

Misoprostol For Prevention of postpartum hemorrhage

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Abstract

Postpartum hemorrhage is the leading cause of maternal deaths in the developing world, accounting for 25% of such deaths in areas where maternal mortality is high, and less than 8% in developed countries. The importance of prevention, particularly where there is limited access to emergency medical is there for obvious.

Objective:

The aim of this study is to compare misoprostol with standard oxytocic regimens in the prevention of primary postpartum hemorrhage .

Study design :

Observational prospective and analytic study.

Setting :

It was carried in Al - Zahraa maternity and childhood teaching hospital in AL-Najaf for period between may 2006 to December 2006.

Sample:

340 women admitted to labor room were randomized to 3 groups there age between 15-40 years old, they divided into 3 groups : 1st group receive 400 mg of misoprostol (no=56). 2nd group receive 0.4 mg of methergin (2 amp) intramuscular (no=144). 3rd group receive 10 unit pitocin (oxytocin) intramuscular or by infusion (no=140).

Main measurements:

The mean blood loss.

PPH> 500 ml.

Needs for additional oxytocic drugs.

Decrease in hemoglobin concentration and hematocrit.

Incidence of manual removal of placenta.

Length of 3rd stage of labor.

The incidence of side effects.

All where the main outcome measures.

Results:

The demographic characteristics occur comparable. There is no significant differences were founded among three groups in the mean blood loss ($p=0.904$), the incidence of PPH more than 500 ml($p=0$), need for additional oxytocic agents ($p=0.647$), decrease in mean hemoglobin concentration ($p=0.920$) , manual removal of placenta ($\chi^2(106.28)0.000^*$) and length of 3rd stage of labor($p=0.572$). A part from significant

difference in temperature between the three groups there is in temperature by about 0.25 in misoprostol group

Nausea, head ach and abdominal pain were less frequent with misoprostol group .diarrhea and vomiting were equal in all groups. The main side effect of misoprostol were shivering.

Conclusion:

The oral misoprostol appears effective as conventional, intramuscular methergin in preventing primary postpartum hemorrhage, and the drug has the advantages of stability at room temperature and ease of administration, be recommended for routine use anywhere for primary PPH prevention.

The oral misoprostol is recommended especially in situations in which methergin and oxytocin are contraindicated or where storage and parental administration of oxytocics is a potential problem.

Introduction

The third stage of labor is potentially the most dangerous part for the mother. The main risk is the occurrence of postpartum hemorrhage, defined as bleeding from the genital tract of 500 mL or more in the first 24 hours following delivery of the baby. The primary cause of postpartum hemorrhage is uterine atony.

Uterine atony and failure of contraction and retraction of myometrial muscle fibers will result in incomplete separation of placenta, inhibition of contraction stability of the uterine muscle to constrict the vascular channels in the placental bed and can sequent excessive bleeding. The non contracted uterus is then distended with blood and has boggy consistency on abdominal examination. This can lead to rapid and severe hemorrhage and hypovolemic shock.

Active management of the third stage of labor was defined as package of interventions designed to speed the delivery of the placenta by increasing uterine contractions and to prevent PPH by averting a uterine atony. Ameta – analysis of these studies, available through the Cochrane database and WHO's reproductive health library, confirmed that active management was associated with reduced maternal blood loss (including PPH > 500 ML and severe PPH > 1000 ML), reduced postpartum anemia, and decreased need for blood transfusion. Active management also was associated with a reduced risk of prolonged third-stage labor, and less use of additional therapeutic uterotonic drugs.

Oxytocicagents:

prophylactic oxytocics resulted in about a 40% reduction in the risk of postpartum hemorrhage

Oxytocin

is a hormone used to help start or continue labor and to control bleeding after delivery. It is also sometimes used to help milk secretion in breast-feeding. Trade name of oxytocin (pitocin or syntocinon). Used for helping to control bleeding after delivery in dose of 10 units injected into a muscle or slowly into a vein. Storage should be away from heat and direct light; protect the medicine from freezing.

Side Effect of oxytocin :- in women who are unusually sensitive to its effects may lead to tearing of uterus, it causes irregular heart beat and increases bleeding after delivery in some women, it has been reported to cause jaundice in some newborn infants, it may cause confusion, convulsion (seizures), difficulty in breathing, dizziness

fast or irregular heart beat , head ache (continuing or sever) , pelvic or abdominal pain (sever) , skin rash
or itching , vaginal bleeding (increase or continuing) , weakness , weight gain , nausea and vomiting .

