A comparison of orally administered misoprostol and membrane sweeping for labour induction in uncomplicated singleton post-term pregnancies

A O Adeniji, S E Akinola

Department of Obstetrics and Gynaecology, Ladoke Akintola University of Technology Teaching Hospital, Osogbo, Nigeria
A O Adeniji, MB BS, FWACS, FMCOG
S E Akinola, MB BS, FWACS, FRCOG

Corresponding author: *A O Adeniji (tunji1802@yahoo.com; aoadeniji@lautech.edu.ng)*

Objectives. This study assessed the efficacy of the two outpatient processes of single-dose 50 µg oral misoprostol (OM) and membrane sweeping (MS) on the outcome of labour induction and the possibility of reducing the need for hospital admission for cervical ripening/labour induction in uncomplicated post-term singleton pregnancies at a tertiary health institution in south-western Nigeria.

Methods. A total of 100 patients were equally randomised into the two groups between April 2007 and March 2010. Primary outcome measures were delivery within 48 hours after the start of induction and route of delivery. Secondary outcome measures were time interval from induction to onset of labour (latency period), time interval from start of induction to delivery (duration of labour), need for oxytocin augmentation, labour complications, Apgar scores at 1 and 5 minutes, and need for neonatal intensive care unit (NICU) admission.

Results. Both groups were similar at the baseline with regard to age, parity and days beyond 40 weeks' gestation. There was a significantly shorter induction to onset of labour (latency) interval in the OM group, with a mean of 17.0 hours compared with 31.9 hours in the MS group (p=0.005), with 82.0% of the patients in the OM group in spontaneous labour within the latency period of 18 hours as opposed to 32.6% of the MS group (p<0.005). Forty-two patients in the OM group and 40 in the MS group had a vaginal delivery (84.0% v. 87.0%, p=0.361), with 12 and 20 patients in the OM and MS groups, respectively, requiring oxytocin augmentation (p=0.023). The duration of labour was significantly shorter in the OM group, in which 78.6% of those who had a vaginal delivery achieved it within 9 hours, compared with 57.5% in the MS group (p=0.036). Overall, neonatal outcomes and need for NICU admission were similar and comparable in the two groups. On a preference scale, 43% of the women in the MS group felt positive about the intervention, compared with 92% of the women in the OM group.

Conclusion. The study demonstrated a shorter latency period, less need for oxytocin augmentation and shorter duration of labour in patients who received OM. The two induction agents were similar with regard to neonatal outcomes and need for NICU admission. Both showed good safety profiles for outpatient care, although further assessment of the safety profile with larger studies will be needed. More patients felt positive about the intervention in the OM group than in the MS group.

S Afr J OG 2013;19(1):4-7. DOI:10.7196/SAJOG.584

Post-term pregnancy is fairly common in obstetric practice and is the most common indication for induction of labour.[1-4] Recent studies have shown that the risks to the fetus[5,6] and to the mother[7,8] of continuing pregnancy beyond the estimated date of delivery are greater than originally thought, and induction of labour remains an accepted means of achieving vaginal delivery. In some cases the status of the cervix is unfavourable for labour induction, the success of which depends to a large extent on the consistency, compliance and configuration of the cervix.[9] Various methods of cervical ripening, from membrane sweeping (MS) and use of a transcervical Foley catheter to administration of prostaglandins (PG) and prostaglandin E_1 (PGE1) analogue, are therefore used.

