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ORIGINAL ARTICLE | OXYTOCIN VS MISOPROSTOL IN PPH

Oxytocin Versus Misoprostol Plus Oxytocin in the Prevention of Postpartum Hemorrhage at a Semi-Urban Hospital in sub-Saharan Africa: A Retrospective Cohort Study

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ABSTRACT

Background: Post-partum hemorrhage (PPH) is a leading cause of maternal mortality. Its first-line of prevention often entails uterotonic drugs like oxytocin and misoprostol which constitute a core point of management in low-resource settings of sub-Saharan Africa. This study aimed to assess the effectiveness of oxytocin alone compared with oxytocin plus misoprostol in two different eras (before and after the advert of misoprostol) of a semi-urban Cameroonian hospital.

Methods: This was a retrospective cohort study carried out between January 2015 to April 2015 and between January 2016 to April 2016 on a group of parturients (group A) who received only oxytocin and another administered oxytocin and misoprostol (group B), respectively. All participants delivered at the Bamenda Regional Hospital, Cameroon. The two different periods represent the era before and after the implementation of misoprostol in the prevention of PPH in this semi-urban hospital. Socio-demographic data, clinical characteristics and details of delivery as well as risk factors for PPH were studied from obstetric records.

Results: We studied the obstetric records of 1778 parturients were studied; 857 in group A and 879 in group B. Their mean age was 26.3 ±5.2 years. Both groups were comparable in several baseline sociodemographic and clinical characteristics. The prevalence of PPH was 2.7% (3.4% vs 2.2%; p = 0.0744). The risk of PPH in the oxytocin only group was about 1.5 times higher than in the oxytocin plus misoprostol group. The estimated blood loss between the two groups was statistically significant (1100 ± 150 vs 800 ± 100 ml, p< 0.0001). The active management of the third stage of labor without misoprostol was the only risk factor for PPH.

Conclusion and Global Health Implications: The implementation of misoprostol plus oxytocin in the prevention of PPH in this low-resource setting improved the obstetrical outcome by reducing the risk and the amount of blood loss during delivery.

Keywords: • Misoprostol • Oxytocin • Postpartum Hemorrhage • Cameroon

1. Introduction

1.1. Background of the Study

Postpartum hemorrhage (PPH) is a life-threatening obstetric emergency that occurs after cesarean section (CS) or normal vaginal delivery (NVD). It is defined as a blood loss of ≥ 500mls after a vaginal delivery or 1000mls after a cesarean delivery.[1] Worldwide, evidence abounds that PPH is the leading cause of maternal mortality, claiming 480,000 global maternal deaths between 2003 to 2009, of which 41.6% of these PPH-related maternal deaths occurred in sub-Saharan Africa (SSA).[2–7] Similarly, in Cameroon, an SSA country, many interventions still need to be done to decrease the contemporary maternal mortality ratio (MMR) from 789 per 100, 000 live births to the targeted global MMR of less than 70 per 100,000 live births by the year 2030.[8] The way forward partly entails curbing the burden of PPH which has been reported as the primary cause of maternal deaths in many hospital-based audit reports,[8,9] as well as tackling a composite of factors which further contribute to a high MMR in this country such as inadequate antenatal care coverage,[8] late hospital presentation of parturients with obstetrical complications, the relatively high cost of health care poverty and the absence of a national health insurance policy.[9] Efforts to curb PPH-related maternal mortality have focused on several medical treatments, mechanical or non-pharmacological measures, uterus preserving surgeries surgery or hysterectomy.[10]