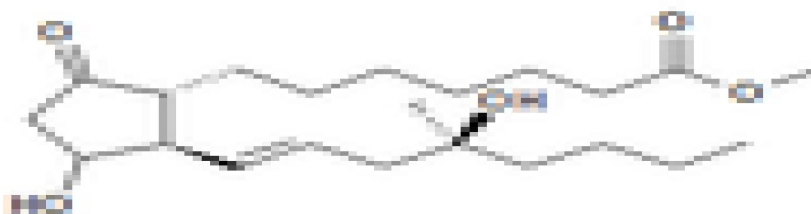
Ergometrine,

however, has significant problems, it is contraindicated in hypertension in pregnancy. It frequently causes nausea and vomiting . It must be given by intra-muscular injection , requiring a clean needle and syringe-an important consideration in the era of hepatitis and HIV infection . Ergometrine is not stable at high temperatures and requires special storage conditions. Studies designed to simulate the storage countries commonly found in developing countries showed that a variety of brands of ergometries lose over 90% of their potency after one year of storage. When syntometrine is stored for prolonged periods of time , it must be kept at between 2 and 8C and protected from light. The ergometrine component of syntometrine has been found to be susceptible to a 21-27% loss in potency after 1 month when stored under conditions simulated to those similar to tropical countries in the developing world.

Ergometrine has been reported to cause cardiac arrest and intracerebral hemorrhage , and these may be attributed to the ergonovine (ergometrine) component . A recent report associated the ergot alkaloid with acute myocardial infarction , cramping , headache , hypertension , dizziness , bradycardia , tachycardia , and some mild gastrointestinal side effects .

Misoprostol

Misoprostol , a prostaglandin E1 analog (methyl -16-hydroxy-PGE, methyl ester)that is marked as tablet trade name (cytotec)



C22 H38 O5

is used orally for the prevention and treatment of gastric / duodenal ulcer caused by the use of non steroidal anti -inflammatory agents (NSAIDs) misoprostol increased secretion of the protective mucus that lines the gastrointestinal tract and increases mucosal blood flow . Its safety for this indication has been established over several years.

In 1985, when the drug came before the Advisory Committee of the USFDA for approval, one reviewer noted that misoprostol's gastrointestinal effects were overshadowed by it's abortifacient effects, and he cautioned the medical community about the potential for misuse by pregnant women.

Obstetric and gynecological applications for which misoprostol-only regimens are being evaluated include induction of first-and second-trimester abortion, treatment of miscarriage, cervical priming, induction of labor, and prevention and management of postpartum hemorrhage. Among the key advantages of misoprostol for these indications

are its effectiveness, low cost, stability (tablets have a shelf life of several years at room temperature), accessibility, and potential to lead to safer reproductive health outcomes than currently used therapies. Interest in misoprostol and its potential to reduce the complications of unsafe abortion and other gynecological and obstetric conditions remains strong around the world, especially for developing countries.

Misoprostol acid is extremely rapid absorption, being detected in the circulation within two minutes of its oral ingestion, shown to be rapid. misoprostol does not increase the blood pressure. Misoprostol is rapidly absorbed after oral, vaginal, and rectal administration, the speaker stated that with oral administration, the half-life is <30 minutes and peak level occurs at 15 minutes; after vaginal administration, there is a gradual rise to a maximum level at 60 to 120 minutes, with the level at 60% of peak at 240 minutes. The speaker noted that vaginal administration has demonstrated greater abortifacient efficacy than oral administration during the first trimester, and is associated with fewer side effects. Tablets do not dissolve in all women who receive misoprostol vaginally which may warrant moistening the tablets prior to insertion.

Misoprostol also has been investigated in the prevention of postpartum hemorrhage, using either the oral or rectal route of administration, and compared with placebo or other oxytocics. Results of most of these studies show a trend toward less postpartum hemorrhage with misoprostol, suggesting that it might be effective for this indication without causing serious side effects.

Side effects ranging from mild (e.g., nausea, vomiting, abdominal pain, diarrhea) to severe (e.g., uterine rupture) have been reported after misoprostol administration that misoprostol-only regimens have the potential to reduce maternal morbidity and mortality resulting from unsafe abortion practices. misoprostol use has reduced the number of infections among women with incomplete abortions as well as the use of other, more invasive forms of illegal abortion. The authors state that teratogenic effects, particularly limb defects, mobius syndrome (congenital facial paralysis 6th and 7th nerve palsies), seizures, slow growth, cranial nerve paralysis and respiratory problems, have been associated with misoprostol used for first-trimester abortion and recommends that clinicians be aware of these risks and counsel patients to complete termination of pregnancy once it is begun they suggest that these teratogenic effects could be the result of anoxia following uterine contraction and constriction of the uterine vessel after misoprostol administration. The author states that misoprostol used for second-trimester abortion has been associated with uterine rupture, particularly when combined with oxytocin infusion; the author cautions clinicians to limit dosage and avoid oxytocin infusions within 6 hours. The author reviews studies reporting on misoprostol used for third-trimester induction of labor and states that the drug has been associated with uterine tachysystole (excessive uterine activity) unrelated to dosage, as well as fetal heart rate changes and increased meconium passage

Patients and methods

Our study was carried out between Jun 2006 and December 2006 in the maternity and children teaching Hospital in Al- Najaf city.

