Scientific Research Publishing

Open Journal of Obstetrics and Gynecology, 2018, 8, 321-328
http://www.scirp.org/journal/ojog
ISSN Online: 2160-8806
ISSN Print: 2160-8792

Efficiency and Tolerance of Misoprostol versus Oxytocin in the Active Management of the Third Period of Delivery at the University Maternity Porto-Novo, Benin

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How to cite this paper: Aguemon, C.T., Ogoudjobi, M., Lokossou, S., Matabishi, B., King, V. and Lawansonou (2018) Efficiency and Tolerance of Misoprostol versus Oxytocin in the Active Management of the Third Period of Delivery at the University Maternity Porto-Novo, Benin. *Open Journal of Obstetrics and Gynecology*, **8**, 321-328.
https://doi.org/10.4236/ojog.2018.84035

Received: February 22, 2018
Accepted: April 7, 2018
Published: April 10, 2018

Abstract

Objective: To assess the efficiency and tolerance of misoprostol versus oxytocin in Active Management of the Third Period of Childbirth. **Framework and Method of Study:** The study was carried out at the Porto-Novo university maternity in Benin. The hospital is level 3. He acted in a randomized clinical trial with a descriptive and comparative aim referred from 1st January 2017 to 31st December 2017. We included all eligible women in labor in the delivery room during the study period and at that gestational age was greater than or equal to 37 weeks of amenorrhea, delivery was done through vaginal birth and delivered with a live birth and agreed to participate in the study. The cases eligible by order of admission were grouped in blocks of two, "Misoprostol" and "Oxytocin" corresponding to the Active Management of the Third Period of delivery. The data collected were captured and analyzed using the SPSS version 20 software. For the comparison of the results, we used the chi-square statistical test and the difference was assumed to be statistically significant for a $p \leq 0.05$. The confidentiality of parturient was respected. **Results:** we recorded 1234 of which were delivered via vaginal birth. The Active Management of the Third Period of Delivery was carried out in 1202 parturients. According to our inclusion criteria, 892 parturients were retained for the study, of which 446 for each group. The average age of parturients was 26.94 ± 5.65 years. Almost pregnancies were mono-fetal (95.7% vs. 93.5%). The average time to expel the placenta after utero-tonic administration was 4.05 ± 0.27 min in the "Misoprostol" group versus 3.82 ± 0.52 min in the "Oxytocin" group ($p >$ 0.05). We had only 9 cases of placental retention in the group "Misoprostol" versus 5 cases in the "Oxytocin" group. Most of the parturients had blood loss

less than 500 ml (96.2% vs. 96.6%). The frequency of delivery hemorrhage was 3.8% in the "Misoprostol" group versus 3.4% in the "Oxytocin" group. The mean blood volume lost was 284.33l ± 13.31 ml in the "Misoprostol" group versus 225.94 ± 21.52 ml in the "oxytocin" group. Maternal prognosis was generally good in both groups. **Conclusion:** Misoprostol may be an alternative in Active Management of the Third Period of Delivery especially in developing countries where the cold chain is often lacking.

Keywords

Misoprostol, Oxytocin, Delivery

1. Introduction

According to WHO data in 2015 [1], about 830 women die every day from preventable causes related to pregnancy and childbirth and 99% of these deaths occur in developing countries. In Benin, the maternal mortality ratio is 347 maternal deaths per 100,000 live births [2]. Immediate postpartum hemorrhage and more precisely the hemorrhage of the delivery, is one of the main causes of these maternal deaths. The Active Management of the Third Period of Delivery, an assisted delivery by the use of an utero-tonic, is a preventive measure of the hemorrhage of the delivery. It is intended to shorten the duration of delivery and to limit the blood loss accompanying it. The molecule of reference in this practice has always been the oxytocin whose conservation is problematic in African maternities where a cold chain is not always available [3]. Misoprostol (a synthetic analogue of prostaglandin E_1) could be an alternative in these maternities. It is a less expensive utero-tonic and stable at room temperature with rapid sublingual bioavailability [4] [5].

