

Comparison between Immediate and Delayed Induction of Labor in Pregnant Women with Spontaneous Pre-Labor Rupture of Membranes at Term

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Abstract: Aim of work Compare the efficacy and safety of immediate induction of labour with intravaginal misoprostol, with those who will have induction of labour with intravenous oxytocin infusion after an expectant period of 12 hours, at term in patients with PROM and a favourable cervix. Patients and methods Randomized control study of 80 women who had either immediate induction of labour with intravaginal misoprostol tablets, or delayed induction with intravenous oxytocin infusion after an expectant period of 12 hours, at sohag teaching Hospital. The outcome of labour was compared in the two groups using the Z test and Chi square test, while, p-value of less than 0.05 was taken as significant. The odds ratio (OR) and 95% confidence interval were also determined where appropriate. Results Immediate induction of labour with intravaginal misoprostol resulted in lower rates of caesarean section and operative vaginal delivery, with a higher rate of spontaneous vaginal delivery. The duration of latent phase of labour and hospital stay before delivery was statistically significantly shorter in the immediate induction group. Neonatal and maternal morbidity were insignificant and comparable between the two groups. Conclusion: Immediate induction of labour with intravaginal misoprostol resulted in significantly lower rates of intervention without compromising fetomaternal outcome. We recommend the immediate induction of labour with proper use of intravaginal misoprostol in women with SPROM at term.

[Mohamed S. Fouad, Mohamed M. Al Kholy, Mohamed S. Hammour, Mohamed Salah Ahmed, **Comparison between Immediate and Delayed Induction of Labor in Pregnant Women with Spontaneous Pre-Labor Rupture of Membranes at Term.** *Nat Sci* 2017;15(3):105-112]. ISSN 1545-0740 (print); ISSN 2375-7167 (online). <http://www.sciencepub.net/nature>. 15. doi:[10.7537/marsnsj150317.15](https://doi.org/10.7537/marsnsj150317.15).

Key words: SPROM at term, immediate vs delayed induction of labour, Outcome.

1. Introduction

Pre-labor rupture of membranes (PROM) occurs in approximately 8% to 10% of term pregnancies (37–42 weeks' gestation). PROM is defined as rupture of membranes at least one hour before the onset of uterine contractions. The management of PROM at term continues to be controversial as best practice has not been established. Approaches to the management of PROM include expectant management and immediate induction of labor. Expectant management is defined as “watchful waiting until spontaneous labor occurs.” (ACOG, 2013)

Early research on PROM noted that 60% to 90% of women at term enter into spontaneous labor within 24 hours of membrane rupture. (Marowitz and Jordan, 2007) Other early studies focused on the best management of PROM: immediate induction or expectant management. Some researches associated immediate induction of labor for women with PROM and an unripe cervix with higher rates of caesarean birth; other studies associated it with higher rates of perinatal infection, prompting further research. (Grant et al, 1992) (Rydhstrom and Ingemarsson, 1991).

In the UK, the National Institute for Health and Care Excellence (NICE) guidelines of term PROM recommend expectant management for 24 hours (NICE, 2009), while in the USA, the American

College of Obstetricians and Gynecologists (ACOG) advises active management of term PROM to reduce the risk of infectious complications (ACOG,2007).

Oral misoprostol (prostaglandin)E1 which is cheap, heat stable and easy to store, with better user acceptability has been found in many studies to be efficient and safe in ripening the cervix and inducing labor when inserted intravaginally in a dose of 50ug tablets every 4-6hours (Wanger 2003 & Patil et al., 2005.)

Medication that will ripen the cervix in a short period of time and compress into a day, the process that generally used to take days will play an important role in modern obstetrics (Patil et al., 2005).

2. Patients and Methods

This study was conducted in the period from January 2016 to June 2016 in Sohag teaching hospital comparing the pregnancy outcome in 80 women with spontaneous pre-labor rupture of membrane at < 37 weeks' gestation with favorable cervix. The patients were randomized to: immediate management group (**Group A** (study)): It included 40 women given 50 µg of vaginal misoprostol In the posterior fornix moistened with saline, and they will be observed closely and the insertion of misoprostol will be repeated after six hours if the women Do not go into labour, or delayed

group (**Group B** (Expectant)): It included 40 women for delayed induction of labour with oxytocin infusion after an expectant period of 12 hours. The patients will be selected according to inclusion and exclusion criteria.