Medical management with uterotonic drugs remains an important integral part of the first-line management of PPH,[10] particularly as the main etiology of PPH in Cameroon and most SSA countries is uterine atony.[11,12] The most commonly used uterotonic agents in hospital-based settings in Cameroon are oxytocin, methyl-ergometrine, misoprostol and carboprost tromethamine.[4] Sulprostone, a potent uterotonic drug is inexistent or scarcely available in Cameroon.[4] The usual protocol used to treat PPH due to uterine atony using uterotonics in this country entails the successive administration of an oxytocin infusion, a single dose of methylergometrine, and then carboprost tromethamine are used in 15-to-20-minute intervals. They are administered parenterally and therefore require skillful health personnel for their administration to parturients. Also, ergometrine requires refrigeration and oxytocin may be inactivated if exposed to high temperatures. Misoprostol, a prostaglandin E_1 analog, is an inexpensive readily available drug and can be absorbed by the following routes of administration: vaginally, rectally, or sublingually.[13,14] Gastrointestinal symptoms (nausea, vomiting, and diarrhea), shivering and fever are the most common adverse effects of misoprostol, which often are mild and self-limited.[15,16] The off-label use of misoprostol has entered into clinical practice for this indication because of its strong uterotonic properties, and its advantages over other synthetic prostaglandin analogs due to the advantage that it does not necessarily requires skilled personnel for its administration. Furthermore, its aforementioned numerous routes of administration, its stability at ambient temperatures, the long half-life, wide availability, and low cost are some additional advantages of misoprostol use.[17,18] A 600 mcg dose of oral misoprostol is safe and effective in preventing PPH.[19,20] It is worth mentioning that the oxytocin is most potent uterotonics at this writing and WHO recommends its only use as first-line uterotonic to prevent PPH.[10] However, due to the aforementioned benefits of misoprostol, the use of misoprostol to prevent PPH has received considerable attention in Cameroon (with an alarming MMR of 789 per 100, 000 live births),[8] where unpublished guidelines by the Cameroon Society of Obstetricians and Gynecologists (CSOG) recommend the concomitant use of oxytocin and misoprostol since 2014 for a more potent synergistic uterotonic effect geared at the prevention of PPH. However, misoprostol was not widely available in Cameroon until September 2015. Prior to this date very few stokes of it where available only in urban parts of Cameroon. The widespread distributions and/or sales of misoprostol to semi-urban and rural areas of Cameroon began in November 2015. Against this background, we sought to evaluate the effectiveness of oxytocin versus oxytocin plus misoprostol in the prevention of PPH in a semi-urban Cameroonian hospital by comparing the era when oxytocin was used alone to the era

when the combined oxytocin-misoprostol protocol was used.

1.2. Objectives of the Study

The study objective was to assess the effectiveness of oxytocin compared to oxytocin and misoprostol alone in the prevention of PPH amongst women delivering at the semi-urban sub-Saharan African Hospital. We hypothesized that misoprostol plus oxytocin will be more efficacious in preventing PPH compared to oxytocin alone.

2. Methods

2.1. Study Design and Setting

This study was a retrospective cohort study. The study setting was the Bamenda Regional Hospital (BRH), Cameroon. The BRH is a state-owned university teaching hospital located in a semi-urban region of the Northwest Region of Cameroon. The BRH is a secondary level health facility in the referral system of Cameroon. It thus serves as a referral hospital for nearby primary health centers in the Northwest Region of Cameroon. The BRH is made up of with the following departments: Pediatrics, Surgery, Obstetrics/Gynecology, Radiology, Nephrology/Hemodialysis, Anesthesiology/Operating room, Intensive Care Unit, Emergency Unit and Internal Medicine department. The study precisely took place in the Obstetrics/Gynecology Unit of the hospital. This unit is further divided into three outpatient consultation rooms which serve for both gynecological consult and antenatal care visits; a family planning unit; an admission ward with a capacity of 33 beds; a labor ward that is sub-divided into six delivery rooms. The Obstetrics/Gynecology Unit is run by three Obstetricians-Gynecologists, two general practitioners and 16 midwives. Averagely, there is one Obstetricians-Gynecologist, one general practitioner and five midwifes per 12 hourly working shifts.

