Evaluate the Potency of Misoprostol for Management of Postpartum Hemorrhage in Maternal Women

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ABSTRACT

The present study to investigate the extent of use of misoprostol in postpartum hemorrhage. To evaluate the knowledge of prevention and treatment of managing PPH among health care providers. To educate the pregnant women and midwives on the treatment approaches for PPH. The present study was conducted in RVS Institute of Medical Sciences, Chittoor, Andhra Pradesh. In the wards of obstetrics and gynecology, especially in the postnatal ward. The materials required for the study are collected from the gynecology and obstetrics department of the hospital included in the study. The study details with all the details of aim, objective, methodology, inclusion criteria, exclusion criteria, expected outcome have been submitted to the ethical committee, and after getting a positive opinion from the institution ethics committee (IEC) towards the study, the work has been started. The study included about 316 maternal women. All the women included in the study have been administered with Misoprostol after giving birth to the neonate to prevent the occurrence of atonic PPH, which is the most widely seen complication resulting in birth of maternal women. The common side effects observed in the maternal women were vomiting, which was reported in 27 women out of 316 women. Diarrhea was reported in 12 women out of all study population. Shivering was accounted in 167 women, thus, shivering is the major side effect noted with administration of misoprostol. One women was reported with an elevated diastolic blood pressure of >100 mm of Hg out of 316 women. Manual removal of placenta was necessitated in 19 women. Misoprostol was administered in all the women (n = 316) after 4-5 hours of delivery. However, it's needed to increase the mandatory guidelines for management of various complications accounted during delivery to prevent maternal mortality rate.

INTRODUCTION

Postpartum hemorrhage (PPH) is a condition in which the failure of the uterus to contract adequately after childbirth, which is known as uterine atony is not adequate (Norman et al., 1991). This results in a condition called postpartum hemorrhage, which very commonly involves heavy blood loss (El-Refaey and Templeton, 1994). Thus, World Health Organization has reported that one third maternal deaths occurred world wide have been accounted from PPH. About 99% of maternal deaths...
Clinical management of PPH

During the third stage of PPH, it can be managed clinically either by following hysterectomy or other surgical procedures to reduce the rate of blood flow (Hofmeyr et al., 2009). But, the major drawback of following a surgical procedure includes, consideration of fertility and the extent of burden of PPH should always be quantified before performing a surgery (Afolabi et al., 2010). Beyond surgery, therapeutic management of PPH includes injectable use of Oxytocin or ergotamine is considered (Çalışkan et al., 2003). But, the major drawbacks of oxytocin and ergotamine includes critical storage conditions, due to their thermolabile properties (International Confederation of Midwives and International Federation of Gynaecology and Obstetrics, 2007).

Misoprostol is the alternative choice of drug for treating PPH in any stage (Baltimore, 2012). Misoprostol is a thermostable drug which can be used either orally or vaginally, which is also effective for inducing abortion and also for initiation of labor by making the uterus to contract, and for use in conditions of peptic ulcer disease caused by prostaglandin synthetase inhibitors (Carroli et al., 2008). Misoprostol is a synthetic analogue of methyl ester of natural prostaglandin E1(14). Misoprostol exhibits good absorption properties, which shows its peak plasma concentrations within 30min after administering orally or sublingually (Prata et al., 2009; Rajbhandari et al., 2006).

Aims and objectives

1. To investigate the extent of use of misoprostol in postpartum hemorrhage.
2. To evaluate the knowledge of prevention and treatment of managing PPH among health care providers.
3. To educate the pregnant women and midwives on the treatment approaches for PPH.
4. To investigate any additional need for administration of oxytocin is required in patients treated with misoprostol.

MATERIALS AND METHODS

The present study was conducted in RVS Institute of Medical Sciences, Chittoor, Andhra Pradesh. In the wards of obstetrics and gynecology, especially in the postnatal ward. The materials required for the study are collected from the gynecology and obstetrics department of the hospital included in the study. The study details with all the details of aim, objective, methodology, inclusion criteria, exclusion criteria, expected outcome have been submitted to the ethical committee, and after getting a positive opinion from the institution ethics committee (IEC) towards the study, the work has been started.

