Can the outcome of induction of labour with oral misoprostol be predicted?

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Objective. To determine predictors of outcome for induction of labour using oral misoprostol.

Setting. Labour ward at Kalafong Hospital in Atteridgeville, Pretoria, that serves an indigent South African urban population.

Methods. Data were collected prospectively on all women undergoing induction of labour with oral misoprostol from 1 March 2004 to 28 February 2005. Patients with contraindications to misoprostol induction were excluded. Univariate analysis and logistical regression analysis were performed to determine the significant predictors of success of induction of labour. Successful induction was defined as a vaginal delivery achieved within 24 hours.

Results. Five hundred and fifty-eight patients were included. There were three major indications for induction of labour, namely hypertension (45%), postdates (22.1%) and prelabour rupture of membranes (20.6%). Vaginal delivery was achieved within 24 hours in 52.4% of patients. The caesarean section rate was 42.1%. Fetal heart rate changes occurred in 25.6% and hyperstimulation in 1.4% of patients. Logistical regression analysis identified the following parameters as independent predictors of vaginal delivery achieved within 24 hours: primiparity ($p < 0.001$), Bishop score < 3 ($p < 0.001$), Bishop score 4 - 6 ($p = 0.029$), ruptured membranes ($p < 0.001$) and pre-eclampsia ($p = 0.006$). A method of scoring (Mbele score) has been developed making use of the results of this analysis in order to predict the successful outcome of induction.

Conclusions. Primigravidity, intact membranes, pre-eclampsia and a low Bishop score were indicators of an unsuccessful outcome for induction of labour. It is thought that the Mbele score will be helpful in counselling patients on methods of delivery when they are admitted for induction of labour.

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Induction of labour is one of the most frequent procedures in pregnant women in both developing and developed countries. In the UK the rate of induction of labour is 19.5%.[1] The decision to induce labour is taken when the risk of continuing with the pregnancy outweighs the benefits. Misoprostol has been the drug of choice for induction of labour in developing countries for almost a decade now because it is cheap, stable at room temperatures, easy to prepare and the route of administration is convenient. Licensed drugs for induction of labour, mostly vaginal prostaglandin gel (Prepidil) and tablets (Prostin), are expensive and some require refrigeration making them unsuitable for resource-poor settings.[2] A recent meta-analysis has shown that low-dose oral misoprostol is as effective as conventional and more expensive agents and does not cause an increase in complications.[3]

Ability to predict the outcome of induction would be valuable in counselling women on the routes of delivery, and would be useful in planning the use of resources in a busy labour ward. The standard protocol for induction of labour at Kalafong Hospital was audited and compared with the Cochrane systematic review in order to ascertain its efficacy and safety and to determine the predictors of successful vaginal delivery within 24 hours.

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Methods

Data were collected on women who underwent an induction of labour with oral misoprostol in the maternity ward at Kalafong Hospital, an academic hospital in Atteridgeville, Pretoria. The study group included live, viable, cephalic, singleton pregnancies where labour was induced with oral misoprostol from 1 March 2004 to 28 February 2005. Patients with multiple pregnancy, intra-uterine death, previous uterine surgery and abnormal fetal lie were excluded. The datasheets were completed by the registrar on call in the labour ward before induction of labour and after delivery of each patient. The Coronation-Liverpool regimen[2] was modified (see below) by administering an extended course of misoprostol for those patients where delivery was urgent, namely patients with pre-eclampsia, prelabour rupture of membranes, chorioamnionitis, and antepartum haemorrhage of unknown origin. The gestational age was recorded if it was regarded as accurate, namely early ultrasound measurements were available or the estimation of uterine size coincided with the estimated gestational age according to the last normal menstrual period provided it was before 16 weeks' gestation. Less than 50% of the patients had accurate gestational ages. In the absence of an accurate gestational age, the estimated fetal weight was used to make management decisions. Prelabour rupture of membranes

was diagnosed if liquor was seen draining from the cervical os on sterile speculum or with the fern test.

The modified Bishop score was used to assess all patients admitted for induction of labour.[4] A poster detailing the components of the Bishop score was displayed in all the rooms in the labour ward and every new registrar was trained in its use. Admission cardiotocography (CTG) was done and was repeated for at least 1 hour after each dose of misoprostol administered. The frequency and duration of contractions were assessed using the abdominal pressure transducer of the cardiotocograph. The fetal heart rate patterns were classified as reassuring, suspicious and pathological according the Royal College of Obstetricians and Gynaecologists (RCOG) guidelines for fetal heart rate monitoring.[5] Hyperstimulation was defined as an abnormal fetal heart rate pattern in the presences of tachysystole (5 or more contractions in 10 minutes). Patients were grouped according to the urgency of delivery, and time limits for induction of labour were specified for each patient. Patients whose induction of labour was urgent were offered a caesarean section if they were not in labour within 24 hours, while those whose indication for induction of labour was elective were offered a second course of misoprostol if not in labour within 24 hours. A 200 µg misoprostol tablet was diluted in 200 ml tap water to make a titrated solution of 1 µg per ml. Patients received 20 ml oral misoprostol every 2 hours for 3 doses, followed by 40 ml every 2 hours for 2 doses and a single dose of 60 ml. Misoprostol was stopped if the attending clinician considered that the patient was experiencing adequate contractions (3 in 10 minutes). If a patient had not delivered after the first course (200 ml = 200 µg), depending on the urgency of delivery, the patient either received an extended course of misoprostol of 60 ml every 2 hours for 3 doses only (urgent induction), or the patient was rested and a second course of diluted misoprostol was re-administered after 24 hours (elective induction).

