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COMPARISON OF ORAL VS VAGINAL MISOPROSTOL IN INDUCTION OF LABOR AT TERM

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KEYWORDS :

INTRODUCTION

Labour is a dynamic process that expel products of conception at or near term. It is well co-ordinated series of physiological events and it is the most integrated neuro endocrine mechanism resulting in successful child birth.

Induction of labour is a deliberate attempt at initiation of uterine contractions before spontaneous onset of labour by surgical or medical means, leading to progressive dilatation and effacement of cervix, then birth of the baby. Of the various modalities prostaglandins are the most popular means of labour induction.

Prostaglandins have been found to have powerful excitatory effect on the myometrium and are involved in the initiation co-oridination and maintenance of cervical ripening and myometrial activity.

If the cervix is unripe (closed, uneffaced, firm, posterior) . Bishop cervical score less than six , then the conventional method of induction of labour by surgical amniotomy is technically difficult and titration with intravenous oxytocin results in prolonged labour with risks of maternal and foetal complications and unsuccessful inductions unnecessarily increasing the rates of cesarean section.

MISOPROSTOL:

Misoprostol, a synthetic methyl ester of PGE_1 originally developed as gastric cytoprotector agent, is an effective myometrial stimulant selectively bind to EP-3 prostanoid receptor.

Intravaginal and oral administration of misoprostol have been studied to effect cervical ripening and induction of labour.Vaginal Misoprostol for induction of labour few studies done all over the world.This study is taken up to see its efficacy orally and compare with vaginal misoprostol

Windrim and associates [1] (1997) reported that orally administered misoprostol was of similar efficacy for cervical ripening and labour induction as intravaginal administration.

Bennet & colleagues[2] (1998)Toppozoda[3] and co workers(1997) found shorter interval to delivery with vaginal application but more frequent foetal heart rate abnormalities.

Adair and colleagues[4] (1998) concluded oral and vaginal applications were of smilar efficacy but that an oral dosage of 200 mcg was associated with more frequent abnormal uterine contractility.

Even though misoprostol has been established as a choice of drug for induction of labour the ideal route, dose and frequency of administration are under investigation.This study aims to compare the safety and efficacy of oral application of misoprostol with vaginal application for cervical ripening and induction of labour

AIMS AND OBJECTIVES

To compare the efficacy of misoprostol in oral and vaginal routes and assess the following parameters in both the routes.

- Induction to delivery interval
- Number of doses required
- Need of oxytocin augmentation
- Mode of delivery
- Maternal outcome
- Fetal outcome

Pharmacokinetics of Oral and Vaginal Misoprostol

Misoprostol is primarily metabolized in the liver, with less than one percent of its active metabolite excreted in urine. Misoprostol has no known drug interactions and does not induce the hepatic cytochrome P-450 enzyme system. The most common adverse effects of misoprostol are nausea, vomiting, diarrhea, abdominal pain, chills, shivering and fever, all of which are dose dependent. Toxic doses of misoprostol have not been determined.

Misoprostol used, in this study is a synthetic analogue of natural PGE1.

It undergoes rapid deesterification to its free acid,misoprostol acid which is responsible for its clinical activity. Misoprostol is extensively and rapidly absorbed orally and vaginally.

Peak plama, level is reached after 30-60 minutes, Oral route of administration achieves earlier peak plasma concentration compared with vaginal administration. Vaginal administration caused longer lasting action. So frequent dosing interval is needed for oral group.

WHICH DOSE SHOULD BE USED?

Multiple dosing regimens have been reported in the literature.

On the basis of our accumulated experience of misoprostol remain concerned about the potent uterotonic effects of misoprostol and advise a careful approach to its use. Our current recommendations are that a dose of 25 ug can be used with similar effectiveness and greater safety than higher dose regimens. The 50 ug dose results in significantly increased tachysytole meconium passage and meconium aspiration compared with prostaglandinE2 (Farah and Colleagues[5] 1997; wing and co-workers[6,7,8,9] 1995a and 1995b). There is also increased incidence of caesarean dlivery due to uterine hyperstimulation when compared with dinoprostone (Buser and Collaborators in 1997).[10]

The 25 ug dose every 4 hrs, was associated with significantly fewer adverse effects than 50 ug dose.

