Basrah Journal Of Surgery

Bas J Surg, March, 17, 2011

EXTRA-AMNIOTIC SALINE VERSUS EXTRA-AMNIOTIC MISOPROSTOL FOR RIPENING THE UNFAVORABLE CERVIX

Ali F Al-Assadi
FICOG, CABOG. Assist. Prof., Dept. of obstetrics & gynecology, Basrah Medical College.

Abstract

This study aimed to compare the efficacy of two methods (extra-amniotic saline instillation and extra-amniotic misoprostol) for ripening the unfavorable cervix.

The study was set at the labour room in Basrah Maternity (teaching) hospital with 300 bed capacity.

It is a prospective comparative study conducted to compare extra-amniotic saline instillation and extra-amniotic Misoprostol for ripening the unfavorable cervix.

Group I (Extra-amniotic saline instillation): Foley's catheter with extra-amniotic normal saline instillation at a rate of 1ml/min.

Group II (extra-amniotic Misoprostol): The cervix was ripped with 25mcg. Misoprostol injected extra-amniotically using a Foley's catheter.

The clinical trial involved a total (121) pregnant women, in group I (57) and in group II (64). The success rates in achieving cervical ripening were 100% for both groups. The mean post ripening Bishop's score in group II (primigravidae (7.5 ± 1.5), multigravidae (7.86 ± 1.39)) were significantly higher than those in group I (primigravidae (6.01±0.4), multigravidae (6.07± 0.47)). The mean ripening time (hrs) in group II (primigravidae (6.15± 2.1), multigravidae (4.03± 1.3)) were significantly shorter than those in group I (primigravidae (7.71± 1.02), multigravidae (6.4± 1.02)). The mean induction-delivery time (hrs) in group II (primigravidae (5.3± 2), multigravidae (3.8± 1.4)) were significantly shorter than those in group I (primigravidae (7,7± 2.03), multigravidae (5.92± 1.9)). The vast majority of women under study had vaginal delivery (80.7% in group I and 96.8% in group II).

In conclusion, EAM was quick and effective method for ripening the cervix, it requires little training for application so that it is a suitable method for patients who require rapid induction of labour.

Introduction

The active approach taken to the management of maternal and fetal problems in modern obstetrics has increased the frequency of induction of labour[1]. Induction of labour in cases with unripe cervix frequently associated with maternal complications and induction failure[1].

The cervical effacement is an essential pre-requisite to its dilatation and one which depend on the softening and ripening of its connective tissue[2].

It is a process by which the cervix undergoes a series of biochemical and physical changes at the end of pregnancy that are manifested as softening, shortening and opening of the cervix[3].

The process of cervical ripening can begin as early as 24 weeks gestation and the time of spontaneous labor has some relation to these changes. There is considerable individual variation in ripening of cervix and about 5 %of patient will reach 42 weeks gestation without such changes having occurred[4].

Pharmaco-dynamic of Misoprostol: Misoprostol is a synthetic PGE1 analogue[5]. Absorption is fast in all routes

of administration, when given vaginally or sublingually takes longer than oral route to start working and has a lower serum level (peak concentration after 60 min) but more sustained effect[5]. Plasma elimination half life is reported to be between 20-30 min.[6] vaginal bleeding and loss of amniotic fluid may have negative effect on absorption through the vagina[5]. Their efficacy depend on the number of PG receptors in the uterus which varies according to whether the women are pregnant or not and what stage of pregnancy she is[5].

Misoprostol is administered sublingually, orally, vaginally & rectally[5].

Dosage of Misoprostol: PG is well established for induction of labour[6]. Using misoprostol tablet, doses employed have been 50µg orally every 4 hour until delivery or 25µg vaginally every 4 hour according to the patient response until delivery[7].

Side effects of misoprostol: Adverse effects include Diarrhea, Abdominal pain, dyspepsia, flatulence, nausea and vomiting[8], uterine hyperstimulation, meconium stained liquor, PG crosses the placenta to stimulate fetal bowel smooth muscle and cause meconium passage, Precipitate delivery labour of less than 2 hour has been described as a complication of misoprostol, rupture of unscarred uterus, increase caesarean section rate & postpartum hemorrhage[3].

This study aims at comparing the efficacy of two different methods (Foley's catheter with extra-amniotic saline installation & Foley's catheter with extra-amniotic Misoprostol) for the ripening of the unfavourable cervix.

Patients & methods

This is a prospective comparative study which was conducted in Basrah maternity & children hospital during the period from March 2008 to June 2009.