Study was conducted in the obstetrics and gynecology departments of the hospital, especially in the labor and postnatal ward. It was carried out during the period of June 2016 and December 2016.

Inclusion criteria

The study included all the age groups of pregnant women brought to labor ward and shifted to postnatal ward within 1-2 days after giving birth to child.

Exclusion criteria

Pregnant women admitted to antenatal ward, maternal women brought to postnatal ward after 2 days of giving birth to the child and other women admitted to the gynecology and obstetrics ward with other menstrual complaints.

REPORTS AND DISCUSSION

The present study was conducted in RVS Institute of Medical Sciences, Chittoor, Andhra Pradesh, in the departments of obstetrics and gynecology. The study has included all the maternal women undergone delivery during the study period of June 2018 and December 2018. The study included about 316 maternal women. All the women included in the study have been administered with Misoprostol after giving birth to the neonate to prevent the occurrence of atonic PPH, which is the most widely
Table 1: Various Demographic Parameters of Maternal Women  

| Parameters                                | Number of women or mean (SD) (Total, n = 316) |
|-------------------------------------------|-----------------------------------------------|
| **Demographic characteristics**           |                                               |
| Maternal age (years)                      | 27.8 (5.9)                                    |
| Maternal weight (kg)                      | 79.4 (12.1)                                   |
| Maternal height (cm)                      | 165.1 (6.6)                                   |
| Primigravidae                             | 145 (51)                                      |
| Gestational age at delivery (weeks)       | 38.9 (2.0)                                    |
| **Labour variables**                      |                                               |
| Spontaneous onset                         | 210 (78)                                      |
| Augmentation of labor                     | 91 (34)                                       |
| Epidural analgesia                        | 176 (56)                                      |
| Narcotic analgesia                        | 92 (37)                                       |
| Episiotomy                                | 43 (23)                                       |
| First and second degree tear              | 123 (55)                                      |
| Instrumental vaginal delivery             | 75 (20)                                       |
| Length of 1st stage (h)                   | 6.6 (4.0)                                     |
| Length of 2nd stage (min)                 | 69 (61)                                       |
| Birth weight (kg)                         | 3.15 (0.60)                                   |

Table 2: Vitals Measured in Study Population before and after Delivery  

| Parameters               | N   | Before delivery | After delivery | Difference | P    |
|--------------------------|-----|-----------------|----------------|------------|------|
| Systolic BP (mm of Hg)   | 316 | 118.8 (12)      | 117.6 (12)     | -1.2 (0.9) | 0.3  |
| Diastolic blood pressure| 316 | 74.5 (7)        | 74.2 (11)      | -0.3 (0.5) | 0.21 |
| Hemoglobin (g/dL)        | 112 | 12.1 (1.1)      | 12.0 (1.2)     | -0.1 (0.13)| 0.04 |
| Haematocrit              | 118 | 0.43 (0.03)     | 0.41 (0.04)    | -0.02 (0.004) | 0.045 |
| Temperature (°C)         | 219 | 36.4 (0.4)      | 37.2 (0.8)     | 0.8 (0.06) | 0.002 |

Table 3: Categorization and Incidence of PPH in Study Population  

| Various parameters                                 | n = 316 (SD or %) |
|---------------------------------------------------|-------------------|
| Blood loss ≤ 500 mL                               | 20 (6.32%)        |
| Blood loss > 100 mL                               | 0 (0%)            |
| Blood loss (mL)                                   | 210 (160-300)     |
| Manual removal of placenta                        | 19 (6.01%)        |
| Required for other uterotonics like oxytocin and ergotamine | 16 (5.06%)  |
| Systolic BP ≥ 150 (mmHg)                          | 4 (1.26%)         |
| Diastolic BP ≥ 100 (mmHg)                         | 1 (0.31%)         |
| Haemoglobin < 9 (g/dL)                            | 12 (3.79%)        |
| Third stage length (min)                          | 5 (4-8)           |
| Third stage length ≥ 30 min                       | 1 (0.5)           |
| Vomiting                                          | 27 (8.54%)        |
| Diarrhea                                          | 12 (3.79%)        |
| Shivering                                         | 167 (52.8%)       |
seen complication resulting in birth of maternal women.