2.2. Study Population and Study Procedure

Through a chart review, were enrolled the obstetric records of all consecutive women with a minimum gestational age of 28 weeks who delivered at the BRH. The files of these parturients were divided into two groups. One group (group A) comprised of all women who gave birth between January 2015 to April 2015, before the implementation of misoprostol use for PPH prevention. This group was routinely administered oxytocin 10 IU intravenously within a minute after vaginal delivery or administration of 10 UI intravenously within a minute after cesarean delivery followed by continuous infusion of 30 IU of oxytocin in Dextrose 5% solution over the next 24 hours of delivery as medical treatment to prevent PPH. The other group (group B) comprised of the obstetric records of all women delivering at the BRH between January 2016 to April 2016 after the implementation of misoprostol in BRH for the PPH prevention. This group was administered 800 mcg of misoprostol sublingually or intra-rectally after within a minute following vaginal/cesarean delivery plus oxytocin 10 IU intravenously within a minute after vaginal delivery or administration of 10 IU intravenously within a minute after caesarean delivery followed by continuous infusion of 30 IU of oxytocin in Dextrose 5% solution over the next 24 hours of delivery as medical treatment to prevent PPH. During the aforementioned chart review, we identified all names women who delivered in the labor room of BRH by consulting the admission registry. Then we proceeded to the archives of the Obstetrics/Gynecology Unit where the files of all these women were retrieved. For women who delivered by cesarean delivery we consulted the operating room register to get details of the operations.

2.3. Study Variables

Overall, through the chart review process we studied the following variables (i) Socio-demographic data: maternal age, level of education, occupation, religion, marital status, urban/rural residence, gestational age, birth weight of the newborn, and gender of the neonate. (ii) Clinical characteristics: maternal comorbidities, parity, gravidity. (iii) Details of delivery: induction of labor, vaginal/cesarean delivery, type/amount/route of uterotonic drugs administered, singleton/multiple pregnancies, spinal/general anesthesia for cesarean section delivery, the occurrence of PPH, etiology of PPH, non-medical and surgical management of PPH, maternal or neonatal death.

2.4. Definition of Terms

PPH was defined as an estimated blood loss greater than 500 ml within 24 hours after vaginal delivery and greater than 1000 ml following cesarean section.[1] Medical management of PPH was defined as the parenteral administration of oxytocin, methyl-ergometrine, and/or misoprostol. Non-medical management of PPH entailed uterine massage, bimanual uterine compression followed by subsequent compression of the abdominal aorta, and/or repair of any vaginal or cervical lacerations and manual uterine revision where appropriate.[10] Uterus preserving surgery was defined as any surgical intervention consisting of ligation of pelvic arteries or application of uterine compression sutures to achieve hemostasis while concomitantly conserving the uterus e.g. Bilateral hypogastric artery ligation, Uterine artery ligation, B-lynch uterine compression suture, Tsirulnikov triples ligation and Hysterorraphy. Tsirulnikov Triple ligation entailed bilateral ligation of the round ligaments, utero-ovarian ligaments and uterine arteries.[10] B-lynch uterine compression suture consisted of making a lower segment transverse hysterotomy or removing the sutures of a recent cesarean section to apply lateral uterine brace sutures to envelop and compress the bleeding uterus to achieve hemostasis.[21] Hysterectomy was defined as a surgical procedure geared at achieving hemostasis through resection of the uterus e.g. subtotal abdominal hysterectomy or total abdominal hysterectomy. Total abdominal hysterectomy consisted of complete resection of the uterus and cervix, while the cervical stump was left in-situ in subtotal abdominal hysterectomy.

2.5. Statistical Analysis

After obtaining data from the patients' files, questionnaires that were not properly filled were sorted out. Questionnaires were then attributed serial numbers that could help match them to the database if there was a need for cross-verification and then the data were then entered into an electronic data entry form by the primary investigator. Data were entered and analyzed using the Statistical Package for Social Sciences (SPSS) Standard version, Release 20.0 (IBM Inc. 2012). Distribution of sociodemographic and clinical characteristics was compared between the misoprostol plus oxytocin group and the oxytocin only group using the Chi-square test. We calculated the relative risk (RR) and their corresponding 95% confidence intervals (95% CI) to measure associations. The original alpha-value was set at 0.05. To reduce the chance of obtaining false-positive results from the multiple analyses performed on the same dependent variable, the Bonferroni adjusted p-value was calculated by dividing the alpha-value by the number of comparisons. The subsequent alpha values calculated were 0.0029, 0.0039 and 0.0056 as seen below in Table 1, 2 and 3 respectively. Hence, any comparison was statistically significant if it was inferior to the Bonferroni adjusted p-value. Variables with too much missing data precluding meaningful analyses were excluded. The study was approved by the Institutional Review Board of the School of Health and Human Sciences, Saint Monica University Higher Institute, Buea, Cameroon and the Ethics committee of the BRH.

