ABSTRACT

Title of abstract: MISOPROSTOL WITH FOLEYS VERSUS MISOPROSTOL ALONE FOR INDUCTION OF LABOUR IN TERM PRIMIGRAVIDAS A PROSPECTIVE RANDOMIZED CONTROL TRIAL

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Objective:

To determine whether use of Foleys in combination with Misoprostol, as opposed to Misoprostol alone, for induction of labour will lead to

i. Decreased induction to delivery interval

ii. Higher probability of achieving vaginal delivery

iii. Lower incidence of Caesarean section

iv. Affect the rates of meconium stained liqour

v. Lower rates of hyperstimulation

vi. Affect incidence of chorioamnionitis/ endomyometritis

vii. Lower rates of atonic post partum haemorrhage

viii. Affect neonatal morbidity

Methods: This is a prospective, randomised control trial to study the efficacy of Foleys and Misoprostol versus Misoprostol alone for induction of labour.

The trial was presented before the Institutional Review Board in Christian Medical College, and protocol was approved prior to start of recruitment. All Primigravida,
low risk, term patients coming to CMC labor room & Obstetrics wards for routine induction of labor were screened for the trial. All primigravidas with singleton pregnancies in longitudinal lie and cephalic presentation at 37 +0 to 40+6 weeks of gestation, with a medical indication for induction, intact membranes and a Bishops score of <6 were counselled for participation in this trial. High risk pregnancies, multigravidas, non vertex pregnancies, those with fever/ sepsis, those undergoing reinduction or those with a known allergy to Misoprostol/ Latex were excluded.

Eligible women who agreed to be part of the trial, were given an information sheet and explained about details of the trial. If they agreed, they were asked to sign a consent form.

Patients were recruited from July 2015 to August 2016 in Christian Medical College, a 2450 bed, tertiary care, teaching hospital. Consenting women were then subjected to a pre induction Non Stress Test, which was carried out for a minimum of 20 minutes. If this was reactive, the Principal Investigator was called in to randomize the patient.

Patients were randomly allotted to two groups – those for induction with Misoprostol plus Foleys catheter and those for induction with only Misoprotol – using computer generated randomization codes in a 1:1 ratio using Block randomisation. Sealed, opaque envelopes were used, and the Principle Investigator was not aware of the randomisation sequence prior to actual randomisation.

However, due to the nature of treatment, after randomization, the patient, principal investigator & caregiver were aware of the arm into which the patient was allocated.

Patients in the combination arm were induced with a 16 Fr Foleys catheter inserted by registrars into the cervix and inflated with 30ml of distilled water. Simultaneously, 25 mcgm of Misoprostol was inserted into the posterior fornix of vagina, which was repeated 4 hourly for a total of 3 doses with Foleys in situ. Foleys was removed
after 12 hrs of insertion, unless there was an indication to do so earlier. Patients were monitored with continuous CTG. Subsequent doses of Misoprostol were withheld if patient developed contractions, ruptured of membranes or fetal heart became non reassuring.

Patients in the Misoprostol Only arm were induced with Misoprostol alone, 25 mcgm Q4th hourly for a total of 3 doses in the posterior fornix of vagina by registrars. Continuous CTG monitoring was done. Indications for abandoning subsequent doses were similar as in the combined treatment arm.

**Results:** This study recruited 300 patients over the period of 1 year from July 2015 to August 2016. Of these patients, 151 were recruited to the Misoprostol arm and 149 patients to the Misoprostol and Foleys Arm. Only Primigravidas with low risk pregnancies were eligible for this trial.

The baseline characteristics of our two groups were similar with regard to age, BMI and risk factors such as anemia and advanced maternal age. There were more patients with primary infertility in the Misoprostol only arm, however this is unlikely to have bearing on the results. Majority of our patients were from Vellore.

Majority of our patients were in the BMI range of 19.5 to 24.9 kg/m2: 72 patients (47.7%) in the Misoprostol only arm and 88 patients (59.1%) in the Misoprostol and Foleys arm. There were 61 patients (40.4%) in the Misoprostol arm and 45 patients (30.2%) in the Misoprostol and Foleys arm in the BMI range of 25 – 29.9. 20.3% of patients had a BMI of <18.5kg/m2. And 28 patients (9.3%) had a BMI of >30kg/m2.

We hypothesized that combining Misoprostol and Foleys catheter for induction of labour, through their synergistic effect, would shorten induction to delivery interval and the overall duration of labour.

Our findings are contrary to this hypothesis.
There was a shorter induction to delivery interval in the Misoprostol only arm by 1 hour 18 minutes compared to the Misoprostol and Foleys arm. This difference was statistically significant (p value 0.017). The latent phase of labour was found to be shorter by 1 hour and 16 minutes in the Misoprostol only group (p value 0.001). The active phase of labour was also shorter in the Misoprostol only group by 44 minutes. Though this was not statistically significant (p value – 0.38), this is of clinical importance. Shortened active phase of labour may help reduce infectious morbidity, the strain on the mother and the baby, as well as allow greater turnover in institutes where patient load is greater and doctors are hard pressed for empty beds.