A total of 121 pregnant women (primigravidae & multigravidae (para 1-4)) were included in this study; they were admitted to the labour ward in Basrah maternity & children hospital with an indication for induction of labour.

The inclusion criteria were gestational age 28-42 week, unfavorable cervix (Bishop score <6), singleton pregnancy, vertex presentation & intact membrane.

The exclusion criteria were known previous uterine surgery (myomectomy, caesarean section & post conization), multiple gestation, abnormal lie & presentation, uterine anomalies, placenta previa, documented episode of mid-trimester or 3rd trimester bleeding & grandmultiparity ≥ 5.

Indications for induction of labour were: prolong gestation ≥42 week and hypertensive disorders. Induction of labour was done at term unless added complication necessitated earlier intervention, Intra-uterine growth restriction, Intrauterine death, diabetic patients with indications for induction.

After obtaining their consent women under study were randomly divided into two groups:

Group I (Foley's catheter with extra-amniotic saline infusion) (EASI):

This control group consisted of 57 patients, those patients were admitted in the morning, under aseptic conditions and with the patients in lithotomy position, the cervical os was exposed with a Sims speculum and a Foley's catheter (22 F.G) was inserted into the extra amniotic space, the balloon was inflated with 50 ml of sterile normal saline, then the catheter was pulled down so that the balloon was applied against the cervical internal os. Normal saline solution was instilled into the extra amniotic space at a constant rate of 1 ml/minute until the catheter fall out of the cervix, gentle traction of the catheter was performed to watch for expulsion of the balloon & assessment of cervical dilatation & effacement was done every 2 hours by same examiner.

After spontaneous expulsion of the catheter, amniotomy was performed if applicable and intravenous oxytocin was

given with increment every 30 minutes until labor was established.

The dose to achieve this being 2-4 unites in 500 ml of 5% dextrose water, the infusion rate was set between 15-60 drops/minute.

Antibiotics were given to the patients to reduce the risk of infection. The patients were followed up for the common complications of balloon application like nausea, vomiting, uterine hyper tonus and febrile morbidity during their hospital stay. Neonatal outcome was assessed by pediatrician using Apgar score.

Group II (Extra-amniotic Misoprostol) (EAM):

This group consisted of 64 patients, those patients were admitted to the hospital at morning and preparation of Misoprostol solution was done under aseptic technique as follow: Misoprostol (Cytotec) 200µg tablet was divided into 2 equal parts in an attempt to obtain 2 pieces each of them containing 100µg which was then dissolved in 8cc normal saline (as it was advice by the pharmacist) and the solution shacked until it become homogenous containing 100µg.

This solution divided into 4 portions each of them containing 2 cc (25µg), under aseptic technique in dorsal position with a pillow under the left hip joint, a 14 French gauge Foley's catheter was inserted into the extra amniotic space and 2cc misoprostol solution (25µg) was injected through the catheter into the extra amniotic space, followed by injection of 4 cc of normal saline to wash any remnant of misoprostol solution inside the catheter.

The patient was advised to remain in left lateral position, monitoring was done every 2 hours to assess the response as in group I. Further management was as in the first group.

Data were analyzed using (t- test) test and the differences were considered to be significant only if P value is <0.05.

Results

Analysis of data revealed that the total number of the women in group I was 57, 35 of them were primigravidae and 22 were multigravidae and in group II was 64, 31 of them were primigravidae and 33 were multigravidae.

Table I, shows the patient characteristics; there were no statistically significant differences regarding the mean gestational age and the mean initial Bishop scores between the two groups in both primigravidae and multiparae.

Table II, shows the indications for induction of labour prolong pregnancy was the most frequent indication in all groups followed by hypertensive disorders, other indications were less frequent.

Table III, shows the Bishops scores and the ripening and induction-delivery times; the mean post-ripening scores were significantly higher in group II compare to group I in both primigravidae and multiparae. Method II required a significantly shorter time than method I to achieve cervical ripening in both primigravidae and multiparae. Primigravidae and multiparae in group II had significantly shorter induction to delivery times.

Both methods were successful in achieving cervical ripening in all cases (100% success rate).

The majority of cases in all groups had vaginal delivery with one primigravida (2.8%) in group-I had vantouos delivery. Caesarean section rates were higher in group I (primigravidae and multiparae) than in group-II. In group-I, 4 cases had caesarean section for failure to progress in cervical dilatation after successful cervical ripening and 6 cases for fetal distress. In group II, one case had caesarean section for failure of descent of the head and one for fetal distress.