MS involves digital separation of the fetal membranes from the lower segment of the uterus. It is an established method of promoting the onset of labour without hospital admission, and is regularly applied to prevent pregnancies extending beyond term.[10,11] This method causes an increase in local PG production,[12,13] which results in ripening of the cervix and ultimately brings about spontaneous onset of labour. The results of trials on the effectiveness of MS have been inconsistent,[3,8,11] possibly owing to methodological differences between studies. A Cochrane review suggested that routine use of MS between 38 and 40 weeks does not seem to produce clinically important benefits;[11] however, it may be beneficial in women with post-term pregnancies.[14,15]

Misoprostol, a PGE1 analogue, has been reported to be an effective and affordable cervical ripening and medical induction agent. It can be used intravaginally or orally and has excellent shelf-life. These factors are immensely advantageous in low-resource tropical countries.[2,4] However, the processes of cervical ripening and labour induction require admission to hospital, resulting in additional costs in terms of both human and material resources. Any safe and effective interventions that also cut costs are therefore desirable.

This study explored the comparative efficacy and safety of the two outpatient techniques of single-dose 50 µg oral misoprostol (OM) and MS on the outcome of labour induction and their effects on reducing the need for hospital admission for cervical ripening/labour induction in uncomplicated post-term singleton pregnancies.

Methods

This study was a prospective, randomised controlled trial of a single dose of 50 µg OM and MS in uncomplicated singleton post-term pregnancies. All patients recruited had had early ultrasound dating of their pregnancy, which was correlated with the expected delivery date to exclude wrong dates. The study was conducted between April 2007 and March 2010 at Ladoke Akintola University of Technology Teaching Hospital, Osogbo, Nigeria. Patients with singleton post-term pregnancies were recruited after giving informed consent. One hundred sealed opaque envelopes containing papers marked OM or MS (50 each) were placed in a box, thoroughly mixed and then numerically labelled. Computer-generated random numbers were used for patient allocation. Patients were allocated sequential numbers in order of recruitment, and the correspondingly numbered envelope was opened for randomisation. The institutional ethical review committee approved the study. Inclusion criteria were a singleton live fetus, post-term pregnancy from 40 weeks and 1 day to 40 weeks and 9 days, intact fetal membranes, Bishop's score ≤5 and cephalic presentation. Exclusion criteria were post-term pregnancies of ≥40 weeks and 10 days, multiple pregnancies, grand multiparity, cephalopelvic disproportion, previous caesarean section or a uterine scar, fetal malpresentation, fetal distress, placenta praevia, antepartum haemorrhage, premature rupture of the membranes and medical disorders.

Study groups

One hundred patients, randomised to 50 in each group, were studied. The OM group received a single 50 µg misoprostol tablet orally on an outpatient basis, and the MS group had MS once only at the antenatal clinic. Patients with unyielding cervices preventing access into the cervical canal were termed 'failed MS'. All patients in both groups who did not go into spontaneous labour after 48 hours were categorised as 'failed labour induction' and together with the women with post-term pregnancies of ≥40 weeks and 10 days managed according to our departmental protocol of cervical ripening and labour induction (transcervical Foley catheter or intravaginal misoprostol) to ensure delivery before 42 weeks' gestation.

To eliminate bias, attending obstetricians in the labour ward were blinded to the labour-inducing agents used in the study groups. Primary outcome measures were delivery within 48 hours after the start of induction and route of delivery. Secondary outcome measures were time interval from the start of induction to onset of labour (latency period), time interval from the start of induction to delivery (duration of labour), need for oxytocin augmentation, labour complications, Apgar scores at 1 and 5 minutes, and need for neonatal intensive care unit (NICU) admission.

Data were entered onto a pre-designed sheet and analysed with SPSS version 17. Mean (± standard deviation (SD)), independent *t*-test, Pearson's chi-square (with Yates' corrections as appropriate), confidence intervals (CIs) and relative risk (RR) were determined as necessary. The level of significance was set at 0.05.

Results

A total of 100 patients (50 in each group) were recruited for the study; 4 in the MS group were categorised as 'failed MS'. At baseline the two groups were similar with regard to mean age, parity and days beyond 40 weeks' gestation (Table 1). Table 2 shows that the latency period was significantly shorter in the OM group than in the MS group, with a mean of 17.0 hours (CI 11.8 - 22.1) as opposed to 31.9 hours (CI 24.7 - 39.0) in the MS group (p=0.005). Eighty-two per cent of the patients in the OM group went into labour spontaneously within the latency period of 18 hours, as opposed to 32.6% in the MS group (p<0.005). Two patients in the OM group and 1 in the MS group went beyond the 48 hours time limit and were categorised as 'failed induction', but subsequently had a vaginal delivery after oxytocin augmentation of labour.

