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ORIGINAL ARTICLE

Comparison of Effectiveness of Induction of Labour between Misoprostol Per Oral and Per Vaginal

SARA GUL[1], TABASSUM ALI[2], AMBER BASHIR[3], ASMA ALI[4], MARYAM BIBI[5], ASIA ASGHAR[6]
[1, 2] *District Gynaecologist, Obs and Gynae, District Head Quarter Teaching Hospital Swabi*
[3] *Consultant Gynaecologist, Agha Khan University Hospital Garden Karachi*
[4] *Medical Officer, Obs and Gynae, Ayub Teaching Hospital Abbottabad*
[5] *Medical Officer, Obs and Gynae, Type D Hospital Charbagh Ughi*
[6] *TMO, Gynae/Obs, Ayub Teaching Hospital Abbottabad*
Corresponding author: Tabassum Ali, Email: drtabassumali77@gmail.com, Cell: +923345088958

ABSTRACT

Introduction: Oral misoprostol as a labor inducing agent (IOL) is quickly attaining popularity under resource constraints due to its cheapness, stability at room temperature, and logistically easier administration in comparison to oxytocin and dinoprostone. We purpose to inspect the effectiveness and safety of a regimen of oral misoprostol in in the Gynae/Obs unit at Rehman Medical Institute, Peshawar Pakistan.

Material and Methods: This was Randomized Controlled Trial conducted at department of Gynecology & Obstetrics, Rehman Medical Institute, Hayatabad, Peshawar, from December, 2016 to May, 2017.In this study a total of 200 (100 in each group) patients were observed. After the drug administration, per vaginal examination was done at 4 hourly intervals to see for labor induction/pains. Data was collected by means of proforma.

Results: In this study, the mean age was 31.2 with SD ± 3.51 in group B and the mean age was 32.80 with SD ± 4.02 in Group A. Oral route (Misoprostol, 50µg) (Group A) was operative in 80% patients and was not effective in 20% patients. While Vaginal route (Misoprostol, 25µg) (Group B) was effective in 88% patients and was not effective in 12% patients.

Conclusion: The oral misoprostol IOL regimen designated in this analysis is effective, safe and logistically practicable to direct with limited resources.

Keywords: Vaginal misoprostol, oral misoprostol, induction of labour.

INTRODUCTION

Globally, labour induction is widely followed in certain conditions of pregnancy that is dangerous to fetus or to the mother. According to a report published internationally it was stated that in 2004-05, 20% of deliveries in the United Kingdom was artificially induced while WHO Global Survey stated that approximately 10% of deliveries require labour induction [(1)]. Moreover, in Africa there are lower rates of labour induction i.e., 1-3% as compared to Asian and Latin Americans with near 40% [(2)]. Labour induction at term is one of the most common interventions with indications of postdates pregnancy, pre-eclampsia, pre-labour rupture of membranes (PROM), oligohydramnios and IUGR. It requires artificial methods to initiate uterine contractions at term and is necessary in about 12-24% of deliveries. Approximately more than 17% of all pregnancies needs artificial drug at term for labour induction [(3, 4)]. Labour is induced to achieve a vaginal delivery, when there is potential risk to continue pregnancy [(5,6)]. There are so many methods present for induction like prostaglandins, oxytocin and mechanical methods etc. Misoprostol is prostaglandin E1, commonly used for labour induction and results in contractions of uterus along with cervical ripening [(7)]. It has many advantages i.e., stability at ambient temperature, less expensive and can be used through various routes i.e vaginal [(9)], oral [(8)], per-rectal and sublingual routes. Thus, misoprostol is safer and more effective than any other prostaglandins for labour induction and cervical ripening [(10)].