In all cases in both groups the placenta was delivered normally with no immediate postpartum complication (post partum bleeding or maternal pyrexia & in

both groups there was no uterine hyper stimulation).

Table V, shows the neonatal outcome, all neonates were active immediately after delivery with a mean Apgar score at 5 minutes equal to 8.5 and above. All neonates had a body weight equal to 3 kg and above.

Discussion

Misoprostol has been used widely in obstetrical and gynecological practice because of it's' effectiveness, low cost, stability in light and hot climate condition and the ease of administration[9].

In this study we found that both EASI and EAM were 100% successful in achieving cervical ripening and this finding is similar to that reported by Al-Dahhan & Al-Assadi[10] and Al-Assadi et al[11] studies respectively.

The mean post-ripening Bishops scores in EASI group (6.01 in primigravidae and 6.07 in multigravidae) is approximate those reported by Al-Assadi et al[12] (6.15 in primigravidae and 6.27 in multigaravidae).

The mean post-ripening Bishops score in EAM group (7.5 in primigravidae and 7.86 in multigravidae) are approximate those reported by Al-Assadi et al[11] (7.77 in primigravidae and 8.06 in multigravidae).

In this study the mean post-ripening Bishops scores in EAM group were significantly higher than those in EASI group.

The mean ripening time in EASI group (7.7 hrs in primigravidae and 6.4 hrs in multiparae close to those reported by Al-Assadi et al[12] (7.54 in primigravidae and 6.33 in multigravidae). The mean ripening time in the EAM group is (6.15 hr.s in primigravidae and 4.03 hr.s in multigravidae) and these are also close to those reported by Al-Assadi et al[11] (6.05 hr.s in primigravidae and 3.97 hrs in multigravidae). This study shows that EAM requires a shorter time to achieve a higher post-ripening score than EASI in both primigravidae and multiparae and the differences were statistically significant and this could be due to the fact that Misoprostol was applied directly to the site of action while EASI act indirectly by stimulating the release of natural PG.

The mean induction-delivery times in EASI group (7.7 hrs in primigravidae and 5.92 hrs in multigravidae) were approximate those reported by Al-Assadi et al[12] (7.9 hrs in primigravidae and 6.19 hr.e in multiparae) and for EAM group were (5.3 hr.s in primigravidae and 3.8 hrs in multigravidae) which also approximate those reported by Al-Assdi et al[11] (5.8 hr.s in primigravidae and 3.7 hrs in multigravidae).

The similarity between the findings of these studies could be due to the same site and patient population under study.

The majority of patients in this study had vaginal delivery (86.3% and above) a finding similar to that reported by above two studies[11,12] except that the caesarean section rate was less in the EASI compared to that reported by Al-Assadi et al[12].

Unlike the finding of Al-Assadi et al[12] (7 cases in the EASI group developed primary postpartum hemorrhage) there was no maternal complication reported in this study. This study confirm the finding of Al-Assadi et al[11] that the use of 25 mcgm. EAM didn't cause uterine hypertonus.

As with the findings of the other 2 studies[11,12] we reported no neonatal complications.

After reviewing the above points EAM requires a significantly shorter time to achieve a higher postripening score than EASI, there was no need for continuous saline infusion as in the EASI and for that reason patients in EAM group can leave the bed after drug administration.

In conclusion; EAM was quick and effective method for ripening the cervix, it requires little training for application so that it is a suitable method for patients who require rapid induction of labour.

Table I: Patient characteristic

parameter	EASI (n=57)		EAM (n=64)	
	Primigravidae	Multigravidae	Primigravidae	Multigravidae
No.(%)	35 (61.4%)	22 (38.6%)	31(48.4%)	33 (51.5%)
Mean patient age ± SD	22±3.9	33±3	24±3.9	28±4
Mean* gestational age ± SD	39±1.5	40.2±1.3	38.5±2.2	39.2±2.5
Mean¤initial Bishop score ±SD	1.2±1.02	1.7±0.8	0.9±1.3	1.5±1.2

*t-test was used for analysis, the P- values for the mean gestational age in primigravidae groups is (0.28) and in multigravidae groups is (0.09).

¤ t-test was used for analysis, P-values for the mean initial Bishop scores in primigravidae groups is (0.29) and in multigravidae groups is (0.49).

