Alexandria Journal of Medicine

ISSN: 2090-5068 (Print) 2090-5076 (Online) Journal homepage: https://www.tandfonline.com/loi/tajm20

Active management of third stage of labor by intravenous ergometrine and rectal versus sublingual misoprostol (a double-center study)

Abd El-Moneim A. Fawzy, Manal Swelem, Amr I. Abdelrehim, Salem Titeli, Zahya S. Elghazal, Milad M. El-Gahwagi & Asma S. Ben Amour

To cite this article: Abd El-Moneim A. Fawzy, Manal Swelem, Amr I. Abdelrehim, Salem Titeli, Zahya S. Elghazal, Milad M. El-Gahwagi & Asma S. Ben Amour (2012) Active management of third stage of labor by intravenous ergometrine and rectal versus sublingual misoprostol (a double-center study), Alexandria Journal of Medicine, 48:4, 381-385, DOI: 10.1016/j.ajme.2012.06.003

To link to this article: https://doi.org/10.1016/j.ajme.2012.06.003

Published online: 17 May 2019.

Alexandria Journal of Medicine (2012) **48**, 381–385

Alexandria University Faculty of Medicine

Alexandria Journal of Medicine

www.sciencedirect.com

ORIGINAL ARTICLE

Active management of third stage of labor by intravenous ergometrine and rectal versus sublingual misoprostol (a double-center study)

Abd El-Moneim A. Fawzy [a], Manal Swelem [a,*], Amr I. Abdelrehim [a], Salem Titeli [b], Zahya S. Elghazal [b], Milad M. El-Gahwagi [b], Asma S. Ben Amour [b]

[a] *El-Shatby University Maternity Hospital, Department of Obstetrics and Gynecology, University of Alexandria, Egypt*
[b] *Al-Jamhoriya Hospital, Department of Obstetrics and Gynecology, University of Benghazi, Libya*

Received 24 December 2011; accepted 11 June 2012
Available online 2 August 2012

KEYWORDS

Third stage of labor;
Active management;
Misopristol

Abstract *Background:* Active management of third stage of labor is a feasible and inexpensive intervention that helps saving thousands of women's lives.
Objective: The aim of the study was to compare the efficacy of IV ergometrine, rectal versus sublingual misoprostol in active management of third stage of labor. The same protocol was applied to Al-Jomhoria Hospital, Garunis University, Benghazi, Libya.
Methods: The study was conducted on 300 primigravida (150 Alexandria University El-Shatby Maternity Hospital, 150 in Al-Jomhoriya Hospital, Benghazi University) who underwent normal vaginal delivery and were divided into 3 groups according to the drug used in management of third stage of labor (ergometrine IV, one rectal tablet of misoprostol, one sublingual tablet of misopristol) All patients were closely observed for time of placental delivery, amount of blood loss by Hb and hematocrit value pre and immediately post delivery (within 1 h), use of oxytocin and any recorded side effects.
Results: During the follow up of Alexandria & Jamhoriya cases, it was found: 200 mcg sublingual misopristol was more effective than 200 mcg rectal misopristol and IV ergometrine immediately

* Corresponding author.
E-mail addresses: moneimfawzy@hotmail.com (A.E.-M.A. Fawzy), manalshafikswelem@gmail.com (M. Swelem), kingamratall@gmail.com (A.I. Abdelrehim), salemtiteli@yahoo.co.uk (S. Titeli), ghazalhia@yahoo.com (Z.S. Elghazal), mila1love@yahoo.com (M.M. El-Gahwagi), asmasbenamour@yahoo.com (A.S. Ben Amour).

Peer review under responsibility of Alexandria University Faculty of Medicine.

ELSEVIER Production and hosting by Elsevier

http://dx.doi.org/10.1016/j.ajme.2012.06.003

after delivery, as it decreased the amount of blood loss [mean estimated blood loss in IV ergometrine group was 331.2 ml/320.33, rectal misopristol group was 310.7/305.9, sublingual misopristol group was 227.6/270.01, respectively. $P1 = 0.001^{*}$, $P2 = 0.001^{*}/P1 = 0.036^{*}$, $P2 = 0.045^{*}$]. The most common side effects occurred in sublingual misopristol group 8% had fever, 30% had shivering in Alexandria group and 98% had shivering in Jamhoriya group.

Conclusion: Misoprostol has a revolutionary potential to reduce death and morbidity from postpartum hemorrhage. Sublingual misopristol is a more effective uterotonic drug in management of third stage of normal labor than IV ergometrine and rectal misoprostol.