The primary aim of this study was to ascertain whether 400 mg oral misoprostol could replace standard oxytocic drugs in the prevention of primary PPH.

The secondary aim was to assess the length of 3rd stage of labor, rate of manual removal of placenta, change in blood pressure, hemoglobin estimation, packed cell volume and

need for additional oxytocic drugs and change in body temperature, and assess incidence of the side effects of all drugs regimens.

Pregnant women were eligible to take part in the study if they were expected to have a vaginal delivery

The exclusion criteria are :-previous caesarian section, hemoglobin level less than 9gm/dl, episodes of ante partum bleeding during the current pregnancy, blood pressure more than 140 mm Hg systolic and 90 mm Hg diastolic, absence of fetal heart sound, multiple pregnancy , non cephalic presentation, known history of bronchial asthma (requiring hospital admission and steroids), history of complication (ante partum hemorrhage / post partum hemorrhage /retained placenta / acute inversion of uterus) during previous pregnancy and high risk conditions including : diabetes, cardiac ailments , seizures , placenta prevail or anticipated breech delivery.

When vaginal delivery was imminent, and in the 2nd stage of labor when it was felt that vaginal delivery soon occur then patient receive 400 Mg misoprostol orally immediately after the delivery of anterior shoulder of the baby and others receive 0.4 mg ergometrin intramuscularly after delivery of the baby or 10 Iu oxytocin intramuscularly After delivery of the baby .

The management of third stage of labor in our teaching hospital usually included active management with controlled cord traction until delivery of the placenta. The data collection form was completed by the doctor caring for the women .This form contained information on maternal characteristics such as age, parity, gestational age at delivery, blood pressure , temperature , hemoglobin hematocrit and blood group. After delivery we record different variable we concern, Blood loss was estimated subjectively by the attend doctor and midwife, as in other randomized trials of the prevention of PPH. Apart from blood loss with delivery of placenta by use labeled kidney shape dish (divide in ML) till complete delivery of placenta and well contracted uterus by massage.

Other variable was recorded after delivery, needed for blood transfusion, using for other oxytocic drugs, length of the third stage of labor, management of the placental delivery whether by controlled cord traction CCT or manually removal, hemoglobin concentration and haematocrit, systolic and diastolic blood pressure (was taking by mercury sphygmomanometer, patient either in sitting or lying on left lateral position). These are the main out come measures of our study for the prevention of primary PPH. And the incidence of the side effects, women were therefore requested to complete questionnaire after delivery before leaving the labor ward, this recorded the women's perception of side effects such as nausea, vomiting, abdominal pain, diarrhea, headache, shivering, elevated temperature (within one hour of delivery).

RESULTS

Table 1: values are given as mean (\pm SE) or n[%] before labour

| | | Misoprostol N=56 Mean (S.E) | Methergin N=144 Mean (S.E) | Oxytocin N=140 Mean (S.E) | P-value |
|----------------------------|-------------------|--------------------------------------|-------------------------------------|------------------------------------|---------|
| Age (year) | | 23.92 (2.074) | 24.63 (1.037) | 23.45 (1.067) | 0.628 |
| Gestational age (weeks) | | 39.21 (0.563) | 39.5 (0.165) | 38.94 (0.334) | 0.350 |
| Parity | primi | 28[50] | 76[52.77] | 64[45.71] | |
| | Para 1-5 | 16[28.57] | 64[44.44] | 72[51.42] | |
| | Para>5 | 12[21.42] | 4[2.77] | 4[2.85] | |
| BP | Systolic mmHg | 123.57 (3.414) | 123.33 (1.497) | 123.42 (1.660) | 0.888 |
| | Diastolic mmHg | 75.71 (2.716) | 76.52 (1.288) | 76.71 (1.808) | 0.526 |
| Hemoglobin g/dl | | 10.60 (0.319) | 10.59 (0.212) | 10.58 (0.202) | 0.941 |
| Haematocrit PCV% | | 34.14 (0.971) | 34.02 (0.707) | 33.94 (0.685) | 0.953 |
| Temperatures c | | 36.7 (0.064) | 36.77 (0.038) | 36.78 (0.046) | 0.545 |

Table 2: The effect of the treatments on amount of blood loss values are given as median [] and mean (\pm SE) . P value>0.05

| | Misoprostol N=56 | Metergin N=144 | Oxytocin N=140 | P- value |
|--------------------------------|---------------------------|---------------------------|-------------------------|-------------|
| Blood loss>500ml | 0 | 0 | 0 | - |
| Blood loss(ml) (within 2hr) | 214.2[150-250] (9.418) | 211.3[150-250] (5.135) | 214[150-300] (6.499) | 0.904 |

This table describes the effect of the trials of treatment on the amount of blood loss which report no case of blood loss 500, and the mean blood loss showed no significant difference between the three groups.