The inclusion criteria

1. Have spontaneously rupture of membrane at 37 weeks of gestation or more, verified from LMP and / or early ultrasound dating;
2. Carrying single fetus in cephalic presentation;
3. Not in labour.
4. Have normal fetal heart rate. 5-Have no meconium staining of the liquor or suspicion of chorio-amnionitis. 6-Have no contraindication to induction of labour or vaginal delivery. 7-Bishop score 4 or more.

The exclusion criteria

Pregnant women who:

- 1- Have previous cesarean section.
- 2-Have multiple pregnancies. 3-Have Bishop score less than 4.
- 4-Meconium staining of liquor. 5-Any contra indication to induction of labour or vaginal delivery 6- In active labour.

All patients were submitted to:

1- Complete history taking.

2- Careful throughout general, abdominal & local vaginal examination

Local vaginal examination: • Examination with a sterile vaginal speculum to confirm the diagnosis of ROM, On examination pooling of amniotic fluid in the posterior vaginal fornix can usually be seen, A Valsalva maneuver or slight fundal pressure may expel fluid from the cervical os.

3-Investigations: CBC, C reactive protein (CRP).

4-Abdominal Ultrasound Done for all women to assess:

Fetal presentation, Gestational age, Fetal size, Fetal wellbeing, Site of placenta, AFT (Amniotic fluid index).

Main outcome of both groups

- 1) Mode of Delivery Among Participants.
- 2) Mean duration of latent phase of labour (hours).
- 3) Mean duration between Pre-labor ROM and delivery in both groups.
- 4) Fetal outcome by Apgar score -need for intubation - admission to ICU.
- 5) Postpartum condition of women in both groups.
- 6) Indications of cesarean section in both groups.

The immediate management group (Misoprostol group: the study group):-

The misoprostol preparation used in this study was: two vagiprost tablets moisted with saline and

administered vaginally in posterior fornix. And repeated after six hours if the women did not go into labour and up to a maximum of four doses whenever needed. There was follow up of the onset, frequency and duration the uterine contractions and cervical dilatation.

The delayed management (oxytocin) [expectant or control] group:-

women admitted and closely monitored for onset of labour for 12 hours (including maternal temperature every 4 hours, hourly maternal pulse rate and hourly, fetal heart rate, white blood cell count if suspicious), before starting induction of labour with oxytocin infusion. if labour didn't start by using Iv infusion of 5 units of oxytocin in 500mls of 5% dextrose which will titrated against uterine contractions starting with 2miu/minute and doubled every30 minutes until 3-5 contractions obtained in 10 minutes which lasting 40-60 sec each or max. infusion of 32ml IU /min. In both groups, vaginal examination done every 4 hours as long as there is no labour pains and hourly when the patient is in active phase. partographic record of laour was used to follow up progress of labour.

Labour monitoring terminated by cesarean section when failure to progress or if fetal distress develops and chorioamnionitis.

Antibiotics were used as a prophylactic therapy in both groups in the form of Ampicillin 1 gm ampoule every 8 hours.

3. Results

Table (1) shows no significant difference between the two groups as regards maternal age, gestational age, parity, gravidity and abortion. This denotes will cross - matching between both groups of the study.

In table (2) No significant difference between the immediate group and the delayed induction group as regards nulliparous and multiparous patients' distribution.

Table3 shows no statistically significant difference could be detected between both groups as regards Bishop score.

Table (4) shows statistically significant difference ($P < 0.05$) between the two groups as regards Duration of latent phase of labour, with shorter latent phase among the immediate induction group, by using the ANOVA test. There was no difference in the rate of progress oflabour in the two groups once active phase was reached.

Table(5) shows significant difference between the two groups as regards duration from rupture of membranes till delivery by using the ANOVA test. as immediate induction group is shorter in duration than delayed group.