Table No.1: Reported treatment regimens for labour induction

Sl. No.	Study	Year	Dosage
1	Kelly Bennett et al[2]	1998	50µ g oral Vs 50 µg Vaginal 4th hourly
2	How et al [11]	2001	25µ g Oral Vs 25 µg Vaginal 4th hourly
3	Abbasi et al [12]	2004	50 µg Oral Vs 50 µg Vaginal 6th hourly
4	Syed et al [13]	2006	100 µg Oral Vs 50 µg Oral 4th hourly
5	Akter .S et al [14]	2007	50 µg Oral Vs 50
6	Sreelatha et al [15]	2012	25µ g Oral Vs 25
7	Mamta Mahajan et al	2012	25 µg Oral Vs 25

8	Pavithra N et al [17]	2012	25µg Oral Vs 25 µg Vaginal 4th hourly
9	Komala et al [18]	2013	50µg Oval Vs 25 µg Vaginal 4th hourly
10	Kavitha Reddy et al[19]	2014	25 µg Vaginally 4th hourly

PATIENTS AND METHODS

SUBJECTS:

The present study comparative study of oral vs vaginal misoprostol for induction of labour at term is a clinical prospective study involving 100 antenatal Women Primi and Multi Gravid (not grand multi) selected for definite indication for induction are taken for the study with following patient selection criteria who were admitted in the department of obstetrics and gynaecology labour room, Kurnool medical college, Kurnool from Jan 2018 to June 2018.

Age more than 18yrs , singleton pregnancy and those who have completed 37 weeks of pregnancy, Vertex presentation, clinically adequate pelvis, Bishop cervical score less than 6,with following indications.

INCLUSION CRITERIA:

1.Prolonged pregnancy
2.Preeclampsia
3.Premature rupture of membranes.

EXCLUSION CRITERIA:

1. Contracted pelvis and cephalopelvic disproportion.
2. Persistent Malpresentation
3. Undiagnosed bleeding per vagina
4. Placenta praevia and abruptio placenta.

5. Multiple pregnancy
6. Pregnancy with previous caesarian section/uterine scar
7. Elderly primigravida specially associated with complicating factors (Obstetric and Medical).
8. Intra uterine foetal death
9. High risk pregnancy with compromised foetus/non reassuring foetal heart rate pattern
10. Pelvic tumor.
11. Hyper sensitivity to prostaglandins

MATERIALS:

Misoprostol tablets. (25 mcg)

PROCEDURE/MANAGEMENT:

Those who were selected for induction of labour were admitted, detailed history taken, physical examination done, investigations done, foetal maturity estimated by clinical dates, clinical examination, ultra sound examination, Obstetric Palpation done, (height of uterus, size, wellbeing of foetus estimated by clinical examination and

confirmed by ultrasound examination.Internal examination done. Pelvis assessment done cephalo pelvic disproportion excluded.

Preinduction cervical scoring done by bishops scoring system as follows:

Table No.2: Bishop's Score

Score	Dilatation(cm)	Effacement (%)	Station	Cervical consistency	Cervical position
0	Closed	0-30	-3	Frim	Posterior
1	1-2	40- 50	-2	Medium	Midposition
2	3-4	60-70	-1.0	Soft	Anterior
3	≥5	≥80	+1,+2	----	---
Total score:	0-5 unfavourable				
	6-13 favourable				

THE PATIENTS WERE STUDIED IN TWO GROUPS:

Group-I:

25 micro grams given orally fourth hourly till the active phase of labour begins or upto 24 hours

Group_II

Misoprostol (PG E1) 25 mcg wet with normal saline and kept in

posterior fornix of vagina and to be continued 4th hourly till the active phase of labour begins or upto 24 hours.

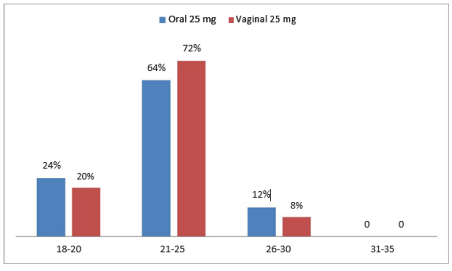
Cervical changes assessed after 4 hours in both the groups.