1. Introduction

The third stage of labor is the time between the delivery of the baby and delivery of the placenta. Separation of the placenta from the uterine wall results from a combination of capillary hemorrhage and uterine muscle contraction. The length of the third stage of labor, and its subsequent complications, depends on the length of time it takes for placental separation and the ability of the uterine muscle to contract. It is a critical stage in the management and prevention of post partum hemorrhage.[1,2]

Postpartum hemorrhage is the most common cause of maternal mortality and accounts for one-quarter of the maternal deaths worldwide. The optimal solution for the vast majority, if not all, of these tragedies is prevention, both before the birth, by assuring that women are sufficiently healthy to withstand postpartum hemorrhage should it occur, and at the time of the birth, by the use of physiological or active management of labor, a management strategy that unfortunately is dependent on circumstances and the availability of uterotonics.[3]

Active management of third stage of normal labor includes administration of uterotonic medications after delivery of the baby, early clamping and cutting the umbilical cord and controlled traction of umbilical cord while separation and delivery of the placenta. Uterotonic medications are oxytocin, ergot alkaloids, syntometrine and misoprostol.[4]

Misoprostol is a prostaglandin E1 analog and it is one of the cheapest prostaglandins, easily used and stored. Misoprostol is available in tablet form that can be administered by oral, sublingual, rectal or vaginal route. It is stable at room temperature and inexpensive. The use of misoprostol is proliferating around the world. It is a life saving treatment for severe postpartum hemorrhage and it is also used to reduce blood loss during labor. It is also used in induction of labor and induction of abortion. Also it has other nonobstetric use as it is used in the treatment of peptic ulcer.[5,6]

2. Methods

The study was conducted on three hundred full term primigravida (150 in Egypt & 150 in Libya) randomly allocated prepared for normal vaginal delivery selected from the inpatient clinics of El-Shatby Maternity University Hospital, University of Alexandria and Al-Jamhoriya, University of Benghazi (from 1 to 6/2011). They were enrolled in the study which started after the protocol was approved by the committee of ethics in medical research in both faculties of medicine in Alexandria and in Benghazi, and obtaining an informed consent from each patient.

All pregnant women were subjected to full history taking (obstetric, medical, and surgical), complete general examination to exclude the presence of any disorders and obstetrical examination where the high risk patients of postpartum hemorrhage ''twins, polyhydramnios, placenta praevia, diabetes mellitus, kidney diseases'' were excluded.

In each center all pregnant women had underwent normal vaginal deliveries and were divided into three groups according to the drug used in management of the third stage of labor. Group I: the third stage of labor was actively managed by one ampoule of ergometrine (10 ml) IV after delivery of anterior shoulder of the baby. Group II: the third stage was actively managed by one rectal tablet of misoprostol. Group III: the third stage of labor was actively managed by one sublingual tablet of misoprostol.

All patients were closely observed for time of placental delivery, amount of blood loss by hemoglobin and hematocrit value pre and immediately post delivery (within 1 h), {then calculation of estimated blood loss using the following equation EBL = (BV)X(HCTO-HCTf)/HCTave where:

EBL = estimated blood loss, BV: blood volume = body weight X600 cc KG&HCTO = initial hematocrit
HCTf = final hematocrit
HCTave = (HCTO + HCTF)/2}[7]

use of oxytocin and any recorded side effects.

The results of the study in Alexandria & Benghazi were tabulated & analyzed with the use of appropriate statistical methods and appropriate figures and diagrams and the study was a double-center study. The data of the study revealed the following results.

3. Results

In Alexandria group: the mean estimated blood loss in ml in group I (IV ergometrine) was 331.2, in group II (rectal misopristol) was 310.7 and in group III (sublingual misopristol) was 227.6 (Fig. 1). In Libyan group: the mean estimated blood loss in ml in group I (IV ergometrine) was 220.33, in group II (rectal misopristol) was 205.9, and in group III was 190.01. It was found that there was statistical significant difference between the studied groups regarding the estimated blood loss ($P < 0.05$) (Table 1).