Table3: Umbilical cord management values are given as n (%). P value<0.05

| Umbilical cord management | DRUGS | | | Chi X2 P value (106.28) |
|----------------------------|---------------------|---------------------|-------------------|-------------------------------|
| | Misoprostol N=56 | Methergin N= 144 | Oxytocin N=140 | |
| Control cord traction | 56 (100) | 136(94.4) | 132(94.2) | 0.000 * |
| Manual removal of placenta | 0 | 8(5.6) | 8(5.8) | |

This table compares the 3 groups of women in regard to the umbilical cord management after administration of oxytotic drugs which is statistically significant as we found no case required manual removal of placenta in misoprostol group.

Table 4: The effect of the treatments on the third stage of labour.

| | Misoprostol N=56 | Methergin N=144 | Oxytocin N=140 | P-value |
|---------------------------------|---------------------|----------------------|-----------------------|---------|
| Length of 3rd stage labor (min) | 5.6[5-8] (0.307) | 6.1[5-10] (0.327) | 6.14[5-10] (0.323) | 0.572 |
| Blood transfusion | 0 | 0 | 0 | - |
| Further oxytotic drugs | 4(7.1) | 16(11.1) | 16(11.4) | 0.647 |

This table describes the effect of treatment trials on the length of the third stage of labour on the need for blood transfusion and on the need for further oxytotic drugs. We found that there is no significance differences between the three groups in the study and we had no patient required blood transfusion

Table 5: Systolic and Diastolic blood pressure before and after delivery was measured in means (\pm S.E).P value >0.05

| Blood Pressure Bp | Misoprostol N=46 Mean (S.E) | Methergin N=145 Mean (S.E) | Oxytocin N=140 Mean (S.E) | P-value |
|------------------------|--------------------------------------|-------------------------------------|------------------------------------|---------|
| Systolic Bp Pre labor | 123.57 (3.414) | 123.33 (1.497) | 123.42 (1.660) | 0.888 |
| Systolic Bp Post labor | 122.14 (1.941) | 123.75 (1.598) | 123.71 (1.878) | 0.287 |
| Diastole Bp pre labor | 75.71 (2.716) | 76.52 (1.288) | 76.71 (1.808) | 0.526 |
| Diastole Bp post labor | 75.0 (2.871) | 75.83 (1.267) | 76 (1.615) | 0.652 |

This table compares between 3groups of patients receiving 3drugs in management of 3rd stage of labor in regard to systolic and diastolic Bp before and after labour within 2hrs (after delivery).

Table6: Hemoglobin and Haematocrit before and after delivery in mean(\pm S.E). P value >0.05

| Blood parameters | Misoprostol N=46 Mean (S.E) | Methergin N=144 Mean (S.E) | Oxytocin N=140 Mean (S.E) | P-value |
|------------------|--------------------------------------|-------------------------------------|------------------------------------|---------|
| Hb pre labor | 10.60 (0.319) | 10.59 (0.212) | 10.5 (0.202) | 0.941 |
| Hb post labor | 9.98 (0.306) | 9.84 (0.197) | 9.87 (0.155) | 0.920 |
| PCV pre labor | 34.14 (0.971) | 34.02 (0.707) | 33.94 (0.685) | 0.953 |
| PCV post labor | 34.00 (0.949) | 33.91 (0.661) | 33.77 (0.629) | 0.968 |

This table shown comparing between 3 groups of patient in regard to hemoglobin and hematocrit before delivery and (1-2hr) after delivery it was reveal that there was slight decrease which is statistically not significant in hemoglobin but hematocrit values showed relatively no change after delivery.

Table7: Temperature before and after delivery in significant differences at P<0.05.

| | Misoprostol N=46 Mean (S.E) | Methergin N=144 Mean (S.E) | Oxytocin N=140 Mean (S.E) | P-value |
|-----------------|--------------------------------------|-------------------------------------|------------------------------------|---------|
| Temp pre labor | 36.7 (0.064) | 36.77 (0.038) | 36.78 (0.046) | 0.545 |
| Temp post labor | 37.14 (0.066) | 36.90 (0.023) | 36.95 (0.021) | 0.000* |

This table has shown comparing between 3 groups of patient in regard to Temperature. Within before delivery and (1-2hr) after delivery it was reveals that there was slight elevation in temperature in those groups receiving misoperstol

Table 8: Mean change in maternal temperature, blood pressure, Hemoglobin concentration and Haematocrit before and after delivery values are given as mean (±SD).significant differences at P<0.05.