3. Results

3.1. Sociodemographic Characteristics of Parturients

During the two study periods, 2056 women delivered at the BRH. Of these 2056 obstetric records, 278 were excluded because the women's gestational ages were below 28 weeks. Hence, 1778 files corresponding to 86.5% of the initial records retrieved were retained for this study. The files were repartitioned as follows: 857 in the oxytocin only group and 879 in the oxytocin plus misoprostol group. The overall mean age of 26.3 ±5.2 years (range: 14 – 48 years) with the most frequent age group being between 18-35 years (93.1%). Both groups were comparable (no statistical difference) in terms of their mean ages, age categories, places of residence (urban versus rural), parity, gravidity, gestational ages, occupations, frequency of preterm deliveries and multiple gestations. On the other hand, being married, being a Christian, being referred to the BRH by another health facility, being HIV-positive, having a history of abortion, and being pregnant of a macrosomic fetus were predictors of

Table 1: Sociodemographic and clinical characteristics of parturients

Variables	Overall, n=1778 (%)	Oxytocin only, n=857 (%)	oxytocin+misoprostol n=879 (%)	RR	95 % CI	p–value
Age (years)				-	-	0.734
<18	37 (2.2)	17 (2.0)	20 (2.3)			
18-35	1617 (93.1)	791 (92.3)	826 (94.0)			
>35	82 (4.7)	49 (5.7)	33 (3.8)			
Mean ± SD	26.28±5.15	26.33±5.22	26.24±5.09	-	-	0.7161
Occupation						
Un-skilled/ informal work	1022 (58.9)	492 (57.4)	530 (60.5)	0.8751	0.79 – 0.97	0.0092
Skilled/Formal work	714 (41.1)	365 (42.6)	349 (39.7)			
Marital Status						
Married	1169 (67.3)	535 (62.4)	634 (72.1)	0.8059	0.74 – 0.87	< 0.0001*
Single	567 (32.7)	322 (37.6)	245 (27.9)			
Religion						
Christian	1622 (93.4)	782 (91.2)	840 (95.6)	0.7264	0.63-0.84	< 0.0001*
Muslim	114 (6.6)	75 (8.8)	39 (4.4)			
Place of residence						
Urban	1646 (94.8)	808 (94.3)	838 (95.3)	0.9016	0.74 – 1.1	0.2987
Rural	90 (5.2)	49 (5.7)	41 (4.7)			
Referral						
Yes	97 (5.6)	21 (2.4)	76 (8.9)	1.64	1.46 – 1.84	< 0.0001*
No	1639 (94.4)	781 (91.1)	858 (97.6)			
Gestational age						
< 37weeks	116 (6.8)	76 (65.5)	40 (34.5)	-	-	0.2478
37 - 42weeks	1561 (91.7)	906 (58)	655 (42)			
> 42weeks	25 (1.5)	16 (64)	9 (36)			
Mean ± S.D	39.24± 2.19	39.24± 2.19	39.24± 2.19		0.0 – 0.21	1.000
Gravidity						
Primigravida	500 (29.1)	234 (27.7)	266 (30.5)	0.94	0.84 – 1.05	0.2478
Multigravida	998 (58.2)	499 (59.1)	499 (57.2)			
Grand multigravida						
Yes	218 (12.3)	111 (12.9)	107 (12.3)	1.0361	0.90 – 1.19	0.6197
No	960 (53.9)	746 (87.1)	772 (87.8)			
Parity						
Nulliparous	608 (35.3)	289 (33.7)	319 (36.3)	0.95	0.85 – 1.05	0.3313
Multiparous	1114 (62.7)	557 (64.9)	557 (63.4)			
HIV Status						
Positive	97 (5.6)	21 (2.4)	76 (8.9)	1.64	1.46 – 185	< 0.0001*
Negative	1639 (94.4)	781 (91.1)	858 (97.6)			
Preterm Delivery						
Yes	33 (2.1)	16 (2.3)	17 (2.0)	1.09	0.77 – 1.57	0.6052
No	1518 (97.9)	670 (97.7)	848 (98.0)			

(*Contd...*)

Table 1: (*Continued*)