Table(6) shows that delayed induction group had a higher frequency of CS delivery compared to immediate induction group with statistically highly significant difference between both groups by using chi square test.

Table (7) demonstrated that 32.5% of the women in the delayed induction group went into spontaneous labour before induction with oxytocin infusion. And 40% delivered by induction with oxytocin.

Table(8) shows that Among the women in the immediate induction group, 80% required only one insertion of misoprostol for induction of labour, while 10% of the women required augmentation of labour with oxytocin infusion. And the last 10% required double dose.

Table9 shows no statistically significant difference could be detected between both groups as regards the indications of cesarean section. Failed progression was the most cause of cesarean section in both groups.

Table (10) shows no statistically significant difference between both groups as regards fetal

weights. But there was statistically significant difference between both groups as regards Mean Apgar score as in misoprostol group was significantly greater than that in the delayed induction group ($P < 0.05$).

In Table11 One of 40 women in the immediate misoprostol group has developed nausea and vomiting and one case in delayed group with no occurrence of diarrhea in both groups so no significant difference between both groups as regards the occurrence gastrointestinal side effects. Also no significant difference between both groups as regards the maternal complication. One case for each of them developed atonic postpartum hemorrhage without need of blood transfusion with no significant difference between them in chorioamnionitis by using the Chi- Square test.

In table (12) No significant difference between the study groups as regards the occurrence of fetal distress or neonatal admission to NICU by using the Chi- Square test.

Table (1): Comparison between the immediate induction group and delayed oxytocin group as regards maternal age, gestational age, gravidity, parity and abortion.

Variables	Immediate group N(40) M±SD	Delayed group N(40) M±SD	P value
Age	27.81±3.270	27.61±3.428	>0.05 NS
Gravidity	2.65±1.191	2.73±1.369	>0.05 NS
Parity	1.29±0.912	1.40±1.078	>0.05 NS
r, Abortion	1.29±0.463	1.47±0.624	>0.05 NS
Gestational Age	38.51±1.057	38.29±1.124	>0.05 NS

Table(2): Comparison between the study groups as regards nulliparity and multiparity:

Variables	Immediate group N(40) M±SD	Delayed group N(40) M±SD	P value
Nulliparous	8(20%)	9(22.5%)	>0.05 NS
Multiparous	32(80%)	31(77.5%)	>0.05 NS

Table3: Comparison between the two groups regarding Bishop Score:

Variables	Immediate group N(40) M±SD	Delayed group N(40) M±SD	P value
Bishop Score	6.51±1.781	6.07±1.803	>0.05 NS

Table (4): Comparison between both groups as regards latent phase of labor and active phase of labor.

Duration(hours)	Immediate group N(40) M±SD	Delayed group N(40) M±SD	P value
Latent phase of labor	3.8±3.1	5.6±3.5	>0.05 NS
Active phase of labor	3.2±2.1	3.4±1.9	<0.05 NS

Table (5): Comparison between both groups as regards interval (in hours) from pre-labor rupture of membranes until delivery.

Interval	Immediate group N(40) M±SD	Delayed group N(40) M±SD	P value
Interval from rupture of membranes till delivery	8.2± 2.154	14.62±4.229	>0.01 HS

Table (6): Comparison between both groups as regards mode of delivery.

Mode of delivery	Immediate group N (40)	Delayed group N (40)	P value
Normal vaginal delivery	37(92.5%)	29(72.5%)	<0.01 HS
Cesarean section	3(7.5%)	11(27.5%)	<0.01 HS

Table (7): Comparison between group (B)cases as regard mode of delivery

Mode of delivery	Delayed group N(40) 100%	P value
Normal vaginal delivery after induction	16(40%)	>0.05 NS
Spontaneous vaginal delivery without induction	13(32.5%)	>0.05 NS
Cesarean section	11(27.5%)	>0.05 NS

Table (8): Comparison between women of immediate induction group (A) as regards misoprostol number of doses.