| | Misoprostol n=56 | Methergin N=144 | Oxytocin N=140 | P- value |
|------------------------------------|---------------------|--------------------|-------------------|----------|
| Temperature (C) | 0.44 (0.007) | 0.13 (0.091) | 0.17 (0.074) | 0.011* |
| Systolic blood Pressure (mmHg) | -1.43 (1.723) | 0.42 (0.232) | -0.29 (1.200) | 0.356 |
| Diastolic blood pressure (mmHg) | -0.71 (0.578) | -0.69 (0.123) | -0.71 (1.1411) | 0.981 |
| Haemoglobin gm/dl | -0.62 (0.049) | -0.75 (0.086) | -0.7 (0.255) | 0.937 |
| Haematocrit %(PCV) | -0.14 (0.112) | -0.11 (0.277) | -0.17 (0.202) | 0.986 |

Table 9: Side effect values are given as n(%),This table summaries the side effect experienced by the women in the three group.

| | Misoprostol n=56 | Methergin N=144 | Oxytocin N=140 |
|----------------|---------------------|--------------------|-------------------|
| Shivering | 20(35.7) | 28(19.44) | 32(22.85) |
| Nausea | 12(21.4) | 48(33.3) | 36(25) |
| Headache | 4(7.1) | 32(22.2) | 24(17.1) |
| Vomiting | 8(14.2) | 24(16.6) | 28(20) |
| Abdominal Pain | 16(28.5) | 52(36.1) | 48(33.3) |
| Diarrhea | 4(7.1) | 12(8.3) | 12(8.5) |

Table (9) Summaries the side effects experienced by the women there were no differences in the incidence of nausea, vomiting, diarrhea, but headache and abdominal pain were reported more often in the oxytocics group, the most prominent side effect of misoprostol was shivering, which occurred twice as often as in the other oxytocics group. Shivering was significantly more common in the women who received epidural analgesia than those who did not receive epidural anesthesia as in 2000 BTOO (Hazimal Refaay). Clear association was found between shivering and a rise in temperature in the misoprostol temperature group a 6°C (small difference in mean change in temperature between shivering and non shivering women (0.25°C) but not in the methergin in group 0 (difference in mean change in temperature between shivering and non shivering women (0.04°C) in the pitocin group (difference in mean change in temperature between shivering and non shivering women (0.1°C).

Discussion

This study has shown that oral misoprostol appears to be as effective in prevention of PPH in third stage of labor as intramuscular oxytocin or methergin the current management recommended by the World Health Organization, so that misoprostol may be an alternative to these drugs. Furthermore, it was easy to use, since it could be given orally to all women in the prevention of PPH. Ergometrine should not be used in women with hypertension, since serious complication and even death may result.(14)

Table 1 and table 2: Shows the number of women who have been submitted to receive misoprostol and oxytocics drugs according to age groups and parity. Shows that more number of women in all groups those within age groups of 18-35 years and both parity group primigravida and (p1-p4) were relatively equally.

Table 4, 5 and 6:- They were compared between 3 groups of women receive (misoprostol, methergin, pitocin) in regard to systolic and diastolic blood pressure. Hemoglobin, hematocrit, temperature before and after delivery within 2 hours. They show no difference in all groups apart from systolic pressure in misoprostol group they decrease the pressure. (-1.43p=). Mild decrease in hemoglobin and no change in Hematocrit and show that slight elevation in temperature in group receive misoprostol by

about (0.34°C) more than other group.

(Table 6):- shows the baseline characteristics and obstetric history of women in the study in regard to age (in years). Gestational age (in weeks), parity, systolic and diastolic blood pressure, Hb, hematocrit and temperature. There were no significant differences between all groups with regard to maternal demographics (baseline character).

Table 7:- this table shows description of the events that occurred during labor and compared between the 3 groups of women. The event was first stage and second stage of labor, whether the labor induced or augmented or spontaneous vaginal delivery mode of delivery (normally or by instrument), episiotomy, tears and management of third stage of labor (usually all labor managed by active management). Length of third stage, management of placental delivery whether by controlled cord traction (CCT) or manually shows that no difference between 3 groups in length of 1st, 2nd and 3rd stage of labor, episiotomy, tears mode of delivery, usually all deliveries vaginally without instrumental interference. Apart from management of placental

delivery showing increase incidence of manual removal of placenta in oxytocic group about 23% comparing to that of no cases reported in misoprostol group. In 1997 (BJOG:EL-Refaey H) has been found that 2% required manual removal of placenta and non required surgical evacuation of uterus with misoprostol. In 1996 (Lancet EL-Refaey H)

has been found that only 2 patient required manual removal of placenta with misoprostal. In 2000 (BJOG John B. Wilson) has been found that the manual removal of placenta were similar in both groups. In (BJOG 107, 1104 Refaey H, R. Nooh) they have been found that the manual removal of placenta in misoprostal group lesser than in oxytocic groups. These result consistent with our result in which lesser percentage of manual removal of placenta in misoprotal group .