Failed induction of labour was defined as vaginal delivery not achieved within 24 hours of initiating induction of labour.[6] The datasheets were collected daily during the audit meeting and entered into an MS Excel database, and data were analysed using STATA version 8. Descriptive statistics were used to describe the population of women requiring induction of labour and to determine the caesarean section rate, presence of hyperstimulation, and serious neonatal morbidity. Univariate analysis making use of the chi-squared (χ^2) test ($p < 0.2$) was perfomed comparing those patients who had a successful induction with those who had a failed induction. From this analysis potential predictors of successful induction of labour that could be included in a logistical regression model were determined. The Mbele score was created making use of odds ratios from the logistical regression analysis. The positive predictive values (PPVs), sensitivity and specificity were determined for each patient's score. The study was approved by the Ethics Committee of the University of Pretoria.

Results

A total of 558 patients were included for the period from 1 March 2004 to 28 February 2005. The mean age of patients was 27.6 years (range 14 - 45 years). Fifty-three per cent of patients were primigravidas. The mean gestational age was 38.14 weeks (range 30 - 44 weeks); 58% of patients were at more than 38 weeks' gestation. The rate of induction of labour was 9.6%. The major indications for induction of labour were hypertension in pregnancy, postdates and prelabour rupture of membranes (Table I). Vaginal delivery was achieved within 24 hours in 52.4% of patients. The caesarean section rate was 42.1%. The indications for caesarean section were fetal heart rate changes (22.8%), cephalopelvic disproportion (3.8%), failed induction (12.4%), abruptio placentae (1.9%), severe pre-eclampsia with organ dysfunction (0.7%), and hyperstimulation (0.2%). In 22.8% of patients caesarean sections were performed for fetal heart rate changes; 60% of these patients had pregnancy-induced hypertension. In 35% of patients induction of labour was urgent, with 15% receiving an extended course of oral misoprostol. The maternal morbidity rate was 6.9% – this included 33 primary postpartum haemorrhage (5.9%), 9 with abruptio placentae (1.6%) and 1 with uterine rupture (0.18%). There was 1 maternal death following uterine rupture, viz. a

Table I. Characteristics of patients induced with oral misoprostol at Kalafong Hospital (*N* = 558)

Characteristics	*N*	%
Mean age (years) (range)	27.8 (14 - 45)	
Parity		
Primigravidas	293	52.3
Multigravidas	265	47.3
Mean gestational age (weeks) (range)	38 (30 - 44)	
Mean estimated fetal weight (g) (range)	2 799 (1 370 - 4 600)	
Bishop score (mean)	4.4	
≤ 3	182	32.6
4 - 6	315	56.5
≥ 7	61	11.0
Urgency of delivery		
Elective	363	65.0
Indicated	195	35.0
Indications		
Hypertension in pregnancy	250	44.8
Postdates	128	23.0
PROM	117	21.0
Non-reassuring CTG	9	1.6
Chorioamnionitis	19	3.4
APH of unknown origin	15	2.7
Eclampsia	6	1.1
IUGR	4	0.7
Reduced fetal movements at term	3	0.5
Poor obstetric history	3	0.5
Diabetes mellitus	4	0.7

PROM = prelabour rupture of membranes; CTG = cardiotocograph; APH = antepartum haemorrhage; IUGR = intrauterine growth restriction.

woman who was a para 2, gravida 3 at 35 weeks' gestation. Labour was induced for poor obstetric history. She received 3 doses of 20 µg misoprostol 2-hourly. This patient had no risk factors for uterine rupture. After the third dose the patient developed vaginal bleeding. It was then thought she had an abruptio placentae. Arrangements were made for an emergency caesarean section. Delay was experienced in getting to theatre because of another case in theatre. At caesarean section a ruptured uterus was diagnosed and the haemorrhage could not be controlled despite a hysterectomy. The neonatal morbidity rate was 3.9%; 15 of the neonates were admitted to neonatal high care for observation because of birth weight less than 2 kg. No neonates were admitted to the neonatal intensive care unit. There was 1 fresh stillbirth delivered during laparotomy in a patient with a ruptured uterus.