Intrapartum management done by monitoring foetal heart rate variabilities, uterine action every one hour, progress of labour noted every 4 hours regularly.Surgical amniotomy done and oxytocin may be started according to necessity.

Inducton- onset of active labour, induction delivery interval noted in both groups and compared.Type of delivery like normal vaginal delivery, instrumental delivery, and caesarian section noted. Neonatal outcome noted with APGAR score at 1 min, and APGAR score at 5 min. In both groups and compared.

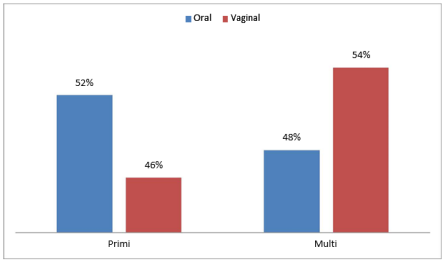
OBSERVATIONS & RESULTS

Graph No.1: The Bar Diagram showing Age Distribution



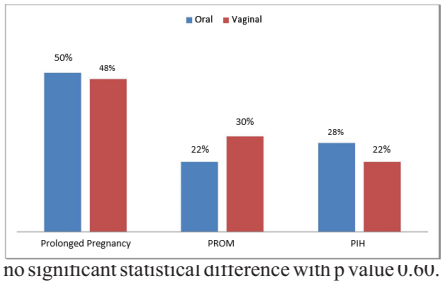
There is no significant difference in the distribution of cases depending on age.

Graph No. 2 : Gravidity based distribution of cases



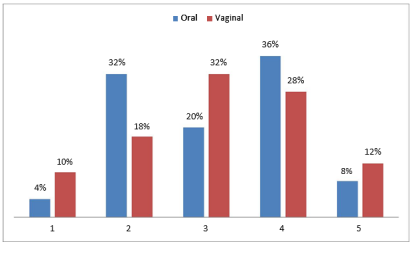
There is no significant difference in distribution of cases with p value 0.54

Graph No.3: Bar Diagram showing indication for induction.



There is no significant statistical difference with p value 0.60.

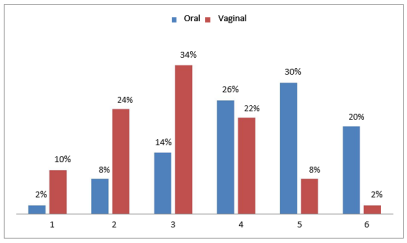
Graph No.4 : Bar diagram showing Bishop Score



The pre induction bishop score was similar and comparable among the

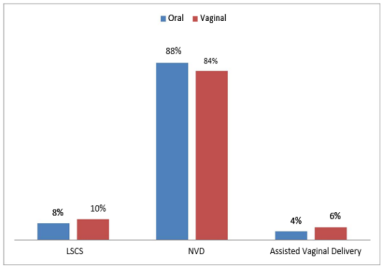
cases in group A and group B, and no significant difference statistically with p value 0.23.

Graph No.5: Bar Diagram shows Number of doses of Misoprostol



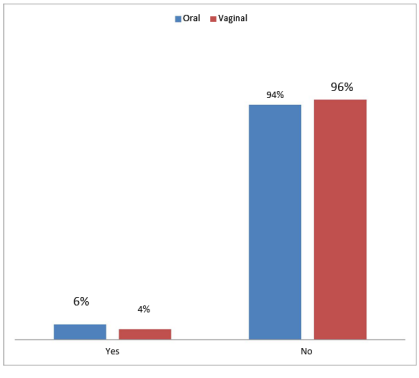
No of doses required among the cases in group A and group B having significant difference as more number of doses required in oral group than in vaginal group which is statistically significant with p value 0.012. The mean number of doses 4.34±1.28 in oral group, 3.06±1.15 in vaginal group.