Table 8 :- in this table comparison had been done in relation to out come variable of women receiving (400Mg oral misoprostal) compared with those receiving I. m. oxytocic 10 I.u. or Im o.4 methergen and their effect on the 3rd stage of labor.Primary out come measure of estimate. * blood loss and that found no women in all group had an estimated blood loss >500ml no women received blood transfusion and maternal death. Median blood loss in all groups relatively equally 214 ml in oxytocin drug group, 214 ml in misoprostal group, 211 ml in methergen group. Secondary out commesures:- *Length of 3rd stage of labor.(5.6 min in misoprostal group and 6.1 min in both group of oxytocic drugs) is relatively lesser in 1st group than other groups. *Use of further oxytocic drugs has been found lesser in misoprostal group about 7.1% than other oxytocic drugs (methergien 11.1% , oxytocic 11.44%)*Manual removal of placenta in misoprostal group 0% and in other group 2.8% *Systolic and diastolic blood pressure, hemoglobin concentration, haematocrit all they have been found no significant difference in all group apart from systolic blood pressure in misoprostol group relatively decrease by about 1.43 mmHg from those in other groups, but they increase in the other groups by about (0.42 methergen group, 0.29 oxytocic group). Diastolic blood pressure, haemoglobin concentration and hemotocrit there were slight similar decrease in all groups. Temperature has been found increase slightly by about 0.34 c in misoprostol while in other groups very slight increase (Methergen 0.13 and 0.2 in oxytocin) but not reach above 37.5c. In 1999 (Surbek D,V) has been found that the length of third stage of abor 8 ± 0.9 min misoprostol group lesser than other group 9 ± 1 min and need for additional oxytocics drugs 16% in misoprostol group and 38% in other group. Mean blood loss 345 ml vs to 417 ml, these results constitute with our result. In 1998 (BJOG Hofimyer GJ) has been found that need for addition oxytocic drug 8.4% in misoprostol group and 13% in other group. Blood loss >1000 ml 6% in misoprostol group vs to 9.2% in other groups. In 1997 (BJOG EL-Refaey H) has been found the blood loss 500ml occur in 6% of patients, lehghth of third stage of labor in misoprostol was 5 min. 5% need for further oxytocic drug and no difference found in systolic/diastolic BP pre and post partum. Temperature significantly increased by 0.5 c all these results constitute with our result. In 2000 (John,B-Willson,Wally RL) they have been found no significant difference in 2 group in Hb concentration, in misoprostol group (10.9) to (10.4) in oxytocin groups estimation of length of the 3rd stage of labor, additional oxytocic Drug and blood loss were similar between the groups. These results constitute with our result apart from use of further oxytocic drug was lesser in misoprostol group in our study. In 2000 (BJOG EL-Refaey H, Nooh -R) they have found Manual removal of the placenta and length of 3rd stage of labor were similar in both groups.Need for further oxytocics drug higher in misoprostol group 14% versus to 10% in other groups. Hb and hemotocrit levels and blood pressure are similar in both groups. Increase in temperature was significantly greater in the misoprostol group mean 0.59 vs 0.25 in other groups. Incidence of PPH was 12% in the misoprostol group compared with 11% with other oxytocics.

Table 9:- shows the changes in the temperature blood pressure, haemoglobin concentration, hematocrit (before and after delivery women in all groups showed slight increase in temperature after delivery but there was significantly great in temperature

with misoprostol (0.34 vs to 0.1 in methergin and 0.2 in oxytocics). There was slightly decrease in systolic BP in misoprostol group after delivery (1.43mmHg) but there were no differences in the changes of diastolic BP, Hb concentration and hemotocrit. In 2000 (BJOG EL-Refaey ETAL) they have been found there is increase in temperature was significantly greater in misoprostol group (mean 0.59 VS 0.25)

Table 10:- This table summaries the side effects experienced by the women it was show the misoprostol was better tolerated than the other oxytocic in terms of nausea, head ache, diarrhea but not in other gastrointestinal side effects. These side effects reduce the acceptability of oxytocic preparations country ergometrine, and have a major stimulus to obstetricians in past 3decades to search for an alternative drug. Shivering and rise in temperature were the main side effects of miso prostol this is likely related to prostaglandin E1 effect on control thermo regular center and then was a clear association between these side effects. Women who reported shivering with misoprostol had a mean rise in temperature of 0.25 c more than women did not shiver, however shivering women who had been given other oxytocics drug did not have a significant increase in their temperature compared with women who did not shiver. Shivering occurs twice as often with misoprostol compared with standard oxytocic drugs, it is occurs after 5-10 of administration of the drug and lasted for 25 to 30 minute. Shivering was not known to be aside effect of misoprostol prior to using it for the third stage of labor. Misoprostol given for induction of abortion in single doses up to 800 mg and total daily dosage up to

