Post-term pregnancy is fairly common in obstetric practice and is the most common indication for induction of labour. Recent studies have shown that the risks to the fetus and to the mother 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.

Various methods of cervical ripening, from membrane sweeping (MS) and use of a transcervical Foley catheter to administration of prostaglandins (PG) and prostaglandin E1 (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. This method causes an increase in local PG production, 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, 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; however, it may be beneficial in women with post-term pregnancies.

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. 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, 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 cervixes 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.
or other labour-inducing agents. However, we did not find any sweeping, and of OM as opposed to intravaginal misoprostol studies have shown individual benefits of MS as opposed to no compare fetomaternal safety profiles of the two methods. Various hospital admission for induction of labour at our institution, and possible impact on the number of post-term women requiring of these two methods for induction of labour, evaluate their an outpatient basis. The intention was to compare the efficacy groups receiving a single-dose 50 µg OM tablet or single MS on beyond 40 weeks but less than 40 weeks and 10 days, into two This study randomised 100 patients, with established gestations 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, and of OM as opposed to intravaginal misoprostol or other labour-inducing agents. 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 likely 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. 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 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. Studies on misoprostol have demonstrated less need for oxytocin augmentation than there was with MS, similar to our findings. 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 0.9, 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 1.3, 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>
<thead>
<tr>
<th>Labour events</th>
<th>OM group (N=50)</th>
<th>MS group (N=46)</th>
<th>p-value (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxytocin augmentation</td>
<td>0.02 (1.1 - 7.0)</td>
<td>0.06 (0.3 - 12.0)</td>
<td>0.867</td>
</tr>
<tr>
<td>Yes</td>
<td>12 (24.0)</td>
<td>20 (43.5)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>38 (76.0)</td>
<td>26 (56.5)</td>
<td></td>
</tr>
<tr>
<td>Mode of delivery</td>
<td>0.36 (0.1 - 1.8)</td>
<td>0.38 (0.2 - 1.1)</td>
<td>0.776</td>
</tr>
<tr>
<td>Vaginal</td>
<td>42 (84.0)</td>
<td>40 (87.0)</td>
<td></td>
</tr>
<tr>
<td>Caesarean section</td>
<td>8 (16.0)</td>
<td>6 (13.0)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Duration of labour (hours)</th>
<th>OM group (N=42)</th>
<th>MS group (N=40)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6</td>
<td>1 (2.4)</td>
<td>4 (10.0)</td>
<td></td>
</tr>
<tr>
<td>&gt;6 - 9</td>
<td>32 (76.2)</td>
<td>19 (47.5)</td>
<td>0.012</td>
</tr>
<tr>
<td>&gt;9 - 10</td>
<td>8 (19.0)</td>
<td>12 (30.0)</td>
<td></td>
</tr>
<tr>
<td>&gt;10 - 12</td>
<td>1 (2.4)</td>
<td>5 (12.5)</td>
<td>0.036</td>
</tr>
</tbody>
</table>

Table 5. Neonatal outcomes in the study groups

<table>
<thead>
<tr>
<th>Neonatal outcome factors</th>
<th>OM group (N=50)</th>
<th>MS group (N=46)</th>
<th>p-value (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight (g), mean (±SD)</td>
<td>3 123 (±328)</td>
<td>3 089 (±302)</td>
<td>0.776</td>
</tr>
<tr>
<td>Apgar score at 1 minute, mean (±SD)</td>
<td>7.7 (±1.0)</td>
<td>7.4 (±0.7)</td>
<td>0.035</td>
</tr>
<tr>
<td>Apgar score at 1 minute &lt;7, n (%)</td>
<td>6 (12.0)</td>
<td>3 (6.2)</td>
<td>0.867</td>
</tr>
<tr>
<td>Apgar score at 5 minutes, mean (±SD)</td>
<td>9.5 (±0.6)</td>
<td>9.478 (±0.4)</td>
<td>0.268</td>
</tr>
<tr>
<td>Apgar score at 5 minutes &lt;7</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>NICU admission, n (%)</td>
<td>2 (4.0)</td>
<td>2 (4.4)</td>
<td>0.930</td>
</tr>
</tbody>
</table>
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 rarely large enough to study rare adverse effects. No harmful adverse effects of MS have been reported in previous studies. 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, 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 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 augmentation and a shorter duration of labour in patients given

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.