Misoprostol dose	Immediate group N(40) 100%
Single dose	32(80%)
Single dose+augmentation by oxytocin	4(10%)
Double dose	4(10%)

Table 9: Comparison between the both groups as regard indication of cesarean sections:

Cause of cesarean section	Immediate group N (3)	Delayed group N(11)	P value
Failed progression	2(66.7%)	8(72.7%).	>0.05 NS
Fetal distress	1(33.3%)	2(18.2%)	>0.05 NS
sign of chorioamnitis	0	1(9.1%)	>0.05 NS
Total(percentage)	3(100%)	11(100%)	

Table (10): Comparison between the two groups regarding baby weight & apgar score:

Variables	Group A Study group mean±SD	Group B High risk group mean±SD	P value
Baby weight	3.075.33±243.20 1	3.1 74.67±284.079	>0.05NS
Apgar score-1	8.93± 0.935	8.43± 1.117	<0.05 S
Apgar score-5	9.96 ± 0.197	9.84 ±0.466	<0.05 S

Table 11: Comparison between both groups as regards the occurrence of maternal gastrointestinal side effects, postpartum hemorrhage and chorioamnionitis.

Variables	Group A Immediate group N (40)	Group B Delayed group N (40)	P value
Nausea and Vomiting	1(2.5%)	1(2.5%)	>0.05 NS
Diarrhea	0(0%)	0(0%)	>0.05 NS
sign of chorioamnionitis	0	1(2.5%)	>0.05 NS
Atonic post partum Hemorrhage	1(2.5%)	1(2.5%)	>0.05 NS

Table (12): Comparison between both groups as regards fetal distress and neonatal admission to the intensive care unit (NICU):

Variables	Immediate group N(40)	Delayed group N(40)	P value
Fetal distress	1(2.5%)	2(5%)	>0.05 NS
Neonatal ICU	0(0%)	1(2.5%)	>0.05 NS

4. Discussion.

The management of Premature rupture of membrane (PROM) at term continues to be controversial as best practice has not been established. Approaches to the management of PROM include expectant management and immediate induction of labor. Expectant management is defined as “watchful waiting until spontaneous labor occurs.” (ACOG, 2013).

In the UK, the National Institute for Health and Care Excellence (NICE) guidelines of term PROM recommend expectant management for 24 hr (NICE, 2009), while in the USA, the American College of Obstetricians and Gynecologists (ACOG) advises active management of term PROM to reduce the risk of infectious complications (ACOG, 2007).

In the present study, 80 women with pre-labor rupture of membranes at term with bishop score > or equal 4 were divided into two groups group (A): 40 women were received vaginal misoprostol 50 ug every 6 hours for a maximum of 4 doses compared with group (B): 40 women managed by delayed induction with intravenous oxytocin infusion after an expectant period of 12 hours. The main outcome measures are: Starting labor pain, the intervals (in

hours) between Pre-labor ROM and significant uterine contractions and delivery in both groups, cesarean section rate and maternal and fetal/neonatal complications, e.g.: chorioamnionitis and fetal distress.

The two groups had similar demographic and ante partum variables. Maternal age, gestational age, parity, and Bishop score were similar in the two groups. This denote well cross matching.

The current study showed that the use of misoprostol has advantage over delayed management, i.e. a decreased interval between pre-labor ROM and delivery. The study demonstrated that the duration of latent phase of labor and interval between pre-Labor ROM and delivery were lower in the group (a) misoprostol group than in group (B) delayed oxytocin management group as (3.8 ±3.1 Vs 5.6 ±3.5: P<0.005) and (8.21 ± 2.154 Vs. 14.62± 4.229 hours; P < 0.001) respectively, so the difference between both groups was significant.

These results were in accordance with those obtained by (Omole et al, 2009), (krupa 2005), (Ghaleh et al. 2012), (Tabasi. 2007), Sanchez-Ramos et al. (1997) & Kramer (1997), Oliver et al 2008. However, (Wing and Paul; 1998) found no

significant difference in the meantime intervals from start of induction to delivery in women with PROM beyond 36 weeks of gestation with either vaginal misoprostol or oxytocin. Also in **(Zeteroglu et al. 2006)** The mean interval from induction to delivery was 10.61 ± 2.45 hours in the misoprostol group and 11.57 ± 1.91 hours in the oxytocin group ($p = 0.063$).