Forty-two patients in the OM group and 40 in the MS group had a vaginal delivery (84.0% v. 87.0%, p=0.361), with 12 and 20 patients, respectively, requiring oxytocin augmentation (p=0.023). Of the caesarean sections (8 in the OM group v. 6 in the MS group), 5 in the OM group were necessitated by presumed fetal distress, compared with 4 in the MS group (Table 3). The duration of labour was significantly shorter in the OM group, with 33/42 patients (78.6%) who had a vaginal delivery achieving it within 9 hours, compared with 23/40 (57.5%) in the MS group (Table 4).

Overall, neonatal outcomes were similar and comparable in the two groups, with more babies in the OM group (6/50) than in the MS group (3/46) having moderate asphyxia at the first minute after birth. However, this was statistically insignificant. NICU admission rates were similar for the two groups. On a preference scale, 43% of the women in the MS group felt positive about the intervention, compared with 92% of the women in OM group

Table 1. Socio-demographic characteristics of study patients

Biodata	OM group (*N*=50)	MS group (*N*=50)	*p*-value
Age (years), mean (±SD)	26.30 (±4.9)	25.38 (±5.1)	0.830
Parity, mean (±SD)	1.70 (±0.8)	1.32 (±0.9)	
Nulliparous, *n* (%)	3 (6.0)	10 (20.0)	
Multiparous, *n* (%)	47 (94.0)	40 (80.0)	0.071
Days beyond 40 weeks, mean (±SD)	5.26 (±1.6)	5.00 (±1.7)	0.290

OM = oral misoprostol; MS = membrane sweeping.

Table 2. Comparison of the agents of induction with regard to latency period

Latency period (hours)	OM group (*N*=50) *n* (%)	MS group (*N*=46) *n* (%)	*p*-value
<6	5 (10.0)	4 (8.7)	
>6 - 12	18 (36.0)	4 (8.7)	
>12 - 18	18 (36.0)	7 (15.2)	
>18 - 24	4 (8.0)	13 (28.3)	
>24 - 48	3 (6.0)	17 (37.0)	
>48	2 (4.0)	1 (2.2)	<0.005

Table 3. Comparison of events and outcomes of labour in the study groups

Labour events	OM group (*N*=50) *n* (%)	MS group (*N*=46) *n* (%)	*p*-value (CI)
Oxytocin augmentation			0.02 (1.1 - 7.0)
Yes	12 (24.0)	20 (43.5)	
No	38 (76.0)	26 (56.5)	
Mode of delivery			0.36 (0.1 - 1.8)
Vaginal	42 (84.0)	40 (87.0)	
Caesarean section	8 (16.0)	6 (13.0)	

Table 4. Comparison of labour duration in the study groups

Duration of labour (hours)	OM group (*N*=42) *n* (%)	MS group (*N*=40) *n* (%)	*p*-value
<6	1 (2.4)	4 (10.0)	
>6 - 9	32 (76.2)	19 (47.5)	
>9 - 10	8 (19.0)	12 (30.0)	
>10 - 12	1 (2.4)	5 (12.5)	0.036

who said that they would agree to use of the drug in another post-term pregnancy.

