(IJRMST) 2020, Vol. No. 10, Jul-Dec **e-ISSN: 2455-5134, p-ISSN: 2455-9059**

# Use of Intravenous Oxytocin Infusion Versus Misoprostol for Induction of Delivery in Cases of PROM at Term

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*Date of Acceptance: 02nd October, 2020; Date of Publication: 19th October, 2020*

**ABSTRACT**

*This research is aiming to a comparison of how administration of misoprostol via vaginal route is efficient and safe versus intravenous oxytocin infusion for induction of delivery in cases with (PROM) at date. Results show that Misoprostol group showed significantly higher mean induction delivery interval than that of oxytocin group. No significantly different results between the both groups regarding the mode of delivery. No significantly different results between the both groups regarding the neonatal admission to (N.I.C.U). No significantly different results between the both groups regarding the mean of Apgar score at 60 seconds and five minutes. No significantly different results between the both groups regarding uterine hyperstimulation. No significantly different results between the both groups regarding postpartum hemorrhage. No significantly different results between the both groups regarding CS indication. No significantly different results between the both groups regarding emergency CS rate due to distress of the fetus. It is concluded that usage of both IV oxytocin infusion with a rate of 2 mU/min which increased by 2 mU/min each twenty minutes up to a rate of 30 mU/min & misoprostol in the vagina 50 µg intravaginally at six hrs. intervals but not exceeding four dosages for safe delivery induction with PROM. It is preferable to use IV oxytocin if the time factor is considered.*

***Keywords:*** *PROM, oxytocin, misoprostol, intravenous, delivery induction.*

## INTRODUCTION

Induction of labor means iatrogenic inducing uterine contractility to start delivery before to the beginning of spontaneous delivery. This is highly performed obstetrical practices in USA **(Martin, 2003)**. Between 1990 and 2004, the rate of delivery induction approximately multiplied by 2, as it was 10.1% and became 21% **(Deborah, 2008)**. An explanation of that increase is the presence of more factors that facilitate ripening of the cervix, doctors and patients prefer arranging a convenient duration of delivery. **(Rayburn, 2002)** Rising induction frequency is due to fear of women or doctors about fetal loss with expectation of managing near date or postdate. **(Deborah, 2008)**

## LITERATURE REVIEW

The pituitary gland - namely its posterior lobe - secretes oxytocin hormone after its production in the hypothalamus. The secretion of that polypeptide takes the form of pulsating manner. It is similar to its synthetic analogous in that it is one of the highly famous strong uterotonic factors. External giving of oxytocin will produce rhythmic uterine contractility as demonstrated firstly at gestational age of nearly twenty weeks, with increase in response with progressing in gestational age. Myometrium is less sensitive concerning response to oxytocin in the last 6 weeks of gestation; but, as spontaneous delivery starts the uterus becomes more sensitive to oxytocin quickly **(Calderyro**, **1959)**. The myometrium becomes more sensitive by advance in pregnancy because of rising in oxytocin receptors in the myometrium. Synthetic oxytocin administration is a proven method of labor induction **(Kelly, 2001)**. On pregnant uterus pharmaceutical oxytocin produces its actions through internal hormone. Uterine respond to oxytocin depends upon the gestational age; after 28 weeks gestation the respond is higher. In the first gestational weeks, oxytocin can establish uterine contractility when a generous dosage is given. Oxytocin is highly efficient at or near term.

The uterine smooth muscular cells are specifically stimulated via enhancement of Na permeability in membranes of myofibrils to induce periodic uterine contractility. This is accompanied by rising the rate & force of present contractility (**O′Brien, 1996**). Recent investigations have demonstrated that oxytocin induces the expression of cyclooxygenase 2 (COX-II) to bring about a sustained release of prostaglandin into the myometrial cells (Molnar et al., 1999). Although the mechanism of this interaction has not been completely clarified, it probably includes provocation of (MAPK) mitogen-activated protein kinase. (**Nohara, 1996**).