Different demographic details of the study population including primiparous and gravidae have been collected from the case reports of individual patients and are observed for time of administration of drug with respect to clinical condition and the outcomes are measured, which are represented in the Table 1. The mean age of maternal women was 27.8 yrs of mean, with a SD of 5.9. The maternal weight of all the women was found to be with a mean of 79.4 years with SD of 12.1, the mean(SD) maternal height of overall study population was found to be 165.1 (6.6), and the primigravidae of aver all population accounted for 145 women., gestational age of all the women with a mean of 38.9 and SD of 38.9 was evaluated.

Spontaneous onset of labor was reported in 210 women, augmentation for labor was done in 91 women, epidural analgesia was given for 176 women, narcotic analgesia was given in 92 women, first and second degree tear was noted in 123 women, 75 women required instrumental vaginal delivery due to complications involved during normal delivery like altered quantities of umbilical fluids etc. episiotomy was performed in 43 women.

Length of first stage of labor was noted with a mean of 6.6 hours in all the women with a SD of 4.0 and the mean of second stage of delivery was found to be 69, with a standard deviation of 61.

The mean birth weight of all the neonates was found to be 3.15kg with a standard deviation of 0.6, which is represented In the Table 1.

Various vital parameters like blood pressure, hemoglobin levels, haematocrit and temperature have been recorded in the study population. The diastolic blood pressure of all the maternal women involved in the study was recorded with a mean of 74.5 (International Confederation of Midwives and International Federation of Gynaecology and Obstetrics, 2007) before delivery and 74.2 (Çalişkan et al., 2003) after delivery with a difference of -0.3, which is interpreted to be nil significant. Thus, diastolic blood pressure does not show any variation with delivery (Derman et al., 2006).

The systolic blood pressure before delivery was noted with a mean of 11.8 (International Confederation of Midwives and International Federation of Gynaecology and Obstetrics, 2007) and 117.6 (International Confederation of Midwives and International Federation of Gynaecology and Obstetrics, 2007) after delivery, thus it has proven that systolic blood pressure does not show any significant difference with delivery. Hemogoblin levels accounted with a mean of 12.1 before delivery and 12.0 after delivery in women, thus, administration of misoprostol has proven to prevent increased blood loss after labor (Carroli et al., 2008) . Haematocrit was noted as 0.43 of mean value before delivery and 0.41 after delivery (Sanghvi et al., 2010) . Temperature was recorded with a mean of 36.4 °C before delivery and 37.2 °C after delivery and the significant difference P was noted as 0.002, which was enlisted in the Table 2.

The stage of PPH and incidence of PPH in all the maternal women were observed (Islamic Republic of Afghanistan Ministry of Public Health, 2005). Blood loss more than or equal to 500 mL is referred to as first stage PPH and blood loss more than or equal to 1000 mL after within 24 hours of delivery is taken as 2nd stage of PPH.

All the women included in the study have been administered with misoprostol within 4-5hrs after delivery. The common side effects observed in the maternal women were vomiting, which was reported in 27 women out of 316 women. Diarrhea was reported in 12 women out of all study population. Shivering was accounted in 167 women, thus, shivering is the major side effect noted with administration of misoprostol. One women was reported with a elevated diastolic blood pressure of >100 mm of Hg out of 316 women. (Tang, 2002). Manual removal of placenta was necessitated in 19 women, which is represented In the Table 3.

CONCLUSIONS

Misoprostol was administered in all the women (n = 316) after 4- 5 hours of delivery. One women was recorded with elevated diastolic blood pressure >100 mm of Hg and no women was reportedly noted with systolic blood pressure >140 mm of Hg. More than 80% of health care team were aware of use of misoprostol for prevention and management of PPH(21). However, it's needed to increase the mandatory guidelines for management of various complications accounted during delivery to prevent maternal mortality rate.

ACKNOWLEDGEMENT

The authors highly acknowledge the Chairperson and Management trustee, Tagore Educational Trust, Rathinamangalam, Chennai, Tamilnadu and B.S.Abdur Rahman Crescent Institute of Science and Technology, Chennai, Tamilnadu, for providing facilities to pursue this research work.

Funding Support
Nil.

Conflict of Interest

The author does not have any Conflict of Interest in this present work.