Discussion

This study randomised 100 patients, with established gestations beyond 40 weeks but less than 40 weeks and 10 days, into two groups receiving a single-dose 50 µg OM tablet or single MS on an outpatient basis. The intention was to compare the efficacy of these two methods for induction of labour, evaluate their possible impact on the number of post-term women requiring hospital admission for induction of labour at our institution, and compare fetomaternal safety profiles of the two methods. Various studies have shown individual benefits of MS as opposed to no sweeping,[16,17] and of OM as opposed to intravaginal misoprostol or other labour-inducing agents.[18,19] However, we did not find any study that compared MS with OM, especially in the outpatient context we adopted in this study. Outpatient management of post-term pregnancies will reduce the financial burden on families by eliminating the cost of hospital admission. It will also allow women to begin labour at home and only come into hospital for delivery, which is more like the natural process of labour and involves fewer interventions.

At baseline the two groups were similar with regard to age distribution and number of days beyond 40 weeks' gestation. Although there were more nulliparous patients in the MS group, this was not statistically significant. Theoretically it has been argued that MS may be more effective in multiparous than nulliparous patients. This assumption has been disputed by de Miranda *et al.*[16] and could not be substantiated by our study, although it is noteworthy that 4 patients in our nulliparous group could not have MS owing to inability to gain access to the cervical canal (failed MS), a technical challenge in this subset of patients that cannot be overlooked. Previous studies[2,4,19,20] have demonstrated that intravaginal misoprostol was more effective at improving cervical effacement and consistency than cervical os dilatation, and also that misoprostol was a better agent for initiating labour than the transcervical Foley catheter.

Our findings suggest that both 50 µg OM and MS, administered on an outpatient basis, are safe and effective agents for inducing labour in uncomplicated post-term singleton pregnancies, with OM having the advantages of a shorter latency period, less need for oxytocin augmentation in labour and shorter duration of labour. Within 12 hours of initiation of the induction at the clinic, 46.0% of the patients in the OM group (23/50) reported back in labour, compared with 17.4% in the MS group (8/46). The proportion increased to 82.0% (41/50) by 18 hours in OM group, whereas it was 32.6% (15/46) in the MS group. The faster effect of induction in the OM group might be due to the reported rapid absorption of this agent after oral administration, peaking about 15 - 30 minutes after administration. We also reason that as misoprostol is a PGE1 analogue and undergoes rapid de-esterification to its active, free acid metabolites, its onset of action will be speedier than the local PG production via a cascade of synthetic processes that would be expected in MS.[21,22] Studies on misoprostol have demonstrated less need for oxytocin augmentation than there was with MS, similar to our findings.[2,23] Of our patients 24.0% in the OM group as opposed to 43.5% in the MS group required oxytocin augmentation (RR 0.5, CI 0.3 - 0.9). This further enhances acceptability of OM, as women perceive their labour as more 'natural' with less intervention.

The proportions of vaginal deliveries were similar in the two groups, (83.3% v. 86.7%, RR 0.1, CI 0.8 - 1.1). When duration of labour was compared, 78.6% of the OM group, but only 57.5% of the MS group achieved vaginal delivery within 9 hours of onset of labour (RR 1.2, CI 0.8 - 1.8). Neonatal outcomes in the two groups were similar and favourable, although the prevalence of moderate birth asphyxia was higher in the OM group. These episodes occurred in babies of relatively low birth weight and recovery was recorded by the Apgar

Table 5. Neonatal outcomes in the study groups

Neonatal outcome factors	OM group (*N*=50)	MS group (*N*=46)	*p*-value (CI)
Birth weight (g), mean (±SD)	3 123 (±328)	3 089 (±302)	
Apgar score at 1 minute, mean (±SD)	7.7 (±1.0)	7.4 (±0.7)	0.150 (-0.1 - 0.6)
Apgar score at 1 minute <7, *n* (%)	6 (12.0)	3 (6.5)	0.358
Apgar score at 5 minutes, mean (±SD)	9.5 (±0.6)	9.478 (±0.4)	0.867 (-0.2 - 0.3)
Apgar score at 5 minutes <7	-	-	-
NICU admission, *n* (%)	2 (4.0)	2 (4.4)	0.930

score at 5 minutes. All admissions to the NICU in both groups were for observation only and the infants were discharged within 24 hours.