Comparing oral misoprostol with placebo in nine trials, it was found that oral misoprostol was more effective as compared to placebo having low rate of C-section and less neonatal complications. Comparing route of misoprostol administration in twelve trials, oral misoprostol showed lower rates of C-section with RR 0.89, at CI of 95% (0.78 - 0.99). Of 9 studies comparing oral misoprostol with I/V oxytocin it was revealed that the C-section proportion was lesser in females induced with oral misoprostol with RR 0.77 at CI of 95% (0.60 - 0.98) but showed high proportion of meconium-stained liquor. 36 trials done in comparing oral and vaginal misoprostol administration which showed that oral route had less rates of babies born with low Apgar score, lesser rates of postpartum hemorrhages and lower rates of caesarean section but had higher rates of meconium-stained liquor with RR= 1.22, at CI of 95% (1.03 - 1.44) [(11)].Being a developing country with scare availability of human, financial and logistic resources, and having high maternal morbidity and mortality it is important to recommend effective drug at term for labour induction with good safety profile for mother as well as fetus and to suggest standard evidence based medical practice. So, this randomized clinical control trial is structured to estimate and compare the effectiveness of oral misoprostol versus vaginal misoprostol at term for labour induction in the Gynae/Obs unit at Rehman Medical Institute, Peshawar Pakistan.

MATERIAL AND METHODS

This was Randomized Controlled Trial conducted at department of Gynecology & Obstetrics, Rehman Medical Institute, Hayatabad, Peshawar, December, 2016 to May, 2017.In this study a total of 194 (97 in each group) patients were observed. After the drug administration, per vaginal examination was done at 4 hourly intervals to see for labor induction/pains. The following operational definitions were used for the study protocol.

Induction of labor: It is the process of evoking uterine contractions during pregnancy before labor begins spontaneously and successful labor induction leads to vaginal delivery.

Term Pregnancy means duration of pregnancy i.e., early term: the period between 37 weeks and 37 weeks, 6 days; full term: between 38 weeks to 40 weeks and late term: 40weeks,1 day and beyond.

Effectiveness was achievement of vaginal delivery by stimulation of uterine contractions by artificial methods, before the onset of natural labour, in women with obstetrical or medical complications of pregnancy. Pregnant females (age 18-45) at term pregnancy having live singleton fetus with cephalic presentation who needs induction of labor with premature rupture of membranes, postdates pregnancy, polyhydramnios, oligohydramnios, intrauterine growth retardation fetal anomalies and mild systemic disease like DM, PIH were included. Pregnant females with severe systemic illnesses like pre-eclampsia, eclampsia, cardiac, renal or hepatic diseases, intra-uterine deaths, cephalo pelvic disproportion, mal presentation, ante partum hemorrhages and previous scar uterus were excluded to control confounders/ bias in study results. The research committee of hospital approved the study. The women admitted to the ward for induction of labour fulfilling the inclusion criteria were included. Informed written consent was taken from all participants. After the drug administration, per vaginal examination

was done at 4 and 8 hours for labor induction/pains. Data was collected by means of proforma. The procedure adopted was follows. Throughout the study the women were monitored for signs of labour initiation along with maternal vitals 1 hourly and fetal heart rate was monitored after every 30 minutes of drug administration for any signs of fetal/ maternal deterioration. A pre induction electronic non stress test for 20 minutes was performed and before the remaining 2 doses CTG was done. A maximum of 3 doses was given if required and then was labeled effective if signs of labour seen i.e., palpable regular uterine contractions, cervical dilatation and effacement leading to delivery of fetus. It was considered failed if up to 24 hours of last dose labour does not start. The next dose of misoprostol was held if cervix is suitable for amniotomy or if the patient is in active labour. In labour induced females, labour was managed according to standard ward protocol.

Treatment Group A: (Oral route) 100 Pregnant Women

One tablets of 200µg misoprostol was divided into four doses of 50µg, and was given orally and repeat after every 4 hours to 3 doses maximum for signs of labour induction.

Treatment Group B: (Vaginal route) 100 Pregnant Women

One tablet of 100µg misoprostol was divided into four doses of 25µg and was positioned in posterior vaginal fornix and repeat after every four hours to 3 doses maximum for signs of labour induction. All the information needed was recorded in a pre-designed proforma. Extreme care was taken of selection bias and responder bias. All the data was analyzed and entered in SPSS20.0. Mean ± SD was calculated for numeric variables such as age, gravidity, parity and period of gestation, number of doses given, induction to delivery and induction of labour interval. The percentages and frequency were premeditated for categorical values such as effectiveness of labour induction. Effectiveness was compared by using chi square test between both groups. Effectiveness was stratified with age, gravidity, parity, period of gestation, number of doses given, induction of delivery interval and induction of labour to see the effect modification. Post stratification chi- square test was applied by keeping p value ≤0.05 as significant.