2200mg did not cause shivering. Shivering is known to be aside effect of epidural analgesia. But shivering occurred with misoprostol regardless of epidural analgesia. Shivering may be dose dependent further research is needed to understand the inter play between pyrexia and shivering and identify methods to over come this side effect. The lack of an effective, stable oxytocic which can be given by mouth is major impediment to the prevention of life threatening postpartum hemorrhage in the developing world. Our randomized study suggestion that misoprostol is as effective as standard oxytocic drugs in the prevention of atonic PPH it dose not increase the blood pressure, has few side effect and is well tolerated shelf life several years, stability at high temperature (i.e. it dose not require refrigeration) oral administration (i.e. it dose not require needle or syringe).

REFERENCE

E medicine>medicine,ob/Gyn, psychiatry, and surgery> ob/Gyn management of the third stage of labor: Article by John R.Smith .MD. Frscs,Facog, head, division of maternal-fetal medicine, associate professor, department of obstetrics and gynecology, united arab emirates university. Last update: September 22,2004.

E medicine->medicine,ob/Gyn, psychiatry, and surgery> ob/Gyn postpartum hemorrhage: article by John R Smith MD FRSSCS FACOG, Head, Division of maternal-fetal medicine, associate professor,department of obstetrics and gynecology, united Arab Emirates university. Last update : November 24,2004.

e medicine-> emergency medicine > ob/Gyn pregnancy postpartum hemorrhage: article by Michael p wainscot MD ,residency director, professor, division of emergency surgery, university of texas southwestern medical center Michael p wainscot, MD, is a number of the following medical societies: American Colleg physicians. last update: November 24,2004.

Barbara Shane. Editorile assistance was provided by Michele Burns. maternal and neonatal health special Issue out look preventing post partum hemorrhage: managing the third stage of labor.program for appropriate technology in health (path),2001.

dewhurst's textbook of obstetrics and gynaecology for postgraduates edited by D. KEITH EDMONDS FRCOG, FRACOG SIXTH EDITION 1999.

Preventing post partum hemorrhage: managing the third stage of labor march 15,2006
American Family Physician preventing postpartum hemorrhage: managing the third stage of labor KAREN L.MAUGHAN,M.D, STEVEN W.HEIM,M.D,M.S.P.H, AND SIM S.GALAZKA,M.D. University of Virginia School of medicine, Charlottesville, Virginia.update march 15,2006. The Merck Manual of Diagnosis and Therapy Section 18. Gynecology And Obsterics Chapter 249. Normal Pregnancy, Labor, And Delivery Topics. Update 5/27/2006. RICHRDE J DERMAN, M.D.Oral Misoprostol for Prevention of Postpartum Hemorrhage-Article National Institute of Child Health and Human Development (NICHD). Update :October 1,2005.

*Hazem EL-Refaey Senior Registrar, *Randa Nooh Research Fellow, The misoprostol third stage of labor study: a randomized controlled comparison between orally administered misoprostol and standard management British Journal of Obstetrics and Gynaecology September 2000, Vol 107, pp. 1104-1110.

* Rbert L. Walley professor, * John B. Wilson consultant, A double-blind placebo controlled randomized trial of misoprostol and oxytocin in the management of the third stage of labor British Journal of Obstetrics and Gynaecology September 2000, Vol 107, pp. 1111-1115.

Joyce Primo Carpenter, M.D., BSc. Pharm. Medical Information Specialist Global Assistance Initiatives Misoprostol Prevention of Postpartum Hemorrhage: An Evidence-based Review by the United States Pharmacopeia Developed: 6/16/2000, Revised:6/30/2001.

Surbek D V , Fehr PM, Holsi I, et al.Oral misoprostol for third stge of labor; a randomized placebo-controlled trial. Obstet Gynecol 1999; 94(2): 255-8.

Amant F, Spitz B, Timmerman D, et al. Misoprostol compared with methylergometrine for the prevention of postpartum hemorrhage: a double – blind randomized trial. Br J Obstet Gynecol 1999; 106:1066-70.

EL- Refaey H, O'Brien P, Morafa W, et al. use of misoprostol in the prevention of postpartum hemorrhage. Br J Obstet Gynaecol 1997;104(3):336-9.

El-Refaey H, O'Brien P, Morafa W, et al. Misoprostol for the third stage of labor. Lancet 1996 [letter]; 347 (9010): 1257.