A major limitation of randomised trials like ours is that they are seldom large enough to study rare adverse effects. No harmful adverse effects of MS have been reported in previous studies.[11] Reported adverse effects of misoprostol, such as vomiting, diarrhoea, tachysystole or hyperstimulation, were not recorded in this study, possibly because of the single low dose administered. However, 20% of the patients in the MS group reported that the procedure was uncomfortable and/or painful, similar to earlier reports,[16,24] and 9% had minimal spotting after the procedure, which subsequently subsided. No case of rupture of the membranes or antepartum haemorrhage was recorded. On a preference scale, 43% of the women in the MS group felt positive about the intervention, compared with 92% of the women in the OM group who would agree to use of the drug in another post-term pregnancy.

Conclusion

This study showed a shorter latency period, less need for oxytocin augmentation and a shorter duration of labour in patients given single-dose OM compared with MS on an outpatient basis. The two induction agents were similar with regard to neonatal outcomes and need for NICU admission, but differences in outcomes cannot be excluded owing to the small numbers studied. Patient preference for the intervention was higher in the OM group than in the MS group.

Conflict of interest. We declare that we have no conflict of interest; no funding/grant was received for this study and there was no commercial relationship. We have full control of all primary data and agree to allow *SAJOG* to review our data if requested.

1. Harman JH, Kim A. Current trends in cervical ripening and labor induction. Am Fam Physician 1999;60(2):477-483.
2. Adeniji OA, Oladokun A, Olayemi O, et al. Pre-induction cervical ripening: Transcervical Foley catheter versus intravaginal misoprostol. J Obstet Gynaecol 2005;25(2):134-139. [http://dx.doi.org/10.1080/01443610500040737]
3. Dare FO, Oboro VO. The role of membrane stripping in prevention of post-term pregnancy: A randomised clinical trial in Ile-lfe, Nigeria. J Obstet Gynaecol 2002;22(3):283-286. [http://dx.doi.org/10.1080/01443610220130571]
4. Ande AB, Ezeanochie CM, Olagbuji NB. Induction of labour in prolonged pregnancy with unfavourable cervix: Comparison of sequential intracervical Foley catheter-intravaginal misoprostol and intravaginal misoprostol. Arch Gynecol Obstet 2012;285(4):967-971. [http://dx.dopi.org/10.1007/s00404-011-2094-4]
5. Caughey AB, Washington AE, Laros RK Jr. Neonatal complications of term pregnancy: Rates by gestational age increase in a continuous, not threshold, fashion. Am J Obstet Gynecol 2005;192(1):185-190. [http://dx.doi.org/10.1016/j.ajog.2004.06.068]
6. Heimstad R, Romundstad PR, Salvesen KA. Induction of labour for post-term pregnancy and risk estimates for intrauterine and perinatal death. Acta Obstet Gynecol Scand 2008;87(2):247-249. [http://dx.doi.org/10.1080/00016340701743165]
7. Caughey AB, Stotland NE, Washington AE, et al. Maternal and obstetric complications of pregnancy are associated with increasing gestational age at term. Am J Obstet Gynecol 2007;196(2):155.e1-155.e6. [http://dx.doi.org/10.1016/j.ajog.2006.08.040]
8. Heimstad R, Romundstad PR, Eik-Nes SH, et al. Outcomes of pregnancy beyond 37 weeks of gestation. Obstet Gynecol 2006;108(3 Pt 1):500-508. [http://dx.doi.org/10.1097/01.AOG.0000227783.65800.0f]