In Alexandria group: the mean of time of placental separation in minutes in group I (IV ergometrine) was 7.20, in, in group II (rectal misopristol) was 6.72 and group III (sublingual misopristol) was 6.21. In Libyan group: the time of placental separation in group I (IV ergometrine) was 15.44, in group

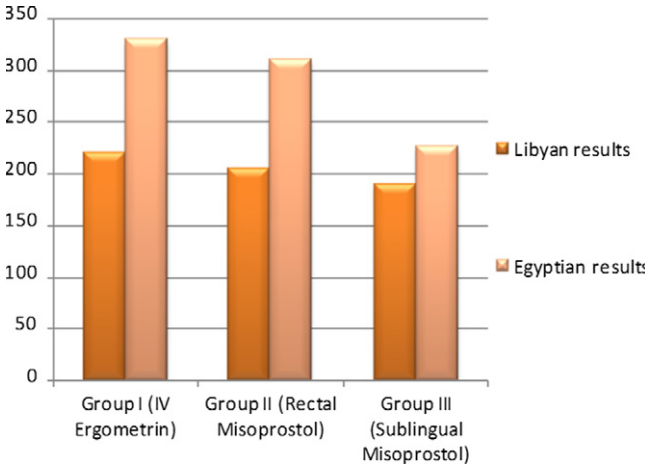

Figure 1 Estimated blood loss in ml.

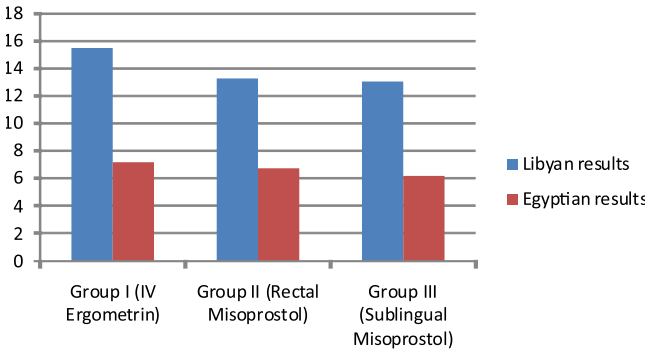

Figure 2 Time of placental separation.

II (rectal misopristol) was 13.2, and in group III (sublingual misopristol) was 13.08 (Fig. 2). It was found that there was statistical significant difference between the studied groups regarding the time of placental separation ($P < 0.05$) (Table 2).

4. Discussion

Even with major advances in prevention of postpartum hemorrhage, approximately 3% of all women in a variety of populations will have severe postpartum hemorrhage with blood loss of 1000 ml or more. Those women will require management with correction of shock, blood and fluid replacement and homeostasis of the source of bleeding.[7]

Active management of labor incorporates three main interventions, administration of uterotonic medication after delivery of the baby, early clamping and cutting the umbilical cord and controlled traction on the umbilical cord while awaiting placental separation & delivery.[8]

In El-Shatby Maternity University Hospital study, it was conducted on 150 primigravidae with low risk of developing postpartum hemorrhage allocated for spontaneous vaginal birth from El-Shatby Maternity University Hospital. The third stage of labor was actively managed in all cases by early clamping and cutting the umbilical cord and controlled traction on the umbilical cord while awaiting placental delivery then they were divided into three groups according to the uterotonic agent used. We compared the three groups according to estimated blood loss, time of placental delivery, use of oxytocin, presence of side effects and presence of postpartum hemorrhage to evaluate the efficacy of IV ergometrine and rectal misopristol versus sublingual misopristol.

In El-Shatby Maternity University Hospital we found that 200 mcg sublingual misopristol was more effective than 200 mcg rectal misopristol and IV ergometrine (10 ml) immediately after delivery of the baby as it decreased the time of placental delivery [mean time of placental separation in minutes in IV ergometrine group was 7.20, in rectal misopristol group was 6.72 and sublingual misopristol group was 6.21 min, $P1 = 0.045^{*}$, $P2 = 0.003^{*}$] and decreased the amount of blood loss [mean of estimated blood loss in ml in IV ergometrine group was 331.2 in rectal misopristol group was 310.7 and in sublingual misopristol group was 227.6. $P1 = 0.001^{*}$, $P2 = 0.001^{*}$]. Also we found that it is more significant in sublingual misopristol than the other two groups regarding final hematocrit level [mean final hematocrit in IV ergometrine group was 34.6, in rectal misopristol group was 35 and in sublingual misopristol group was 35.8, $P1 = 0.021^{*}$, $P2 = 0.038^{*}$]. The most common side effects to occur in IV ergometrine group were: 20% had nausea or vomiting, 14% had increase in blood pressure and 16% had headache. While in rectal misopristol group 10% had fever, 32% had shivering and 2% had nausea or vomiting. In sublingual misopristol group 8% had fever and 30% had shivering. Cases which had atonic postpartum hemorrhage [IV ergometrine group: 6%, rectal misopristol group 2% and sublingual misopristol group no patients (0%)] were managed by giving higher doses of misopristol, IV oxytocin and fluid transfusion, all responded to management without need for further intervention.