Hofmeyr GJ, Nikodem VC, De Jager M, et al. A randomized placebo-controlled trial of oral misoprostol in the third stage of labor. Br J obstet Gynaecol 1998; 105 (9); 971-5.

Murad AL-Momani E-mail : abeer_f@PM.GOV.JO. Is oral or rectal misoprostol effective to prevented post partum Hg.

website for the global network for women's and children's health research triangle institute international K.L.E. Society's Jawaharlal Nehru medical college. Oral misoprostol for prevention of post partum hemorrhage. Last update: December 8,2005.American Journal of obstetrics and Gynecology Kenneth W. Jackson, Jr MD, John R. Allbert MD. Available online 9 may 2002.

American Journal of obstetrics and gynecology Eray Caliskan MD, M. Mutlu Meydanli MD. Is rectal misoprostol really effective in the treatment of third stage of labor. Available online 23 October 2002.

American Journal of obstetrics and Gynecology. Rectal misoprostol versus intravenous oxytocin for the prevention of postpartum hemorrhage after vaginal delivery. Tammy S. Gerstenfeld DO and Deborah A. Wing MD. AVILABLE ONLINE 9 MAY 2002.

PATH: PREVENTING POSTPARTUM HEMORRHAGE. Saving mother's lives. 1995-2006,path. misoprostol-Wikipedia, the free encyclopedia. Last update 11 June

2006. Entrez PubMed Quiroga Diaz R, Esparza Arechiga M, Vaginal misoprostol in the prevention of postpartum hemorrhage. Update 2002 Nov.
- INTERNATIONAL JOURNAL OF GYNECOLOGY BY FAX . BOARD OF AUTHORS: M. BIRKHAUSER, L CABERO ROURA, R. THE USE OF MISOPROSTOL IN POSTPARTUM HEMORRHAGE. Sept 2003
- medlineplus drug information: oxytocin (systemic). Thomson Micromedex, Inc.DISCLAIMER. last update 10 Aug 2006. Ratnam SS, Viegas OAC, Singh K.
- Magnitude and causes of maternal mortality as a basis for its prevention in: Kassel E, Awan AK, editors. Maternal and child care in developing countries Zurich, Switzerland: Ott publishers; 1989.p.80-90.
- Kwast BE. Postpartum hemorrhage: its contribution to maternal mortality. Midwifery 1991; 7: 64-70.
- cook CM, Spurrett MM, Murray, H. A randomized clinical trial comparing oral misoprostol with synthetic oxytocin or syntometrine in the third stage of labor. Aust NZJ obstet Gynaecol 1999;39:4:414-9.
- O'Brien P, EL-Refaey H. The management of the third stage of labor using misoprostol in low risk women. Contemp Rev Obstet Gynecol 1997;9(1);27-32.
- Lawson JB. Obstetric hemorrhage. In: Lawson JB, Steward DB, editors. Obstetrics and gynecology in the tropics. London: Edward Arnold; 1967.p.155-9.
- Sleep J: Physiology and management of the third stage of labor. In: Bennett VR, Brown Myles Textbook for Midwives. 12th ed. London, UK: Churchill Livingstone; 1993: 216-29.
- Cunningham FG, Gant NF, Leveno KJ, et al: Conduct of normal labor and delivery. In: Obstetrics. 21st ed. New York, NY: McGraw-Hill; 2001:320-5.
- For man JB, Sullivan RL. The effects of intravenous injections of ergonovine and methergine on the postpartum patients. Am J Obstet Gynecol 1952;63: 640-4.
- Prendiville, W.J. et al. Active versus expectant management in the third stage of labor (Cochrane Review, March 9,2000). In: the Cochrane library, issue 4, 2001. oxford: Update software, Ltd.
- WHO. Reproductive Health Library [CD ROM]. Geneva: WHO/HPR (2001). For information, contract RHL@ who.int.
- Rogers J, Wood J, Mc Candlish R, Et al. Active versus expectant management of third stage of labor: the Hinchingsbrooke randomized trail. Lancet 1998;351(9104):693-9.
- Sorbe B. Active pharmacologic management of the third stage of labor. A comparison of oxytocin and ergometrine. Obstet Gynecol 1978;52(6):694-7.
- Kelsey JJ, provost RR. Drug therapy during labor and delivery. Am J Hosp Pharm 1994;51:2394-402.
- Inman WH. Report on current PEM studies: drugs for peptic ulcer or reflux. Prescription Event Monitoring News 1991;7:32-4.
- Hofmeyer GJ, Bamigboye AA. In reply [letter to the editor]. Am J Obstet Gynecol 1999;6(pt 1):1601-2.
- Bamigboye AA, Hofmeyer GJ, Merrell DA. Rectal misoprostol in the prevention of postpartum hemorrhage: a placebo-controlled trial. Am J Obstet Gynecol 1998;179:1043-6.