Variables	Overall, n=1778 (%)	Oxytocin only, n=857 (%)	oxytocin+misoprostol n=879 (%)	RR	95 % CI	p–value
Abortion						
Yes	358 (22.9)	171 (19.7)	187 (26.9)	1.23	1.09 – 1.39	0.0005*
No	1204 (77.1)	509 (74.1)	695 (80.3)			
Multiple Pregnancy						
Yes	46 (2.6)	28 (3.3)	18 (2.0)	1.24	0.97 – 1.57	0.0740
No	1690 (97.4)	829 (96.7)	861 (98.0)			
Macrosomia						
Yes	145 (8.4)	91 (10.6)	54 (6.1)	1.30	1.39 – 1.49	0.0001*
No	1591 (91.6)	766 (89.4)	825 (93.9)			

*Bonferroni corrected p-value < 0.0029. RR: Relative Risk; 95% CI: 95% Confidence interval

being administered oxytocin plus misoprostol, not attenuated by Bonferonni correction (Table 1).

3.2. Peripartal Factors

Amongst the women included in this study (n=1778), 48 had PPH, giving an overall prevalence rate of PPH of 2.7%. Table 2 summarizes the proportion of women with PPH and those without PPH in the two treatment groups. The risk of PPH in the oxytocin only group was about 1.5 times higher than in the oxytocin plus misoprostol group (3.4% vs 2.2%). The amount of blood lost was significantly higher in the oxytocin group compared with the oxytocin plus misoprostol group (1100 ± 150 vs 800 ± 100 ml; p< 0.0001). Unlike cesarean delivery, vaginal delivery conveyed protection against the only use of oxytocin (RR: 0.78; < 0.0001).

3.3. Factors Associated with Postpartum Hemorrhage

In this study, 33 (68.6%) of patients with PPH required a doubled dose of 600 micrograms of misoprostol for PPH management while 15 (31.4%) of patients with PPH received adjuvant intravenous oxytocin. About 66.7% of patients with PPH had surgery for better management despite receiving medical management with oxytocin and/or misoprostol. The active management of the third stage of labor without misoprostol was the only risk factor for PPH (RR: 1.04; 95 % CI: 1.02-1.05; p: 0.0008) which was not attenuated by Bonferroni correction (Table 3).

4. Discussion

This study aimed to assess the effectiveness of oxytocin only compared with oxytocin plus misoprostol in the prevention of PPH amongst women delivering at the semi-urban sub-Saharan African Hospital between an era where misoprostol was not used and an era where it was used combined with oxytocin. We found the prevalence of PPH was 2.7%. The risk of PPH in the oxytocin only group was about 1.5-fold higher than in the oxytocin plus misoprostol group and the amount of blood lost was higher in the oxytocin only group (1100 ± 150 vs 800 ± 100 ml, p< 0.0001). The active management of the third stage of labor without misoprostol was the only risk factor for PPH.

The mean age of our study participants was 26.28±5.15 years which concurs with findings obtained by Ngwenya in Zimbabwe.[22] The most frequent age group was between 18-35 years (93.1%). There was no significant difference in the mean ages and age categories of the two study groups (p=0.734) probably explained by the fact that most women tend to have children during their most reproductive time frame.

The mean gestational age was 39.24 ±2.19 weeks. This gestational age differs from the previous reports, perhaps suggesting several factors influence the progression of a pregnancy, and the onset of labor in different environments, especially in sub-Saharan Africa where complementary and