2. Objective

Appreciate the efficiency and tolerance of misoprostol versus oxytocin in Active Management of the Third Period of Childbirth.

3. Patients and Method of Study

The study was carried out at the Obstetric Gynecology Department of University hospital centerin Porto-Novo, the political capital of Benin republic. The hospital is level 3. This was a cross-sectional study with a descriptive and comparative aim with prospective data collection from January 1st, 2017 to December 1st, 2017. Were included all parturient admitted to the delivery room during the study period and in whom gestational age was greater than or equal to 37 weeks of amenorrhea (WA), delivery was with the newborn live and who agreed to participate in the study. We excluded all women in labor with known bleeding disorder or a history of hypersensitivity to misoprostol or oxytocin. The parturient eligible by order of admission in the study were grouped in blocks of two.

In two sealed envelopes, we recorded the terms "Misoprostol" or "Oxytocin" respectively corresponding to the active management of the third period of delivery (AMTPD) or assisted delivery by sublingual administration of 600 µg of misoprostol or intramuscular injection of 10ui oxytocin within one minute of the expulsion of the fetus. For each pair of parturient, the first one had drawn one of the two envelopes. The envelope was then opened allowing to know to which protocol the parturient was assigned so that if this first parturient derived the protocol "Misoprostol", the second systematically received the protocol "Oxytocin". The efficacy of the protocol was assessed through the time of placenta expulsion, blood loss, change in hemoglobin and hematocrit between admission and 24 hours after delivery, and possible complications of delivery. Tolerance was assessed by the occurrence or absence of side effects. The data collected were captured and analyzed using the SPSS version 20 software. For the comparison of the results, we used the chi-square statistical test and the difference was assumed to be statistically significant for a p less than or equal to 0.05. The confidentiality of the data, the anonymity and the consent of the parturient were respected.

We have also the authorization from the hospital authorities and the service head.

4. Results

The emergency admission in this period was 2800 patients. We recorded 2378 deliveries, 1234 of which were delivered via vaginal birth. The active management of the third period of delivery was carried out in 1202 parturients or a realization rate of 97.4%. Taking into account our inclusion criteria, 892 parturients were retained for the study, of which 446 for the group "Misoprostol" and 446 for the group "Oxytocin".

4.1. Characteristics of the Sample

The average age of parturients was 26.94 ± 5.65 years with extremes of 15 and 42 years (26.88 ± 5.62 vs. 27.01 ± 5.62 years, $p = 0.317$). The gynaecological and obstetric histories were statistically comparable between the two groups (Table 1).

4.2. Pregnancy and Childbirth Data

Almost of pregnancies were mono-fetal (95.7% vs. 93.5%) and these pregnancies were followed in most cases (90.4% vs. 92.4%). Data on pregnancy (pathologies presented during pregnancy) and childbirth (gestational age at delivery, mode of entry into labor, type of delivery, duration of Labor, birth weight) were statistically identical between the two groups (Table 2). The mean duration of labor in our study was 6.84 ± 1.65 hours for the group "Misoprostol" and 6.96 ± 1.83 hours for the group "Oxytocin".

4.3. Results of Issuance

The average time to expel the placenta after utero-tonic administration was 4.05

Table 1. Distribution of parturients according to the gynecological and obstetric histories.

	Misoprostol, N (%)	Oxytocin, N (%)	*p*
Gestity			
Primigestous (1)	118 (26.5)	125 (28.0)	0.302
Paucigestous (2 - 3)	187 (41.9)	170 (38.1)	
Multigestous (≥4)	141 (31.6)	151 (33.9)	
Parity			
Nulliparous (O)	144 (32.3)	144 (32.3)	
Primiparous (1)	122 (27.4)	96 (21.5)	0.824
Pauciparous (2 - 3)	108 (24.2)	120 (26.9)	
Multiparous (4 - 5)	60 (13.4)	79 (17.7)	
Large Multiparous (≥6)	12 (2.7)	7 (1.6)	
Other gynecological and obstetric histories			
Curettage	31 (6.9)	24 (5.4)	0.330
Hemorrhage of delivery	14 (3.1)	14 (3.1)	0.442
Myome	12 (2.7)	17 (3.8)	0.345
Scare uterus	21 (4.7)	31 (6.9)	0.153

Table 2. Distribution of parturients according to the data of pregnancy and childbirth.

