was statistically no significant association.

The maternal complications encountered in this study are shown in Table 4. One case of ruptured uterus occurred in the misoprostol Group.There was no maternal death recorded. Of the 34 patients that received misoprostol 4 developed nausea/ vomiting. The mean dose of misoprostol used was 71.4μg ± 30.4μg with a range of 50–150μg.

DISCUSSION

During the period of study, 1462 deliveries were conducted giving an induction rate of 4.2%. This figure is low compared with a recent Nigerian study[18]. The commonest indication of induction of labour in this study was hypertensive disorder in pregnancy (notably pre-eclampsia/eclampsia) accounting for more than one-third of cases. The recent report referred to above documented prolonged pregnancy as the commonest indication for labour induction. The mean induction-delivery interval of 12.1 hours among patients that were induced with misoprostol was higher than that reported by Nigram et al[19] but comparable to 13 hours quoted in a Nigerian study[18] and much less than the 25 hours reported by Gemund et al[20]. The diverse dosage regimen among other factors may explain these differences. However our mean value for the oxytocin group was comparable to that reported by Nigram et al[18] from India and Zeteroglu et al[21] from Turkey. In this report, there was no significant difference in the duration of labour among our study groups. In the report of Nigram et al,[19] the mean duration of labour in the misoprostol group was almost half of that of patients induced with oxytocin. A possible explanation for the differences may emanate from patient selection- the Nigram report considered only patients at term while our study spanned from 28 weeks to term.

There was no significant difference in the caesarean section rate between the two groups in our study (0.34% for misoprostol vs 0.27% for oxytocin; p=0.599). This is consistent with earlier reports.[19,21] The similarity of perinatal outcome in the study groups also agrees with previous reports.[19,21]

In this study, there was one case of ruptured uterus in a 30- years old para 4 woman who had 50μg of misoprostol, developed hyperstimulation and foetal distress after about three hours of insertion. Anterior rupture was diagnosed intraoperatively. Yolande et al[14] reported two cases of ruptured uterus in their series of 104 cases, while Onafowokan et al[18] reported one case of uterine rupture in their study involving 100 patients. Uterine rupture was not reported by several others[17,19-21].

In our patients with pre-eclampsia/eclampsia and induced with misoprostol, there was no case of placenta abruption. Fontenot et al[22] reported *abruptio placenta* complicating misoprostol used in pre-eclamptic patients. Side effects of misoprostol encountered in this study were minor mainly nausea and vomiting. This is consistent with earlier reports.[14-21] Although our sample was small, the mean dose of misoprostol in this study (71.4μg ± 30.4μg [amounting to a cost of USD1.5 and comparable to USD 2.0 for oxytocin] is far less than the 226μg reported by Yolande et al[14].

It can be concluded that the efficacy of misoprostol is comparable to oxytocin in the induction of third trimester singleton pregnancies, even in low resource setting. However, its potential for hyperstimulation with subsequent uterine rupture call for close monitoring of patients. Further studies are needed to substantiate this observation in our setting.

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