RES ULTS

In this study, the age distribution between the two groups was analyzed as in A group; 15 (15%) patients were 18-25 years old; 65 (65%) patients were 26-35 years old and 20 (20%) patients were aged 36-45 years of age. The mean age was 31.2 with SD ± 3.51. In group B, 15 (15%) patients were 18-25 years old, 66 (68%) 26-30 years old, and 16 (17%) 31-35 years old. The mean age was 32.80 with SD ± 4.02. (As shown in table 1)

Table 1: shows the age distribution of the patients

Age Distribution	Group A	Group B
18-25 Years	15(15%)	18(18%)
26-35 Years	65(65%)	68(68%)
36-45 Years	20(20%)	14(14%)
Total	100(100%)	100(100%)
Mean and SD	31.2±3.51	32.80±4.02

Gravida among two groups was analyzed as in Group A 36(36%) patients were primigravida, 64(64%) patients were multigravida. In Group B 42(42%) patients were primigravida, 58(58%) patients were multi para. (As shown in table no 2)

Table 2: shows the gravida details of the patients

Gravida	Group A(n=100)	Group B(n=100)
Multigravida	64(64%)	58(58%)
Primigravida	36(36%)	42(42%)
Total	100(100%)	100(100%)
P- value	0.81	

Parity among two groups was analyzed as in Group A 48(48%) patients were primipara, 52(52%) patients were multipara. In Group B 46(46%) patients were primipara, 54(54%) patients were multipara. (As shown in table no 3)

Table 3: shows the parity of the patients

Parity	Group A(n=100)	Group B(n=100)
Primipara	48(48%)	46(46%)
Multipara	52(52%)	54(54%)
Total	100(100%)	100(100%)
P- value	0.81	

Period of gestation among two groups was analyzed as in Group A 83(83%) patients had POG <41 weeks, 17(17%) patients had > 41 weeks. In Group B 75(75%) patients had POG <41 weeks, 25(25%) patients had > 41 weeks. (As shown in table no 4)

Table 4: shows the gestation period of the patients

Gestation Period	Group A(n=100)	Group B(n=100)
< 41 weeks	83(83%)	75(75%)
=41 weeks	17(17%)	25(25%)
Total	100(100%)	100(100%)
Mean and SD	41.21±3.12	39.87±4.02
P-value	0.21	

Indication among two groups was analyzed as in Group A 42(42%) patients had postdates, 16(16%) patients had PROM, 8(8%) patients had Diabetes mellitus, 10(10%) patients had Oligohydramnios, 15(15%) patients had Fetal anomalies and Preeclampsia in 19(19%) of the patients. In Group B 33(33%) patients had postdates, 16(16%) patients had PROM, 9(9%) patients had Diabetes mellitus, 16(16%) patients had Oligohydramnios, 10(10%) patient had fetal anomalies. (As shown in table no 5)

Table 5: shows the indication of labour

Indication	Group A(n=100)	Group B(n=100)
Post-dates	42(42%)	33(33%)
Prom	16(16%)	15(15%)
Preeclampsia/ PIH	19(19%)	18(18%)
Oligoydraminos	10(10%)	16(16%)
Diabetes mellitus	8(8%)	9(9%)
Fetal Anomalies	15(15%)	10(10%)
Total	100(100%)	100(100%)
P-value	0.97	

Delivery interval among two groups was analyzed as in Group A 68(68%) patients had delivery interval <12 hours, 32(32%) patients had delivery interval >12 hours. In Group B 55(55%) patients had delivery interval <12 hours, 45(45%) patients had delivery interval >12 hours. (As shown in table no 6)

Total no of doses given among two groups was analyzed as in Group A 93(93%) patients had 1-3 doses while 7(7%) patients had 4-5 doses. In Group B 88(88%) patients had 1-3 doses while 12(12%) patients had 4-5 doses.

Oral route (Misoprostol, 50µg) (Group A) was operative in 80% patients and was not effective in 20% patients. While Vaginal route (Misoprostol, 25µg) (Group B) was effective in 88% patients and was not effective in 12% patients.