Table 1 Comparison between the different studied groups regarding estimated blood loss (Fig. 1).

Estimated blood loss (ml)	Group I (IV ergometrine)	Group II (rectal misoprostol)	Group III (sublingual misoprostol)
Egyptian results			
Range	114.92–719.29	116.72–490.72	112.51–364.24
Mean	331.1955	310.69	227.5612
SD	140.26643	101.0	73.24817
Libyan results			
Range	50.17–853.9	25.0–890.22	20.42–702.0
Mean	220.33	205.9	190.01
SD	190.84	180.1	177.54
P	0.001	0.001	0.001

Table 2 Comparison between the different studied groups regarding time of placental separation (Fig. 2).

Time of placental separation (minute)	Group I (IV ergometrine)	Group II (rectal misoprostol)	Group III (sublingual misoprostol)
Egyptian results			
Range	2–14	5–8	4–8
Mean	7.20	6.72	6.21
SD	2.814	1.025	1.98
Libyan results			
Range	5–40	5–45	10–30
Mean	15.44	13.2	13.08
SD	8.13	5.5	3.87
P	0.001	0.001	0.001

In Al-Jamhoriya Hospital, Garyounis University study they found that sublingual misopristol was more effective than IV ergometrine in shortening the time of placental delivery but had the same effect as rectal misopristol [mean time of placental delivery in minutes in IV ergometrine group was 15.44, in rectal misopristol group was 13.2 and sublingual misopristol group was 13.0 min, $P1 = 0.033^{*}$, $P2 = 0.433$]. Also they found that sublingual misopristol was more effective than rectal misopristol and IV ergometrine in decreasing blood loss in third stage of labor [mean of estimated blood loss in ml in IV ergometrine group was 220.33, in rectal misopristol group was 205.9 and in sublingual misopristol group was 190.01. $P1 = 0.036^{*}$, $P2 = 0.045^{*}$]. Also they found that it was more significant in sublingual misopristol than the other two groups regarding final hematocrit level [mean final hematocrit in IV ergometrine group was 34.27, in rectal misopristol group was 31.2 and in sublingual misopristol group was 31.77, $P1 = 0.046^{*}$, $P2 = 0.0008^{*}$]. The most common side effects to occur in IV ergometrine group were 18% had nausea and vomiting and 8% had shivering. While in rectal misopristol group 10% had shivering. In sublingual misopristol group 28% had shivering. Cases which had atonic postpartum hemorrhage [IV ergometrine group 10%, rectal misopristol group 2% and sublingual misopristol group no patients (0%)] were managed by giving higher doses of misopristol, IV oxytocin and fluid transfusion, all responded to management without need for further intervention.

Singh et al.[9] have suggested that administration of sublingual misoprostol was more effective than intravenous oxytocin, and intravenous methylergometrine for active management of the third stage of labor in a double-blind randomized trial of 300 women with a healthy singleton pregnancy allocated into groups to receive either: 400 mcg or of sublingual misoprostol, 5 IU of intravenous oxytocin, or 200 mcg of intravenous methylergometrine. This is matching with our results.

Winikoff et al.[10] have suggested that in settings in which use of oxytocin is not feasible, sublingual misoprostol might be a suitable first-line treatment alternative for post-partum hemorrhage. As in this double-blind, 9348 women not exposed to prophylactic oxytocin had blood loss measured after vaginal delivery at four hospitals in Ecuador, Egypt, and Vietnam. Of them: 978 (10%) women were diagnosed with primary post-partum hemorrhage and were randomly assigned to receive 800 μg misoprostol ($n = 488$) or 40 IU intravenous oxytocin ($n = 490$). Primary endpoints were cessation of active bleeding within 20 min and additional blood loss of 300 ml or more after treatment. Clinical equivalence of misoprostol would be accepted if the upper bound of the 97·5% CI fell below the predefined margin of 6%. All outcomes were assessed from the time of initial treatment. Active bleeding was controlled within 20 min with study treatment alone for 440 (90%) women given misoprostol and 468 (96%) given oxytocin (relative risk [RR] 0.94, 95% CI 0.91–0.98; crude difference 5.3%, 95% CI 2.6–8.6). Additional blood loss of 300 ml or greater after treatment occurred for 147 (30%) women receiving misoprostol and 83 (17%) receiving oxytocin (RR 1.78, 95% CI 1.40–2.26). Shivering (229 [47%] vs 82 [17%]; RR 2.80, 95% CI 2.25–3.49) and fever (217 [44%] vs 27 [6%]; 8.07, 5.52–11.8) were significantly more common with misoprostol than with oxytocin. No women had hysterectomies or died. Our results concluded better efficacy of sublingual misopristol group as it included only low risk primigravidas.