Different researches have demonstrated that PGs E2 are effectient to ripen the cervix and to induce delivery **(Alfirevic, 2006)**. In those studies, there was no clarification of the difference between formal induction and ripening of the cervix. In the USA, PG E2 or E1 is typically given intravaginally for ripening of the cervix as the primary measure to induce delivery. This initiates labor in many women without addition measure. If delivery is not started or is not progressed in a fair rate, oxytocin may be given. Alternatively, repeated doses of prostaglandins can be given. In randomized trials, prostaglandins appear to be as good as or better than oxytocin for labor induction. Up till now, no determination for optimal dosage & type of PGs has been established for induction of labor. One option is a dinoprostone insertion in the vagina of ten mg of prostaglandin E2 in a timely release formula (the medicine is released by a rate 0.3 milligram/hour). We leave the suppository vaginally until starting of active labor or up to 12 hrs. Another option is prostaglandin E2 in 3 mg doses administered every 6 hrs. Oxytocin might be started, if required, 40 to 60 minutes following removal of dinoprostone insertion **(Keirse, 2006)**. Unlike oxytocin, receptors for PGE and PGF are present in both pregnant and non-pregnant uteri. There are eight divisions and subdivisions of PG receptors. They include thromboxane A2, prostacyclin, PGF, and PGD receptors and 4 subdivisions of PGE binding sites (EP.1, EP.2, EP.3, and EP.4) **(Narumiya, 1999)**. Those receptors are coded by various genes so they have been expressed in cultured cells; the binding properties and transduction pathways have been characterized. They are coupled to G proteins, and the receptor–G protein complexes are coupled to different effector systems. The receptors are specific for the pentane ring structure but do not distinguish changes in the fatty acid backbone of the molecule **(Williams, 2000)**. There are four subtypes of PGE receptors. They couple to two major effector pathways leading to increased intracellular calcium and muscle contraction (EP1), to stimulation of the adenyl-cyclase system leading to muscle relaxation (EP2 and EP4), and to inhibition to adenyl-cyclase system will provide muscular contractility (EP3). For this reason, PGE may be stimulatory at lower doses and inhibitory at large doses in vitro experiments. The distribution of PGE receptors is different among different tissues: EP2 is expressed mainly in spleen, lung, and testis, EP3 in liver and kidney, EP1 in muscular tissue, and the most ubiquitously expressed is EP4 (**Boie, 1997**). There are PGE receptors in the cervix, but their concentration is lower than in the myometrium. Inflammatory cytokines stimulate EP1 receptor

expression by the amniotic membranes (**Spaziani, 1999**). Misoprostol acid, the biologically active form of misoprostol, binds to EP3 and EP4 receptors (**Breyer, 1996**)

## METHODOLOGY

This is randomized study with a total of 60 pregnant women at full term (≥ 37weeks) with premature rupture of membrane. I divided the cases in two groups (A - B) each consisting of 30 patients as follow:

- *Group A, given 50 µg misoprostol intravaginally. The doses administered every 6 hrs. not exceeding four dosages.*
- *Group B, given intravenous oxytocin infusion. I used a solution of ringer that contains 10mU oxytocin/ml and started with a rate of 2 mU/min that raised by 2 mU/minutes at 20 min. intervals not exceeding rate of 30 mU/min.* The infusion rate was adjusted manually assuming that 1ml=20 drops. Optimum response assumed when 3efficient contractions were obtained in 10 minutes period.

In the events of contraction more than 3 per 10 minutes the solution rate was decreased by step (2 mU/min) and response was reevaluated in 20 minutes.

The *1ry outcome* measure was the induction-delivery period (duration from inserting the drug to deliver), while 2*ary outcomes* monitor: uterine hyperstimulation, mode of delivery, abnormal patterns of fetal heart rate, Apgar score at 1-5 minutes, NICU admissions and CS indication.

## RESULTS & DISCUSSION

**Table (1) Comparison between both groups as regards induction delivery period**

| Induction delivery interval | Misoprostol | Oxytocin |
|---|---|---|
| **Mean (hour)** | 11.97 | 8.97 |
| **SD** | 0.999 | 0.944 |
| **P value** | <0.001 | |

P<0.001 highly significant

There was statistically significant difference between both groups as regards the mean of *induction delivery period*, as the mean is higher when using misoprostol (11.97 ±0.999) than that of oxytocin group (8.97± 0.944), (P<0.001) as shown in table (1). This goes with (**Escudero, 1997)** However, (**Kramer, 1997**) and (**Tabasi, 2007**) found significant difference as the mean was higher when oxytocin was given. That can be explained by a smaller dose of misoprostol used in those studies (25µg).

**Table (2) Comparing both groups as regards delivery mode**

| MOD | misoprostol | | oxytocin | | total | | P Value |
|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | 0.754 |
| **CS** | 7 | 23.3 | 6 | 20.0 | 13 | 21.7 | (NS) |
| **VD** | 23 | 76.7 | 24 | 80.0 | 47 | 78.3 | |

P>0.05 insignificant

When giving misoprostol, 23 women (76.6%) were delivered vaginally and 7 cases (23.3%) were *delivered by CS*, while when giving oxytocin, 24 cases (80%) vaginal delivery occurred and 6 cases (20%) by CS. No significantly different results between the both groups regarding the mode of delivery (p=0.754) as shown in table (2). This goes

with (**Wing, 1998**) and (**Abedi-Asl, 2007**) However, (**Tarik, 2006**) found that the frequency of CS when giving oxytocin was 4.7%. This low percentage may be due to the lower number of nulliparous (25.9%) in oxytocin group in their study versus 33.3% in my study.