9. Trofatter KF, Bowers D. Stanby RN, Gall A, Killam AP. Preinduction cervical ripening with prostaglandin E2 gel. Am J Obstet Gynecol 1985;153:268-271.
10. Munro KJ, Johnson RW, Philips MH. Historical Review of British Obstetrics and Gynaecology, 1800-1950. Edinburgh: Livingstone, 1954.
11. Boulvain M, Stan CM, Irion O. Membrane sweeping for induction of labour. Cochrane Database of Systematic Reviews 2005, Issue 1. Art. No.: CD000451. [http://dx.doi.org/10.1002/14651858.CD000451.pub2]
12. Mitchell MD, Flint AP, Bibby J, et al. Rapid increases in plasma prostaglandin concentrations after vaginal examination and amniotomy. Br Med J 1977;2:1183-1185. [http://dx.doi.org/10.1136/Fbmj.2.6096.1183]
13. Keirse MJ, Thiery M, Parewijck W, Mitchell MD. Chronic stimulation of uterine prostaglandin synthesis during cervical ripening before the onset of labor. Prostaglandins 1983;25(5):671-682. [http://dx.doi.org/10.1016/0090-6980%2883%2990121-1]
14. el Torkey M, Grant JM. Sweeping of the membranes is an effective method of induction of labour in prolonged pregnancy: A report of a randomized trial. Br J Obstet Gynaecol 1992;99(6):455-458. [http://dx.doi.org/10.1111/j.1471-0528.1992.tb13780.x]
15. Goldenberg M, Dulitzky M, Feldman B, Zolti M, Bider D. Stretching of the cervix and stripping of the membranes at term: A randomised controlled study. Eur J Obstet Gynecol Reprod Biol 1996;66(2):129-132. [http://dx.doi.org/10.1016/0301-2115%2896%2902405-0]
16. de Miranda E, van der Bom J, Bonsel G, Bleker O, Rosendaal F. Membrane sweeping and prevention of post-term pregnancy in low-risk pregnancies: A randomised controlled trial. Br J Obstet Gynaecol 2006;113(4):402-408. [http://dx.doi.org/10.1111/j.1471-0528.2006.00870.x]
17. Wong SF, Hui SK, Choi H, Ho LC. Does sweeping of membranes beyond 40 weeks reduce the need for formal induction of labour? Br J Obstet Gynaecol 2002;109(6):632-636. [http://dx.doi.org/10.1016/S1470-0328(028)01193-X]
18. Akter S, Chowdhury SB, Fatema N. A comparison of orally administered misoprostol with vaginally administered misoprostol for cervical ripening and labour induction. Orion Medical Journal 2010;33(1):710-713.
19. How HY, Leaseburge L, Khoury JC, Siddiqi TA, Spinnato JA, Sibai BM. A comparision of various routes and doses of misoprostol for cervical ripening and the induction of labour. Am J Obstet Gynecol 2001;185(4):L911-915.
20. Adeniji AO, Olayemi O, Odukogbe AA. Intravaginal misoprostol versus transcervical Foley catheter in pre-induction cervical ripening. Int J Gynaecol Obstet 2006;92(2):130-132. [http://dx.doi.org/10.1016/j.ijgo.2005.10.010]
21. Tang OS, Schweer H, Seyberth HW, Lee SWH, Ho PC. Pharmacokinetics of different routes of administration of misoprostol. Hum Reprod 2002;17(2):332-336. [http://dx.doi.org/10.1093/humrep%2F17.2.332]
22. Brian C. Misoprostol: Pharmacokinetics and pharmacodynamics. HRB PhD Scholar Health Services Research TCD/CWIUH/RCSI. 2010. http://www.medicine.tcd.ie/obstetrics-gynaecology/assets/pdf/Brian-Cleary-Feb-2010.pdf (accessed 3 July 2012).
23. Alfirevic Z, Weeks A. Oral misoprostol for induction of labour. Cochrane Database of Systematic Reviews 2006, Issue 2. Art. No.: CD001338. [http://dx.doi.org/10.1002/14651858.CD001338.pub2]
24. Boulvain M, Fraser WD, Marcoux S, et al. Does sweeping of the membranes reduce the need for formal induction of labour? A randomised controlled trial. Br J Obstet Gynaecol 1998;105:34-40.