Table 6: shows the delivery interval

Delivery Interval	Group A(n=100)	Group B(n=100)
=12 hrs	68(68%)	55(55%)
> 12 hrs	32(32%)	45(45%)
Total	100(100%)	100(100%)
Mean and SD	19 ±2.64	23± 3.96
P-value	0.0001	

DISCUSSION

Globally, labour induction is widely followed in certain conditions of pregnancy that is dangerous to fetus or to the mother[12-13].

According to a report published internationally it was stated that in 2004-05, 20% of deliveries in the United Kingdom was artificially induced while WHO Global Survey stated that approximately 10% of deliveries require labour induction [(1)]. Moreover, in Africa there are lower rates of labour induction i.e., 1-3% as compared to Asian and Latin Americans with near 40% [(2)]. In this study, the mean age was 31.2 with SD ± 3.51 in group B and the mean age was 32.80 with SD ± 4.02 in Group A. Oral route (Misoprostol, 50µg) (Group A) was operative in 80% patients and was not effective in 20% patients. While Vaginal route (Misoprostol, 25µg) (Group B) was effective in 88% patients and was not effective in 12% patients. When comparing the route of administration of misoprostol in twelve studies, oral misoprostol showed lower rates of caesarean section with a 95% CI (0.78 to 0.99) and a RR of 0.88. Of the nine studies comparing oral misoprostol to oxytocin, I / V, women induced with oral misoprostol with a 95% CI (0.60 to 0.98) and a RR of 0.77 had a lower frequency of cesarean sections but showed a higher percentage of meconium-colored fluids[14-15]. Thirty-six studies comparing oral and vaginal misoprostol administration showed that oral and vaginal misoprostol administration showed that oral administration had a lower Apgar birth rate, lower postpartum hemorrhage rate, and lower cesarean section but higher meconium colored fluid. RR = 1.22, with a 95% CI (1.03-1.44) (11). A comparable opinion was stated in alternative analysis by Jindal P et al where the labor interval was significantly shorter (16.47 hours vs.9.79) in the group receiving vaginal misoprostol induction, and effective induction was significantly longer (90.38 vs.9.79). 74.51%) group, within 24hour of induction. Regarding the dose required, 40.38% of the females in the vaginal group needed 2 doses for delivery and 36.2% of the oral group required all-out of six doses[16-17]. Shetty et al reported fewer failures at 50 µg vaginal compared to oral misoprostol (2.5 vs 6.77%, RR 2.8, 95% CI 0.8-10.0), and also found a shorter interval between induction of administration, 10.1 hours[18-19]. Even Latika et al detected a 100% achievement percentage with 50 mcg of vaginal misoprostol and 100 mcg of oral misoprostol. Total no of doses given among two groups was analyzed as in Group A 93(93%) patients had 1-3 doses while 7(7%) patients had 4-5 doses. In Group B 88(88%) patients had 1-3 doses while 12(12%) patients had 4-5 doses[20-21]. In our study, the interval between labor induction was shorter and amounted to 5.30 hours at 50 µg vaginal misoprostol (17.20 hours vs. 10.21 hours, RR 0.79, 95% CI, 0.27–1.31). When 50 µg vaginal misoprostol was compared to the oxytocin, the effective induction was 91.20% compared with 77.21% in the vaginal misoprostol group, and the induction-delivery interval was shorter at 7.87 hours. Compared to the oral route, it is longer, causes faster progress of labor and causes more women to give birth within 24 hours of giving birth (70.1% vs 55.8%). The incidence of uterine contraction disorders following the vaginal administration of 50 µg misoprostol was reported as 5.1%, 9.6%, 13% and 25.80%. At 100 and 50 µg oral misoprostol, the incidence of uterine hyperstimulation was 0.9% and 6.5%, respectively. Oxytocin, which is measured safer than misoprostol, also has a 19.2% incidence rate of uterine abnormalities. In addition, PGE2 has fewer complications than misoprostol[22-23].

CONCLUSION

The oral misoprostol IOL regimen designated in this analysis is effective, safe and logistically practicable to direct with limited resources.

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