Graph No.6: Bar diagram showing Mode of Delivery



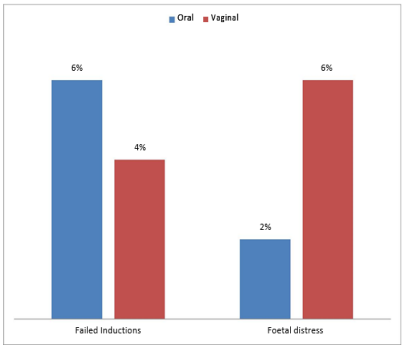
There is no significant difference between oral and vaginal group depending on mode of delivery with p value 0.83.

Graph No.7: Failed Induction



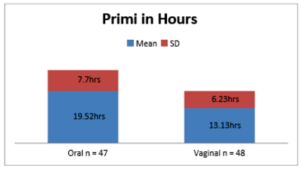
There is no significant difference statistically in between oral and vaginal group with p value 0.64.

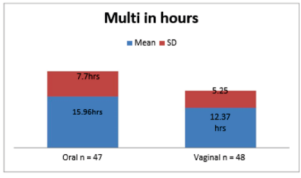
Graph No.8: LSCS Rate



The LSCS rate between oral and vaginal group 6% are due to failed inductions and 2% are due to foetal distress in oral group and 4% due to failed inductions and6% due to foetal distress in vaginal group,which is statistically not significant with p value 0.29.

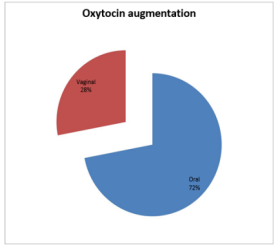
Graph No.9: IDI (MEAN)





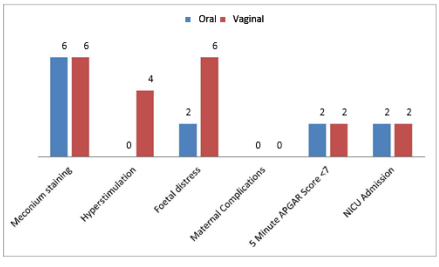
There is less significant difference of Mean induction- delivery interval in oral and vaginal groups with p value0.02

Graph No.10: Need of Oxytocin augmentation



Need of oxytocin augmentation was more in oral group (72%),than in vaginal group(28%),which is statistically significant with p value0.013

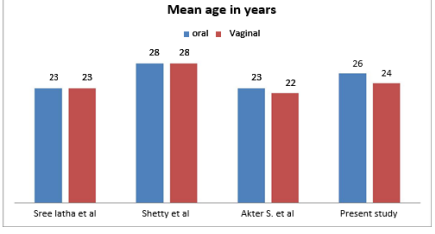
Graph No.11: Maternal and Fetal out come



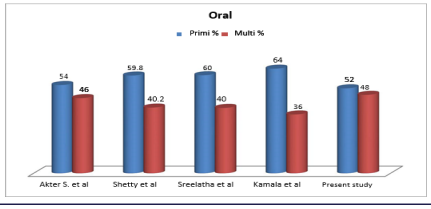
The incidence of meconium staining was similar in both groups. Hyper stimulation was observed in Vaginal group. Foetal distress was more in Vaginal group. Maternal complications were nil in both groups. Foetal outcome with respect to APGAR Score < 7 at 5 min & NICU admission were similar in both the groups.

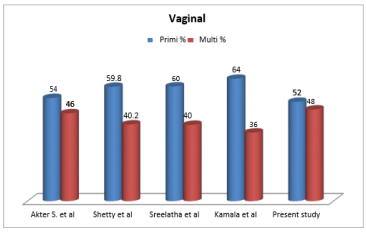
DISCUSSION

Graph No.12: Comparison of Age distribution with other studies

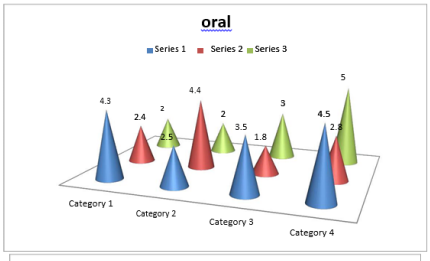


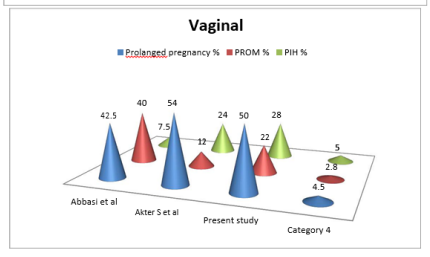
Graph No.13: Comparision depending on Gravidity based distribution with other studies