	Misoprostol, N (%)	Oxytocin, N (%)	*p*
Pathologies presented during pregnancy			
Hypertension/Pre-eclampsia	98 (22.0)	80 (17.9)	0.131
Placenta prævia	7 (1.6)	5 (1.1)	0.561
In Admission Pathologies			
Hydramnios	6 (1,3)	5 (1,1)	0.761
Premature rupture of membranes	76 (17.0)	92 (20.6)	0.171
Severe Anemia < 7 g/dl	3 (0.7)	7 (1.6)	0.340
Delivery			
Mean gestational age (WA)	39.15 ± 1.53	39.21 ± 1.51	0.160
Labor of spontaneous birth	429 (96.2)	432 (96.9)	0.583
Directed delivery	393 (88.1)	398 (89.2)	0.597
Natural delivery	53 (11.9)	48 (10.8)	
Average working time (hours)	8.80 ± 2.05	8.83 ± 2.04	0.219
Mean birth weight (g)	3017 ± 515	3083 ± 517	0.603

± 0.27 min in the "Misoprostol" group versus 3.82 ± 0.52 min in the "Oxytocin" group ($p > 0.05$). The AMTPD was a success for the majority of the parturients (98% vs 98.9%). We had only 9 cases of placental retention in the group "Misoprostol" versus 5 cases in the "Oxytocin" group. Most of the parturients had

blood loss less than 500 ml (96.2% vs. 96.6%). The frequency of delivery hemorrhage was 3.8% in the "Misoprostol" group versus 3.4% in the "Oxytocin" group. The mean blood volume lost was 284.33 ± 13.31 ml in the "Misoprostol" group versus 225.94 ± 21.52 ml in the "oxytocin" group. The mean fall in hemoglobin in the "Misoprostol" group was 1.22 ± 0.11 g/dl and 0.81 ± 0.18 g/dl in the Oxytocin group ($p = 0.402$).The mean fall in hematocrit in the "Misoprostol" group was 2.62% ± 0.28% vs 2.34% ± 0.21% in the oxytocin group ($p = 0.186$). Maternal prognosis was generally good in both groups. Recorded hemorrhagic cases of the delivery had received medication and obstetrical care. No case of hemorrhage required heavy treatment (vascular ligation, hysterectomy). We had more chills, hyperthermia and nausea or vomiting in the "Misoprostol" group than in the "Oxytocin" group (Table 3). However, these side effects were minor and did not require any cumbersome treatment. No cases of maternal death were recorded in our series.

5. Discussion

5.1. Comparative Efficiency of Misoprostol and Oxytocin in AMTPD

The efficiency of misoprostol versus oxytocin in the active management of the third period of childbirth was assessed through the rate of delivery, duration of placenta expulsion, blood loss.

5.2. Average Time to Expel Placenta

Active management of the third period of childbirth was a success for the majority of the women in our series (98% vs 98.9%) with an average delay of placenta ejection in both groups (4.05 ± 0.27 min vs. 3.82 ± 0.52 min; $p > 0.05$). Our results agree with those obtained in the various studies that have addressed the importance of sublingual misoprostol in the management of the third period of

Table 3. Results of delivery according to the protocol used (complications and side effects).