**Table (3) Comparison between the two groups as regards neonatal ICU admission**

| | **misoprostol** | | **oxytocin** | | **total** | | **P Value** |
|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | 0.718 |
| **Normal** | 25 | 83.3 | 26 | 86.7 | 51 | 85.0 | (NS) |
| **NICU** | 5 | 16.7 | 4 | 13.3 | 9 | 15.0 | |

P>0.05 insignificant

The number of *neonatal ICU admission* was slightly high when giving misoprostol in contrast to giving oxytocin [5 cases (16.7%) and 4 cases (13.3%) respectively]. there was 2 cases in the misoprostol group was admitted to neonatal ICU due to thick meconium and 3 cases was admitted to neonatal ICU due to fetal distress. there was 1 cases in the oxytocin group was admitted to neonatal ICU due to thick meconium and 3 cases was admitted to neonatal ICU due to fetal distress. No significantly different results between the both groups regarding neonatal ICU admission (p= 0.718) as shown in the table (3). This goes with (**Zetroglu, 2006)** and (**Abedi-Asl, 2007**)

**Table (4) Comparing both groups regarding Apgar score**

**(At 60 seconds and 5 minute)**

| **Apgar score** | **Misoprostol** | | **Oxytocin** | | |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | P value |
| **at 60 seconds** | 6.57 | 1.073 | 6.43 | 1.006 | 0.416 |
| **at 5 min.** | 8.13 | 0.900 | 8.07 | 0.980 | 0.872 |

P>0.05 insignificant

No significantly different results between the both groups regarding the mean of ***Apgar score at 60 seconds***, as the mean was slightly higher in the misoprostol group (6.57 ±1.073) than that of oxytocin group (6.43± 1.006) which denotes homogeneity of 2 groups (p=0.416). No significantly different results between the both groups regarding the mean of Apgar score at five minute, the mean was slightly higher in the misoprostol group (8.13 ±0.900) than that of oxytocin group (8.07± 0.980)which denotes homogeneity of 2 groups (p=0.872). This goes with (**Zeteroglu, 2006**) and (**Escudero, 1997**)

Only one patient (3.3%) in the misoprostol experienced ***uterine hyperstimulation*** and none of the patients in the oxytocin group experienced uterine hyperstimulation which is defined as a persistent pattern of more than 5 uterine contractions in ten minutes, contractions persisting more than 2 minutes, or those of normal period that occur one minute after each other, accompanied or not by changing heart rate of the fetus. There was no significant difference between the two groups as regards uterine hyperstimulation (p=0.313). This goes with (**Zeteroglu, 2006**) and (**Sanchez, 1997**)

There were 2 patients (6.7%) when giving misoprostol who suffered ***postpartum bleeding*** and none of the patients when giving oxytocin suffered postpartum bleeding. No significantly different results between the both groups regarding postpartum hemorrhage (p=0.150). This goes with (**Zeteroglu, 2006**) and (**Sanchez, 1997**)

When giving misoprostol, 3 cases (10%) undergone CS due to fetal distress and 4 cases (13.3%) undergone CS due to induction failure, while when giving oxytocin, 4 cases (13.3%) undergone CS due to fetal distress and only 1 case (3.3%) by CS due to failed induction. No significantly different results between the both groups regarding ***CS***

***indication*** (p= 0.198). This is similar to (**Zeteroglu, 2006**) who reported No significantly different results between the both groups regarding incidence of failed induction. (**Sanchez, 1997**) and (**Abedi-Asl, 2007**) also found No significantly different results between the both groups regarding the occurrence of fetal distress. But (**Zeteroglu, 2006**) found higher number of fetal distress when giving vaginal misoprostol more than in the current study. This may be due to shorter interval between doses (50µg every 4 hours) while it is (50µg every 6 hours) in this study.

## CONCLUSIONS

1. Misoprostol group showed significantly higher mean induction delivery interval than that of oxytocin group.
2. No significantly different results between the both groups regarding the mode of delivery.
3. No significantly different results between the both groups regarding the neonatal admission to the intensive care unit (N.I.C.U)
4. No significantly different results between the both groups regarding the mean of Apgar score at 60 seconds and five minutes.
5. No significantly different results between the both groups regarding uterine hyperstimulation.
6. No significantly different results between the both groups regarding postpartum hemorrhage.
7. No significantly different results between the both groups regarding CS indication.
8. No significantly different results between the both groups regarding emergency CS rate as a response to fetal distress.
9. Usage of both IV oxytocin infusion *with a rate of 2 milli-unit/minute which increased by 2 milli-unit/minute at 20 minutes gaps not exceeding rate of 30 milli-unit/minute* & vaginal misoprostol *50 µg intravaginally every six hours not exceeding four dosages* for safe induction of delivery with PROM.
10. It is preferable to use IV oxytocin if the time factor is considered.

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