Chhabra et al.[11] have suggested that a low dose of sublingual misoprostol appears to be as effective as a low dose of IV methylergometrine in the prevention of post-partum hemorrhage in low-risk cases. So given the advantages of its stability at room temperature, low cost and easy route of administration, misoprostol appears to be a better choice. However, we found that sublingual misoprostol is more effective than IV ergometrine.[11]

Shivering and hyperpyrexia were the most common side effects of misoprostol. Patted et al.[12] mentioned in their study that misoprostol is associated with a significant increase in postpartum maternal shivering and fever. Given its proven efficacy for the prevention of postpartum hemorrhage, the benefits of misoprostol are greater than the associated risks. As in their study 1620 women delivering at home or sub-centers in rural India were randomized to receive misoprostol or placebo in the third stage of labor. Women were evaluated for shivering, fever, nausea, vomiting and diarrhea at 2 and 24 h postpartum. Symptoms were graded as absent, mild-to-moderate or severe. The result of this study was women who received misoprostol had a significantly greater incidence of shivering (52% vs. 17%, $p < 0.001$) and fever (4.2% vs. 1.1%, $p < 0.001$) at 2 h postpartum compared with women who received placebo. At 24 h, women in the misoprostol group experienced significantly more shivering (4.6% vs. 1.4%, $p < 0.001$) and fever (1.4% vs. 0.4%, $p < 0.03$). There were no differences in nausea, vomiting or diarrhea between the two groups. These results are not matching with our results that revealed an incidence of fever in sublingual misopristol group 8% and incidence of shivering was 30%, but this may be explained by the difference in number of cases.

Finally, misoprostol is a drug of low-cost, easy-to-administer, powerful uterotonic with an excellent safety profile and

long shelf-life, misoprostol has a revolutionary potential to reduce death and morbidity from postpartum hemorrhage in precisely those situations where it is most common – delivery at home without a skilled birth attendant and sublingual route is the most rapidly absorbable route, and a more effective uterotonic drug in the management of the third stage of the normal labor, with excellent safety.

References

1. Arias F. Post partum complications*Practical guide to high risk pregnancy and delivery*. 2nd ed. Mosby; 1993.
2. AbouZahr C. Antepartum and postpartum haemorrhage. In: Murray CJL, Lopez AD, editors. *Health dimensions of sex and reproduction*. Boston: Harvard University Press; 1998. p. 172–81.
3. World Health Organization. Take every mother and child count. Geneva: the World Health Organization, 2005:62–3.
4. WHO Recommendations on Prevention of Postpartum Hemorrhage. Geneva: WHO, 2007.
5. Lagenbach C. Misoprostol in preventing postpartum hemorrhage: a meta-analysis. *Int J Gynecol Obstet* 2006;**92**:10–8.
6. Gemezell-Danielsson. Misoprostol pharmacokinetic profiles and side effects. *Int J Gynecol Obstet*. 2007;**99**:S160–7.
7. Høj L, Cardoso P, Nielsen BB, Hvidman L, Nielsen J, Aaby P. Effect of sublingual misoprostol on severe postpartum haemorrhage in a primary health centre in Guinea-Bissau: randomised double blind clinical trial. *BMJ* 2005;**331**:723.
8. Prendiville WJ, Elbourne D, McDonald S. Active versus expectant management in the third stage of labor. *Cochrane Database Syst Rev* 2007(3);CD000007.
9. Singh G, Radhakrishnan G, Guleria K. Comparison of sublingual misoprostol, intravenous oxytocin, and intravenous methylergometrine in active management of the third stage of labor. *Int J Gynaecol Obstet*. 2009;**107**(2):130–4.
10. Winikoff B, Dabash R, Darwish E. Treatment of post-partum haemorrhage with sublingual misoprostol versus oxytocin. *The Lancet* 2010;**375**(9710):210–6.
11. Chhabra S, Tickoo C. Low-dose sublingual misoprostol versus methylergometrine for active management of the third stage of labor. *J Obstet Gynaecol Res* 2008;**34**(5):820–3.
12. Patted SS, Goudar SS, Naik VA. Side effects of oral misoprostol for the prevention of postpartum hemorrhage: results of a community-based randomised controlled trial in rural India. *J Matern Fetal Neonatal Med* 2009;**22**(1):24–8.