Table 2: Intrapartum characteristics and management of postpartum hemorrhage

Variables	Overall, n=1778 (%)	Oxytocin only, n=857 (%)	Oxytocin + misoprostol n=879 (%)	RR	95 % CI	p–value
Induction of labor						
Oxytocin	11 (0.6)	6 (0.7)	5 (0.6)	1.38	0.74 – 2.57	0.3181
Misoprostol	58 (3.3)	23(2.7)	35 (3.9)			
Mode of delivery						
Vaginal delivery	1522 (85.6)	726 (84.7)	796 (90.6)	0.78	0.69 – 0.88	< 0.0001*
Cesarean delivery	214 (12)	131 (15.3)	83 (9.4)			
Anesthesia used for cesarean section						
General anesthesia	50 (56.8)	25 (53.2)	25 (61.0)	0.8636	0.59 – 1.27	0.4587
Spinal anesthesia	38 (43.2)	22 (46.8)	16 (39.0)			
Gender of neonate						
Male	852 (50.2)	405 (49.0)	447 (51.3)	0.96	0.87 – 1.06	0.4250
Female	798 (47.0)	395 (47.8)	403 (46.3)			
Number of fetuses						
Singleton pregnancy	1691 (97.7)	861(98.0)	830 (97.4)	1.13	0.80 – 1.59	0.4838
Multiple pregnancy	40 (2.3)	18 (2.0)	22 (2.6)			
Birth weight						
< 2500	79 (4.4)	31 (3.6)	48 (5.5)	0.81	0.61 – 1.08	0.1489
≥ 2500	1657 (93.2)	773 (90.2)	831 (94.5)			
Estimated blood loss (mls.)	48 (2.7)	1100 ± 150	800 ± 100	-	-	< 0.0001*
PPH						
Yes	48 (2.7)	29 (3.4)	19 (2.2)	1.24	0.98 – 1.56	0.0744
No	1696 (97.6)	828 (96.4)	868 (98.8)			
Etiology of PPH				-	-	0.3563
Uterine atony	19 (52.8)	13 (50.0)	6 (60.0)			
Retained Tissue	9 (25.0)	8 (30.8)	1 (10.0)			
Laceration	7 (19.4)	5 (19.2)	2 (20.0)			
Coagulopathy	1 (2.8)	0 (0.0)	1 (10.0)			
Blood transfusion						
Yes	11 (40.7)	4 (26.7)	7 (58.3)	0.53	0.23 – 1.24	0.1413
No	16 (59.3)	11 (73.3)	5 (41.7)			
Surgical intervention						
Yes	10 (76.9)	6 (85.7)	4 (66.7)	1.8	0.34 – 9. 64	0.4925
No	3 (23.1)	1 (14.3	2 (33.3)			
Surgical intervention						
TAH	1 (8.3)	0 (0.0)	1 (25.0)	-	-	0.463
B-Lynch	3 (25.0)	2 (25.0)	1 (25.0)			
TAL	1 (8.2)	1 (12.5)	0 (0.0)			
Repair of tear	7 (18.3)	5 (62.5)	2 (50.0)			
Episiotomy						
Yes	11 (1.1)	4 (2.3)	7 (0.8)	2.26	1.02 – 4.99	0.069
No	1036 (98.9)	167 (97.7)	869 (99.2)			

*Bonferroni corrected p-value < 0.0039; RR: Relative Risk; 95% CI: 95% Confidence interval; TAL: Tsirulnikov artery ligation; TAH: Total abdominal hysterectomy; PPH: Postpartum hemorrhage

Table 3: Factors associated with postpartum hemorrhage

Variables	PPH (-) N=1730	PPH (+) N=48	RR	95 % CI	p–value
Referral					
Yes	44 (93.6)	3(6.4)	0.95	0.88-1.03	0.1985
No	1593 (98.7)	27 (1.1)			
Gestational age (weeks)					
< 37	97 (49.0)	1 (1.0)	1.01		
≥ 37	1384 (98.2)	26 (1.8)		0.99-1.03	0.4428
Multiple Gestation					
Yes	42 (95.5)	2 (4.5)	0.97	0.91-1.03	0.3879
No	1654 (98.2)	30 (1.8)			
Macrosomia					
Yes	142 (99.3)	1 (0.7)	1.01	0.99-1.02	0.1199
No	1546 (98.1)	30 (1.9)			
Labor Induction					
No	1645 (95.7)	74 (4.3)	0.97	0.94-1.01	0.1123
Yes	60 (98.4)	1 (1.6)			
Mode of Delivery					
Normal Delivery	1446 (98.4)	23 (1.6)	1.03	0.99-1.06	0.0582
Cesarean section	197 (95.6)	9 (4.4)			
Birth Weight (g)					
< 2500	73 (4.3)	2 (6.7)	0.63	0.15-2.72	0.382
2500- 4000	1497 (88.7)	26 (86.7)			
4000	117 (6.9)	2 (6.7)			
Not precised	1023 (98.8)	12 (1.2)			
Placental Retention					
Yes	26 (86.7)	4 (13.5)	0.88	0.76-1.01	0.0696
No	994 (98.4)	13 (1.3)			
Drugs					
AMSTL	835 (97.4)	22 (2.6)	1.04	1.02-1.05	0.0008*
MISO+AMSTL	870 (94-3)	53 (5.7)			