There were more patients with a Bishops score of 2 or 3 randomised to the Misoprostol and Foleys arm compared to the Misoprostol only arm (118 versus 85). Those with a higher Bishops score (4,5 or 6) were randomised in larger numbers to the Misoprostol only arm (66 versus 31 patients).

Gestational age wise, for patients from 37+0/7 to 38+6/7 weeks, there were 5 patients each with a Bishops score of 2/3 and 4/5/6. Of the Bishops score of 2 or 3, two patients were in the Misoprostol arm and 3 patients were in the Misoprostol and Foleys arm. Of a Bishops score of 4,5 or 6; there was one patient in the Misoprostol arm and 4 patients in the Misoprostol and Foleys arm. Above 39 weeks to 41+0/7 weeks, there were 198 patients (68.3%) with Bishops score of 2 and 3 compared to 92 patients (31.7%) with a Bishops score score

Inspite of randomisation of the sample, only 85 patients (55.6%) with a Bishops score of 2 and 3 were in the Misoprostol arm. In contrast, there were 118 patients (79.2%) with a Bishops Score of 2 and 3 in the Misoprostol and Foleys arm. Despite this uneven distribution, it was found that those patients with a lower Bishops score in the Misoprostol only arm had a significantly shorter latent phase of labour (30 minutes, p value 0.35).
There were more patients with meconium stained liquor in the Misoprostol only arm (40 patients, 26.5%) compared to the Misoprostol and Foleys arm (15 patients, 9.4%). These findings were statistically significant (p value 0.001). More patients with meconium stained liquor ultimately underwent Caesarean sections/Instrumental deliveries. Of the 40 patients in the Misoprostol arm with meconium staining, 21.2% underwent normal vaginal delivery, whereas 62.5% had either Instrumental/Caesarean delivery. These findings were statistically significant, with a p value of 0.157. Of the 15 patients with meconium stained liquor in the Misoprostol and Foleys arm, only one patient had a normal vaginal delivery whereas 14 patients underwent either Instrumental or LSCS deliveries. These findings were also statistically significant (p value 0.034). Other studies (Lanka et al, Rust et al, Chen et al) did not find a statistically significant difference in the rates of Vaginal/Instrumental/Caesarean deliveries in the two groups.

21 patients (13.9%) in the Misoprostol arm required Inj. Terbutaline for hyperstimulation as compared to 15 patients (10.1%) in the Misoprostol and Foleys arm. However, this difference was not found to be statistically significant (p value 0.3). Cheng et al analysed 5 trials that studied this outcome and found the combination group had a significantly decreased incidence of tachysystole.

Women in the BMI range of 25 to 29.9 kg/m2 had a statistically significant reduction in both the latent and the active phase of labour, both being significantly shorter in the Misoprostol only arm. The latent phase was shorter by 1 hour 51 minutes (p value 0.001) and the active phase by 35 minutes (p value 0.002). The total duration of labour was thus reduced by 2 hours 39 minutes in the Misoprostol only group. Although labour was shorter in BMI of <25 and >30 kg/m2 for the Misoprostol only arm, this was not statistically significant.

The incidence of chorioamnionitis was nearly equal in both arms contrary to the findings in Chen et al meta analysis where combination arm had higher incidence of chorioamnionitis.
Post partum haemorrhage was slightly higher in the Misoprostol only group, but this was not statistically significant.

Endomyometritis seemed to be more frequent in the Misoprostol Only arm, and wound infections more common in the Misoprostol and Foleys arms. Neither of these findings reached statistical significance.

More babies in the Misoprostol group (27 babies, 17.9%) were diagnosed with neonatal sepsis compared to the Misoprostol and Foleys arm (20 babies, 13.4%), however this was not statistically significant.

When using Misoprostol alone, there is a higher risk for meconium staining of liquor, hyperstimulation and ultimately Caesarean section/Instrumental deliveries.

**Conclusion:** Misoprostol alone seems to have the following advantages as compared to misoprostol with Foleys together:

1. Shorter induction to delivery interval
2. Shorter overall duration of labour
3. Useful in unfavourable cervix (bishop score < 4)
4. After subgroup analysis, in overweight women (BMI 25 to 29.9 kg/m2), it shortened duration of labour (statistically significant)

- Even though these findings are statistically significant in our study, our numbers are underpowered to advocate Misoprostol as the best agent for induction of labour.
- Use of Misoprostol alone results in higher rates of Meconium stained liquor, hyperstimulation requiring Terbutaline and subsequently a higher Caesarean rates/Instrumental deliveries in these patients.
- There is no statistical difference in infectious and neonatal morbidity in the two groups.