REFERENCES

Afolabi, E. O., Kuti, O., Orji, E. O., Ogunniyi, S. O. 2010. Oral misoprostol versus intramuscular oxytocin in the active management of the third stage of labour. *Singapore Medical Journal*, 51(3):207–211.

Baltimore, M. D. 2012. Health Services Support Project Final Report. *Jhpiego*.

Çalişkan, E., Dilbaz, B., Meydanlı, M. M., Öztürk, N., Narin, M. A., Haberal, A. 2003. Oral Misoprostol for the Third Stage of Labor. *Obstetrics & Gynecology*, 101(5, Part 1):921–928.

Carroli, G., Cuesta, C., Abalos, E., Gülmezoglu, A. M. 2008. Epidemiology of postpartum haemorrhage: a systematic review. *Best Practice & Research Clinical Obstetrics & Gynaecology*, 22(6):999–1012.

Derman, R. J., Kodkany, B. S., Goudar, S. S., Geller, S. E., Naik, V. A., Bellad, M. B., Patted, S. S., Patel, A., Edlavitch, S. A., Hartwell, T., Chakraborty, H., Moss, N. 2006. Oral misoprostol in preventing postpartum haemorrhage in resource-poor communities: a randomised controlled trial. *The Lancet*, 368(9543):1248–1253.

El-Refaey, H., Templeton, A. 1994. Early abortion induction by a combination of mifepristone and oral misoprostol: a comparison between two dose regimens of misoprostol and their effect on blood pressure. *BJOG: An International Journal of Obstetrics and Gynaecology*, 101(9):792–796.

Hofmeyr, G. J., Gülmezoglu, A. M., Novikova, N., Lindner, V., Ferreira, S., Piaggio, G. 2009. Misoprostol to prevent and treat postpartum haemorrhage: a systematic review and meta-analysis of maternal deaths and dose-related effects. *Bulletin of the World Health Organization*, 87(9):666–667.

International Confederation of Midwives and International Federation of Gynaecology and Obstetrics 2007. Prevention and treatment of post-partum haemorrhage: new advances for low resource settings. *Int J Gynecol Obstet*, 97:160–163.

Islamic Republic of Afghanistan Ministry of Public Health 2005.

McDonald, S. J., Prendiville, W. J., Blair, E. 1993. Randomised controlled trial of oxytocin alone versus oxytocin and ergometrine in active management of third stage of labour. *BMJ*, 307(6913):1167–1171.

Norman, J. E., Thong, K. J., Baird, D. T. 1991. Uterine contractility and induction of abortion in early pregnancy by misoprostol and mifepristone.

Prata, N., Gessessew, A., Abraha, A. K., Holston, M., Potts, M. 2009. Prevention of postpartum hemorrhage: options for home births in rural Ethiopia. *African Journal of Reproductive Health*, 13(2):87–95.

Rajbhandari, S., Pun, A., Hodgins, S., Rajendra, P. K. 2006. Prevention of postpartum haemorrhage at homebirth with use of misoprostol in Banke District, Nepal. *International Journal of Gynecology & Obstetrics*, 94:S143–S144.

Sanghvi, H., Ansari, N., Prata, N. J., Gibson, H., Ehsan, A. T., Smith, J. M. 2010. Prevention of postpartum hemorrhage at home birth in Afghanistan. *International Journal of Gynecology & Obstetrics*, 108(3):276–281.

Tang, O. S. 2002. Pharmacokinetics of different routes of administration of misoprostol. *Human Reproduction*, 17(2):332–336.

Toppozada, M., El-Bossaty, M., El-Rahman, H. A., El-Din, A. H. 1981. Control of intractable atonic postpartum hemorrhage by 15-methyl prostaglandin F2 alpha. *Obstetrics and Gynecology*, 58(3):327–330.

World Health Organization 1989.

World Health Organization 1991. Mortality: A Global Factbook.

Zuberi, N. F., Durocher, J., Sikander, R., Baber, N., Blum, J., Walraven, G. 2008. Misoprostol in addition to routine treatment of postpartum hemorrhage: A hospital-based randomized-controlled trial in Karachi, Pakistan. *BMC Pregnancy and Childbirth*, 8(1).