In the current study there was a significant difference between both groups as regards the rate of cesarean section. It was (7.5%Vs 27.5%; $p < 0.05$) in the misoprostol group compared to the delayed management group, and the rate of normal vaginal delivery was (92.5%; Vs 72.5%; $p < 0.05$) respectively. This current study came in agreement with the study of **(Omole et al., 2009)**, **(Tabasi 2007)**, **(Ghaleh et al. 2012)** **(Oliver et al 2008)** **(sanchez-ramus et al., 1993)**. In the **Sanchez-Ramos et al. (1997)** meta-analysis compared the use of intravaginal misoprostol for cervical ripening and labor induction with that of dinoprostone, oxytocin or placebo. Misoprostol was associated with a significantly lower overall rate of cesarean section, a higher incidence of vaginal delivery within 24 hours of application and a reduced need for oxytocin augmentation. Spontaneous labor occurred in nearly 85 percent of the women studied. In **(Zeteroglu et al; 2006)** The rates of vaginal delivery were 83.3% and 91.8% and cesarean delivery were 16.7% and 8.2% in the misoprostol and oxytocin groups, respectively. This is a doubling of the cesarean section rate, and so was not significant. In **Wingand Paul, (1998)**, were not in agreement of current study as no significant difference in the mode of delivery. The incidence of cesarean birth was 13.3% in vaginal misoprostol group versus 14.1% in oxytocin group.

Also in the study of **Zamzami, 2006**, who compared the outcomes of expectant versus induction of labor management of patients presenting with pre-labor rupture of membranes at term there was no statistically significant difference between both groups. This may be due to the difference in method of active management (induction of labor).

In the current study The misoprostol dose required to induce labor ranged from only 50ug (single insertion) in 89.3% women to 100ug in 10.7% of women. These results were in the agreement with **Omole et al. (2009)** that among the women in the immediate induction group, 94% required only one insertion (50ug) of misoprostol for induction of labour.

Also in **Oliver et al 2008** The total misoprostol dose required to induce labour ranged from 100ug (single insertion) in (85.6%) patients to 300ug (three insertions) in (4.2%) patient. And (10.2%) patients had two insertions, By **Sanchez-Ramos and associates, (1997)**, 85.7% of patients in the misoprostol group, needed only one vaginal dose for

successful labor induction. Also in **Ozden et al., (2002)**, found that 71 % of patients in the vaginal misoprostol group received single dose for active labor, the higher percentage in current study may be explained as women in current study of bishop score of \geq or = 4 but in this study of low bishop score.

In the current study: in group B there were 25 (33.3%) women went into spontaneous labour before induction with oxytocin.

Which in agreement of the study of **(Omole et al., 2009)** there were Thirty-three percent of the women in the delayed induction group went into spontaneous labour before induction with oxytocin infusion. Also **(Chaudhuri Snehamay et al 2006)** were in agreement of current study as in delayed induction group 32.14 % (3611 12) women went into spontaneous labor while under observation.

In current study Failure of progression in both misoprostol and oxytocin groups accounted for most of the indications for cesarean section cases (66.7%) and 8 cases (72.7%) respectively. This finding is in agreement with **Tarik, (2006)**, where he found the all the cesarean sections performed in the oxytocin group were due to failure to progress (7.4%). The other hand in **(oliver et al., 2008)** A large percentage of caesarean section in oxytocin arm was for prolonged labour as against cephalopelvic disproportion in the misoprostol arm. The emergency CS rate due to fetal distress (pathological fetal heart rates) in this study was 0 case (0%) to 2 cases (18.1%) in misoprostol and oxytocin respectively. in **Sanchez- Ramos et al., (1997)**, also found no significant difference between the vaginal misoprostol and oxytocin groups as regards the occurrence of fetal distress (8.6%) in vaginal misoprostol versus (9.9%) in oxytocin group.

Also in **(omole et al. 2009)** There was no statistically significant difference ($P > 0.05$) between the two groups in the occurrence of fetal distress. While in **(Krupp 2005)**. There were no differences between the two group regarding fetal wellbeing. Also in **(oliver et al., 2008)** There were no significant difference in the fetal distress rate ($p=0.46$).