*Bonferroni corrected p-value < 0.0056; RR: Relative Risk; 95% CI: 95% Confidence interval; PPH: Postpartum hemorrhage; AMSTL: Active management of the third stage of labor; MISO: misoprostol

alternative medicine has been reported to induce and augment labor.[23]

The prevalence of PPH in the current study was 2.7% which is quite lower than the PPH prevalence rates of 25.7% in Africa and 10.5% in sub-Saharan Africa obtained from a recent systematic review.[24] The low prevalence rate of PPH in the present study may be explained by the fact that there is generally a gross under-reporting of PPH in our health facility due to the method of estimating blood loss which often visual and subjective. It has been shown that visual estimation of blood loss underestimates the amount of blood lost by 30 %.[8] The method of estimating blood loss was the same across the two study periods permitting relative comparisons to be made without being biased. But given that the method of determining blood loss is not standard with the other studies, it is not surprising that the prevalence given in our study is in contrast with the findings of other studies.

We found that the prevalence of PPH amongst women who received oxytocin only was significantly higher compared with the prevalence amongst women who were administered oxytocin plus misoprostol (3.4% vs 2.2%). This finding corroborates with a Pakistan study that obtained similar findings after the administration of 600mcg of misoprostol sublingually with parenteral oxytocin after delivery. This helped to reduce the amount of blood loss, and PPH.[8]

Similar to other studies carried out in sub-Saharan Africa,[25] the causes of PPH were uterine atony, placenta retention, genital tract lacerations and coagulopathy. The amount of blood loss in women who received oxytocin only was significantly higher (1100 ± 150 ml) compared with those who received misoprostol plus oxytocin (800 ± 100 ml). This observation concurs with those of Blum et al in Egypt who found that the administration of oxytocin plus sublingual misoprostol versus oxytocin only was more effective in preventing and managing PPH due to uterine atony.[8] Likewise, an India study also showed misoprostol-oxytocin combination to be more effective than either misoprostol only and oxytocin only in the prevention and management of PPH.[8,25]

4.1. Limitations

With an extensive literature search, to the best of our knowledge, this study is one of the first comparative studies on oxytocin alone versus oxytocin plus misoprostol in the prevention of PPH in Cameroon. Its strength lies in its large sample size (N = 1778) and cohort design over two different eras to assess this comparison. Its main limitation is its retrospective design because the obstetric records studied were not filled to carry out a study later on. However, we noticed the records were well filled with little missing data.

4.2. Recommendations for Further Studies

We recommend the conduct of similar studies with a prospective cohort design on a larger scale of participants at multicenter levels to yield better quality evidence which can be generalizable in Cameroon. Although WHO guidelines recommend the use of oxytocin only as the first-line uterotonic in the prevention of PPH.[10] Perhaps multinational studies evaluating the effectiveness of oxytocin plus misoprostol compared to oxytocin only as the first-line uterotonic in the prevention of PPH, may show a superiority of oxytocin plus misoprostol in this regards which may call for a revision of WHO guidelines.[10]

5. Conclusion and Global Health Implications

The administration of misoprostol concomitantly with oxytocin in resource-limited setting of Cameroon improved the delivery and post-delivery conditions by reducing the prevalence of PPH through a reduction in the total amount of blood loss.

Compliance with Ethical Standards

Conflicts of Interests: *The authors declare that they have no competing interests.* ***Financial Disclosure:*** *None. Funding/Support: None.* ***Ethics Approval:*** *The study was approved by the Institutional Review Board of the School of Health and Human Sciences, Saint Monica University Higher Institute, Buea, Cameroon and the Ethics committee of the Bamenda Regional Hospital, Cameroon.* ***Acknowledgments:*** *We would like to thank the entire staff of the Bamenda Regional Hospital, Cameroon, for their detailed hospital file reporting approach and their good file keeping system.*

Key Messages

- The main finding of this study suggests that the combined used of misoprostol and oxytocin in the prevention and management of postpartum hemmorhhage in a low-resource setting reduces the risk of postpartum hemorrhage as well as the amount of blood loss during delivery.

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