Univariate analysis showed that the following factors influenced the outcome of vaginal delivery achieved within 24 hours, namely parity, hypertension, rupture of membranes, oligohydramnios with intact membranes, suspicious CTG and Bishop score (Table II). Gestational age was not found to be associated with vaginal delivery, probably because of the large number of missing values. The backward logistical regression analysis showed that the following factors were independent predictors of outcome, namely multiparity, Bishop score, pre-eclampsia and prelabour rupture of membranes (Table III). The parameters found in the logistical regression analysis, including the odds ratios, were then used to design a scoring system for patients admitted for induction of labour to predict which of these patients would achieve vaginal delivery within 24 hours (Table IV). Applying the score in the study group the predictive values were calculated and the results are shown in Table V. A patient with a score of 0 was found to have a PPV of 16%, whereas a patient with a score of 8 had a PPV of 89% for successful induction.

Table II. Univariate analysis – factors influencing vaginal delivery achieved within 24 hours

Parameters	*p*-value
Multiparity	< 0.001
Hypertension	0.012
Pre-eclampsia	0.003
Non-reassuring CTG	0.024
Oligohydramnios (AFI < 5)	0.008
Bishop score	< 0.001
Ruptured membranes	< 0.001

CTG = cardiotocograph; AFI = amniotic fluid index.

Discussion

The Pretoria regimen for induction of labour is effective, with vaginal delivery achieved within 24 hours in 52.4% of patients. There is a low rate of hyperstimulation, and low neonatal and maternal morbidity. This is in keeping with studies done in other institutions in South Africa and with the Cochrane systematic review.[3,7,8] However the caesarean section rate was 42.1%. This may possibly be due to the large number of cases where labour was induced for hypertensive disease in pregnancy (44.8%). A similar result was found by Ferreira.[8] Twenty-three per cent of caesarean sections were performed for fetal heart rate pattern changes; this contributed to the high caesarean rate, but without fetal scalp pH facilities the appropriateness of the caesarean sections cannot be determined. A randomised control trial by Rozenberg *et al*.[9] demonstrated that misoprostol does not significantly cause fetal distress compared with dinoprostone in patients at risk of fetal distress. All the patients who had suspicious fetal heart rate patterns on admission CTG developed fetal distress during induction and were delivered by caesarean section. Patients with suspicious CTG patterns should probably not undergo an induction of labour, but rather have a caesarean section.

Of concern, there was 1 patient with uterine rupture without any risk factors for uterine rupture. The rupture of the uterus was unexpected at that low dose of misoprostol. Hofmeyr and Gülmezoglu[10] reported that rupture of the uterus has been documented in a nulliparous patient who received as little as 100 µg of oral misoprostol. Misoprostol can cause excessive uterine activity and uterine rupture, meaning that it is a prerequisite for a patient to be monitored during labour induction or termination of pregnancy.[11] Large multicentre trials are still needed to determine the safety of misoprostol for induction of labour.[10]

Wing *et al*.[12] found that parity, initial cervical dilatation and gestational age at entry were predictors of likelihood for success of induction of labour. In a similar study by

Table III. Logistical regression analysis – independent predictors of vaginal delivery achieved within 24 hours

Parameters	*p*-value	Odds ratios (95% confidence intervals)
Primiparity	< 0.01	0.45 (0.31 - 0.66)
Bishop score (4 - 6)	0.029	0.49 (0.26 - 0.93)
Bishop score < 3	< 0.01	0.26 (0.13 - 0.51)
Pre-eclampsia	0.006	0.55 (0.36 - 0.84)
Ruptured membranes	< 0.001	4.6 (1.2 - 17.6)

Table IV. Mbele score

	Score			
Parameters	0	1	2	3
Parity	Primiparous	Multiparous		
Pre-eclampsia	Yes		No	
Ruptured membranes	No		Yes	
Bishop score	≤ 3		4 - 6	≥ 7

Table V. Positive predictive values (PPVs) for successful induction of labour with oral misoprostol at Kalafong Hospital

Mbele score	PPV for successful induction (%)
0	16
1	21
2	31
3	48
4	53
5	63
6	68
7	77
8	89

Caliskan *et al*.[13] poor Bishop score and nulliparity were found to be predictors of failed induction of labour. A randomised controlled trial by Krupa *et al*.[14] demonstrated that 73.3% of patients with prelabour rupture of membranes at term will achieve vaginal delivery within 24 hours when induced with oral misoprostol versus expectant management. Findings of these studies were similar to our findings except that no independent association with gestational age was found in this study.

A score was developed to predict the likelihood of successful induction. The value of each criterion for the score was determined by the strength of association for successful outcome and ease of remembering the values. As expected, the PPV for success was high using the score, with low scores having a very low chance of successful induction and high scores having a very good chance of success. This information may be useful in counselling women on methods of delivery when they are admitted for induction of labour. It is not suggested that a woman with a low score should have a caesarean section, but that the woman be counselled that the chance of success is low and that caesarean section might be an option. It would be for the patient to decide, and dependent on the clinical condition. However, the score should be tested prospectively on a new population to determine the real value of the score.

Conclusion

This study confirms that cervical ripeness, parity, ruptured fetal membranes, and placental insufficiency resulting from pre-eclampsia influence likelihood of induction success. The scoring system that has been designed may be useful in counselling women on methods of delivery when they are admitted for induction of labour.

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