In the current study Mean Apgar score (at 1 min) was 8.93 ± 0.935 in misoprostol group and 8.43 ± 1.117 in the delayed induction group, which in misoprostol group was significantly greater than that in the expectation treatment group ($P < 0.05$). These was in agreement of **(Ghaleh et al. 2012)** that Mean Apgar score was 9 ± 0.14 in misoprostol group and 8.7 ± 0.7 in the expectation treatment group, which in misoprostol group was significantly greater than that in the expectation treatment group ($P = 0.02$). While in **(omole et al., 2009)** There was no statistically significant difference ($P > 0.05$) between the two groups in apgar score. Also **Zeteroglu et al., (2006)**, who found that there was no significant difference

between the vaginal misoprostol and oxytocin groups as regards Apgar score at 1 and 5 minutes (7.16 ± 1.19 , 7.32 ± 1.14) at 1 minute (8.9 ± 0.88 , 8.95 ± 0.95) at 5 minutes respectively, though no statistically significant difference between the 2 groups.

In our current study there were no significant difference between the vaginal misoprostol and oxytocin groups as regards the occurrence of fetal distress 1 case (2.5%) in vaginal misoprostol versus 2 cases (5%) in oxytocin group. Also these came in the agreement of (**Omole et al., 2009**) that There was no statistically significant difference in the occurrence of fetal distress, ($P > 0.05$). (3 cases) in the misoprostol group and (4 cases) in delayed oxytocin group.

Sanchez- Ramos et al., (1997), also found no significant difference between the vaginal misoprostol and oxytocin groups as regards the occurrence of fetal distress (8.6%) in vaginal misoprostol versus (9.9%) in oxytocin group. Also in (**Tabasi et al., 2007**) there were no difference between the two group as regard fetal distress. (**Oliver et al., 2008**) also came in agreement of our study as There were no significant difference in the fetal distress rate ($p=0.46$).

No significant difference was found between the two groups in our study as regards the occurrence of atonic postpartum hemorrhage as there was only 1 case (2.5%) in the vaginal misoprostol group and 1 case (2.5%) in oxytocin group who did not require blood transfusion. These came in agreement of (**omole et al., 2009**). (**Zeteroglu et al., (2006)**). In (**Krupa 2005**) Also in the study done by **Sanchez Ramos et al., (1997)**, there was no significant difference between the study groups 2 (2.9%) cases in vaginal misoprostol group and 2 cases (2.8%) in oxytocin group and the authors did not comment on the requirement of blood transfusion in these cases. The conservative small dosing regimen in this study (50 µg) might participate in the rare occurrence of this postpartum complication.

In our study there were no significant differences between both groups as regard maternal and neonatal outcome. these was in agreement of **Omole et al., (2009)**, **Krupa (2005)**, **Sanchez Ramos et al., (1997)**. The rate of chorioamnionitis in the expectant management group was 2.5%; it was not recorded in the immediate induction group. This result is in accordance with those obtained by **Javaid et al. [2008]**. These results are different from those obtained by **Hannah and co-workers [1997]**, who stated that there was significant difference between the studied groups in the rate of chorioamnionitis. This difference may be due to the larger scales they studied; a total of 5041 women from six different countries were included in their study. This wide scale allows significant differences between the groups.

It can be concluded that immediate induction of

labour in pre-labor rupture of membranes with a favorable cervix with intravaginal misoprostol appear to be at a lower risk of intervention and to have shorter duration of hospital stay without compromising fetomaternal outcome, with low rates of cesarean sections than expectation treatment. We recommend the proper use of intravaginal misoprostol 50ug every 6hours tablets for immediate induction of labour.

Conclusion

Women who had immediate induction of labour with intravaginal misoprostol appear to be at a lower risk of intervention and to have shorter duration of hospital stay without compromising fetomaternal outcome.

Recommendations

We recommend the proper use of intravaginal misoprostol tablets for immediate induction of labour in women with SPROM at term with Bishop score 4 Or more. However, more studies will be required in order to accept this method of induction of labour as the method of choice.

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