	Misoprostol, N (%)	Oxytocin, N (%)	*p*
Complications of delivery			
Hemorrhage from delivery	17 (3.8)	15 (3.4)	0.719
Placental retention	9 (2.0)	5 (1.1)	0.281
Atone uterine	8 (1.8)	10 (2.2)	0.634
Ripped cord	7 (1.6)	5 (1.1)	0.561
Side effects			
Headache	31 (6.9)	21 (4.7)	0.153
Chills	103 (23.1)	17 (3.8)	0.000
Temperature ≥ 38˚C	92 (20.6)	7 (1.6)	0.000
Nausea/Vomiting	43 (9.6)	5 (1.1)	0.000

childbirth in comparison with intramuscular oxytocin. Although the mean expulsion time varies from one study to another with variable doses of misoprostol, the results obtained are statistically identical between the group "Misoprostol" and the group "Oxytocin". Indeed, in a double-blind randomized clinical trial conducted by Esther in Uganda between 2012 and 2013 with 600 µg misoprostol, the mean time to expulsion of the placenta was comparable (4.4 ± 2.0 min in the misoprostol group And 4.4 ± 1.9 min in the oxytocin group [6]. The same is true of a study carried out in Nigeria in 2010 with 400 µg of misoprostol and which noted an average delay of placenta expulsion of 4.6 min in the misoprostol group and 4.5 min in the oxytocin group with no significant difference [7]. As for the Walley team in 2000, the mean time to expulsion from the placenta is slightly higher (6.2 min in the group Misoprostol vs 7.3 min in the oxytocin group with $p = 0.26$ [8].

5.3. Evaluation of Blood Loss

The mean blood volume lost in our series was statistically identical between the two groups (284.33 ± 13.31 ml vs 225.94 ± 21.52 ml; $p > 0.05$). In the literature, the mean volume of blood loss varies from one study to another, with no significant difference between the "Misoprostol" group and the "oxytocin" group (**Table 4**).

In our series, cases of delivery hemorrhage were recorded with a frequency of 3.8% in the "Misoprostol" group versus 3.4% in the "Oxytocin" group with no significant difference. Our results are consistent with most literature data that there is no difference in the results of active management of the third period of labor with misoprostol or with oxytocin [7] [11] [14] [15] [16].

On the other hand, in Uganda and France, studies have reported a significantly higher frequency of delivery hemorrhage in the "Misoprostol" group than in the "Oxytocin" group (28.6% vs 17.4%; $P < 0.05$ [6] and 27.27% vs 14.79%, $p < 0.05$ [17]).

Differences from one series to another may be related to techniques used to quantify blood loss. The main cause of delivery hemorrhage in our study was placental retention (2% vs 1.1%, $p = 0.281$). It is also the most common cause in the literature with no significant difference between misoprostol and oxytocin. This is the case of Benchimol (4.30% vs 5.10%, $p > 0.05$) [17].

5.4. Tolerance of Misoprostol and Oxytocin in AMTDP

Chills (23.1% vs. 3.8%, $p < 0.05$) and hyperthermia (20.6% vs. 1.6%; $p < 0.05$) were

Table 4. Average volume of blood lost according to authors.

Authors	Misoprostol	Oxytocin	*p*
Aziz [9]	302.86 ± 160 ml	267 ± 140 ml	0.236
Al-Harazi [10]	362 ± 170 ml	342 ± 154 ml	>0.05
Uthman [12]	327.68 ± 3.95 ml	388.04 ± 3.95 ml	0.26
Musa [13]	325.85 ± 164.72 ml	303.95 ± 163.33	0.391

the main side effects found in our study. These are known side effects of prostaglandins by central action, as well as nausea and vomiting [18] [19] [20]. It is therefore normal that their proportions are higher in the group "Misoprostol" than in the group "Oxytocin" as disassembled by other authors [9].

6. Conclusion

The efficiency of misoprostol and oxytocin was comparable for the active management of the third period of labor. Misoprostol was responsible for more side effects than oxytocin. However, these side effects were mild. Misoprostol may be an alternative in Active Management of the Third Period of Delivery especially in developing countries where the cold chain is often lacking.

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