Graph No.14: Comparision depending on indication for inductions with other studies





In the present study, distribution of cases depending upon indication for induction of Labour were similar and comparable in both the groups with Post dated Pregnancy being the most common indication.It is comparable with the above studies.

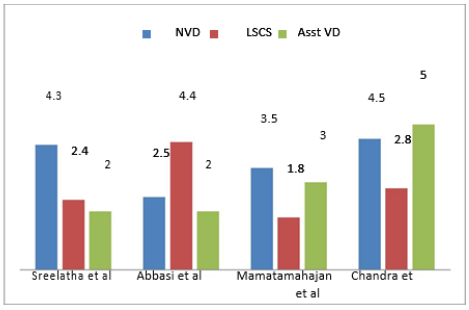
Comparison of No. of doses required with other studies

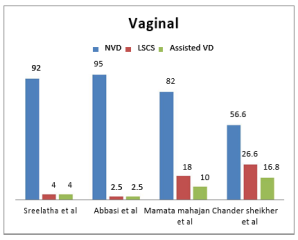
S.No.	Study	Mean no. of doses	
		Oral	Vaginal
1	Shaheen et al	2.21	1.39
2	Present study	4.34±1.28	3.06±1.15

When comparing the number of doses of misoprostol necessary to induce labour in women who were given oral required more number of doses which is statistically significant. The mean no of doses 4.34±1.28 in oral group,3.06± 1.15 in vaginal group. This is slightly significant with p=0.012.

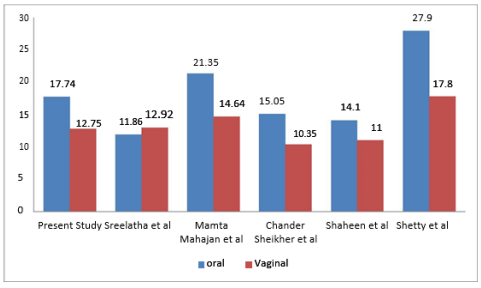
This is attributed to pharmacokinetics of misoprostol which is different for each route.Although the bioavailability of vaginal misoprostol is greater, the peak plasma concentration attained by oral misoprostol is higher than the peak attained by vaginal route.Also misoprostol is rapidly absorbed orally with the time for onset of action being shorter for oral route(8mins) compared to vaginal route(20mins)There is also a great variation in bioavailability between women with vaginal administration.

Graph No.15 : Comparision by mode of delivery with other studies



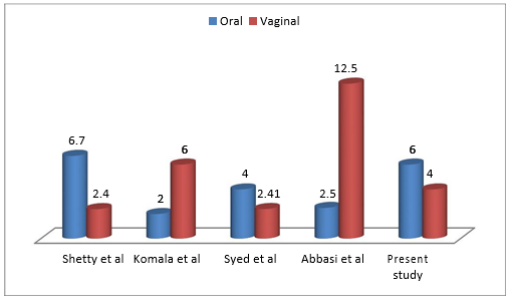


Graph No.16: Comparision of IDI Table with other studies



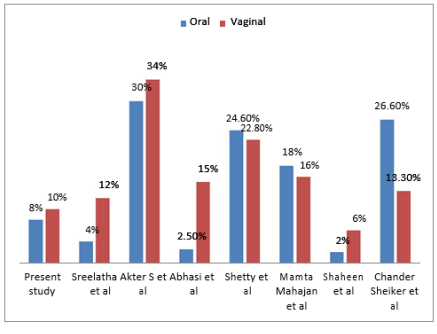
In the Present study,the mean Induction delivery Interval is 17.74±7.7 hrs in Oral group and 12.75±5.74 hrs in Vaginal group and there is slightly significant difference in between the two groups with P value 0.02 attributed to