Table II: Indications for induction of labour

Indication	EASI (n=57)		EAM (n=64)	
	Primigravidae (n=35)	Multigravidae (n=22)	Primigravidae (n=31)	Multigravidae (n=33)
Prolong pregnancy	14 (40%)	8 (36.3%)	15(48%)	14 (42.4%)
Hypertensive disorder	8 (22.8%)	4 (18.18%)	6 (16.35%)	9 (27.2%)
IUGR	6 (17.14%)	2 (9.09%)	4 (13.9%)	5 (15.15%)
IUD	3 (8.5%)	3 (13.63%)	3 (8.6%)	2 (6.06%)
Others (congenital anomalies and reduced fetal movement)	3 (8.5%)	5 (22.7%)	3 (8.6%)	3 (9.09%)

Table III: Bishop scores, Ripening & induction-delivery times

Parameter	EASI (n=57)		EAM (n=64)	
	Primigravidae (n=35)	Multigravidae (n=22)	Primigravidae (n=31)	Multigravidae (n=33)
Mean initial Bishop score	1.2 ±1.02	1.7±0.8	0.9±1.3	1.5± 1.2
Mean post-ripening score	6.01±0.4	6.07±0.47	7.5±1.5	7.86±1.39
Mean ripening time (hr.)	7.71±1	6.4±1.02	6.15±2.1	4.03±1.3
Mean induction-delivery time (hr.)	7.7±2.03	5.92±1.9	5.3±2	3.8±1.4

t-test values

Parameter	Primigravidae (group 1 versus group 2)	Multiparae (group 1 versus group 2)
Mean initial Bishop score	0.298	0.495
Mean post-ripening score	0.00	0.00
Ripening time (hr.)	0.0005	0.00
Induction-delivery time (hr.)	0.00	0.00

Table IV: Mode of delivery

Mode of delivery	EASI (n=57)		EAM (n=64)	
	Primigravidae (n=35)	Multigravidae (n=22)	Primigravidae (n=31)	Multigravidae (n=33)
Spontaneous vaginal delivery	27 (77.1%)	19 (86.3%)	30 (96.7%)	32 (96.9%)
Instrumental	1 (2.8%)	0	0	0
Caesarean section	7 (20%)	3 (13.6%)	1 (3.22%)	1 (3%)

Table V: Neonatal outcome

parameter	EASI		EAM	
	Primigravidae	Multigravidae	Primigravidae	Multigravidae
Apgar score (5 Min.)	8.67±1.02	8.58±0.8	8.5±2.9	9.4±2.05
Body wt.(kg)	3.6±1.32	3.05±1.09	3.07±0.58	3.004±0.4

References

1. Schreyer P., Sherman D.J., Ariely S. et al. Ripening the highly unfavourable cervixwith extra-amniotic saline instillation or vaginal PG E2 application. Obestetric and Gynaecology. 1998;73:938.
2. Calder A. Normal labour. In: Edmonds D K, (editor). Dewhurst's textbook of Obstetrics & Gynecology. 6th ed. London. BlackWell Puplishing. 1999:242-47.
3. Hofmeyr G.J. Induction and augmentation of labour. In: Edmond D K, (editor). Dewhurt`s textbook of Obstetrics & Gynaecology. 7th ed. London. BlackWell. 2006: 205-10.
4. Osmann I, young A, Ledingham M.A. et al. Leukocyte density and proinflamatory cytokine expression & myometrium before & during labour at term. Mol-Hum-Reпord; 2003:41-45.
5. Lurence D R & Bennett. (B.N.F) British National Formulary. 2006. 105,45.
6. Schoenhard G. Metabolism & pharmacokinetic studies of Misoprostol. Diag Dis Sci. 1985; 30(suppl): 1265-85.
7. Margulies M. Misoprostol to induce labour. Lancet .1992; 339: 64.
8. Coldberg A B, Greenberg M B & Darney P D. Misoprostol & pregnancy. N-Engl-J-Med. 2001, 2002; 344:59-60 and 61.
9. Song J. Use of Misoprostol in Obstetrics & Gynecology. Obstet Gynaecol Surv.2000;55:503-10.
10. Fouad Hamad Al –Dahhan, Ali Falih Al-Assadi. A comparison of four methods of ripening the unfavorable cervix . Basrah J. of surgery.2005(September); 11(2):55-63 .
11. Al-Assadi A., Al-Waeely F., Ahmed H. et al. Extra amniotic Versus Vaginal Misoprostol for Ripening the Unfavourable Cervix.JBMS.2009 (January- March);21(1):207-211.
12. Al-Assadi A., Al-Waeely F.& Khadim S. The use of Extra amniotic Dexamethasone for Ripening the Unfavourable cervix.JBMS.2007 (October); 19(4):148-153.