Graph No.17: Comparision by failed induction with other studies

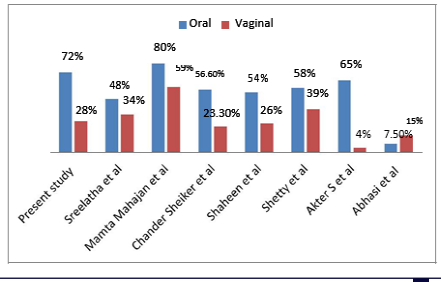


In the Present study, 6% of cases in Oral and 4% of case in Vaginal group were Failed to have significant cervical changes after 24 hrs of Induction and it is comparable with the studies above.

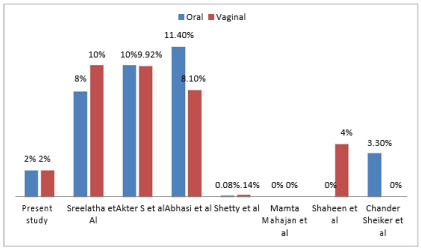
Graph No.18: Comparison of Caesarean Section Rate with other studies



Graph No.19: Comparision of need of oxytocin Augmentation



Graph No.20: Comparision of APGAR <7 at 5 minutes



In the Present study, APGAR <7 at 5minutes were 2% in both Oral and Vaginal group and it is comparable with the above studies.There is no significant difference in the Foetal Outcome between two groups.

Meconium staining of liquor was seen similar in both oral and vaginal group with 6% Inspite of increase in abnormal fetal heart rate pattern there was no significant adverse neornatal outcome in both the groups.

CONCLUSIONS

- Misoprostol effectively induces labour in vaginal route resulting inshorter induction delivery interval and fewer doses per patient.
- Contractile abnormalities, Intervention rate for fetal distress andmaternal complications were less in the oral group, could mean that the preferred route might be oral.
- Oral misoprostol 25µg is as effective as vaginal misoprostol 25 µg. But need of oxytocin augmentation is more in oral group.
- Lower is the parity, higher is the induction delivery interval.
- Lesser is the Bishop score, higher is the induction delivery interval
- Higher is the dose of misoprostol, higher is the hyper stimulation syndrome.
- Maternal and foetal outcome comparable between both groups.
- Misoprostol compared to other methods of induction of labour has good safety profile with predictable side effects, low cost, long shelf life, no need of refrigeration and availability world wide.

SUMMARY

In the present study two routes of administration of misoprostol (oral vs vaginal) for induction of labour in term pregnancy were compared with respect to safety, efficacy, maternal and foetal out come.Divided in two groups.

- Group A: 50 women for oral administration of 25 mcg of misoprostol every fourth hourly for 24 hours or till the active phase of labour
- Group B:50 women for vaginal administration of 25mcg of misoprostol

every fourth hourly for 24 hours or till the active phase of labour

1. The maternal characteristic of two series of patients were similar with respect to mean age, gravidity and preinduction Bishop score
2. Number of doses required by the oral group was more when compared with vaginal group (p=0.012)
3. Post dated pregnancy was the most common indicaton for induction of labour in both groups with 50% in oral and 48% in vaginal group.
4. More number of doses required in oral than in vaginal group.
5. Induction delivery interval was relatively prolonged in the oral group (p=0.02) mean, standard deviation for oral and vaginal group was17.74±7.7 and 12.75±5.74 hours respectively, thus inference as 25mcg dose orally as effective as 25 mcg vaginal dose with timely needed oxytocin augmentation.
6. Failed induction was more in the oral group series (p=0.29) implies that there is no significant difference between the two groups.
7. Percentage of vaginal delivery was similar in both the series(p=0.83)implies that there is no significant difference between the two groups
8. More cases of tachysystole were noted in the vaginal group.
9. Abnormal fetal heart rate pattern in the oral and vaginal group were 2% and6% respectively which was not statistically significant.
10. Neonatal outcome comparable between both the groups and no adverse outcome was seen
11. No maternal complications were seen in both groups.

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