When compared to the carbetocin and oxytocin plus the misoprostol groups, the oxytocin group had a statistically significant lower hemoglobin level and greater blood loss (p=0.0001). The TA + oxytocin group had a statistically significant higher hemoglobin level and less blood loss than the carbetocin group (p=0.004 and 0.043, respectively) (Table 2).

PPH was more common in the oxytocin group (9.1 percent) than in the carbetocin group (2.5 percent) or the oxytocin plus the misoprostol group (0.83 percent) (p=0.0001).

There was no significant difference in the incidence of PPH between the carbetocin group and the oxytocin plus misoprostol group (p=0.298), therefore the oxytocin group used more extra uterotonics than the other two groups. Only 14 (10.8 percent) women in the oxytocin group required blood transfusion.

The oxytocin + misoprostol group had a higher rate of diarrhea and increase temperature (6.6 percent) than the carbetocin group (0 percent) or the oxytocin group (0 percent). There were no significant differences in the incidence of nausea, vomiting, or diarrhea across the three groups (Table 3).

Discussion

This research was designed to compare the efficacy of intravenous 100 µg carbetocin against 20 units of oxytocin infusion in 500 ml lactated ringer's solution 125 ml/h with 400 µg sublingual misoprostol, as well as 20 units of oxytocin infusion in 500 ml lactated ringer's solution 125 ml/h alone, in reducing blood loss in pregnant women who are having a vaginal birth and experience blood loss>500 ml. Our research found that using oxytocin in combination with sublingual misoprostol or IV carbetocin reduces determined blood loss, the incidence of PPH, and hence the requirement for further uterotonics, compared to oxytocin alone.

In comparison to oxytocin, carbetocin dramatically reduced postpartum blood loss and reduced the need for extra uterotonics in women with atonic PPH, with no notable adverse effects or hemodynamic abnormalities. This is often thanks to Carbetocin's longer half-life, which causes a greater uterine response in terms of frequency and amplitude of uterine contractions [10]. These findings were also the results of several studies published within the literature [12-15].

Our findings matched those of Samimi et al., who gave carbetocin or Syntometrine to 200 women undergoing childbirth to avoid PPH. the need for extra uterotonics was observed to be considerably reduced within the carbetocin group. Carbetocin was shown to be more efficient than syntometrine in preventing PPH [13].

Our findings matched those of one study, which randomly assigned 200 women who delivered vaginally and had at least two risk factors for atonic PPH to receive either 100 µg IM carbetocin or 5 IU IM oxytocin. The quantity of bleeding, the prevalence of PPH, and therefore the requirement for extra uterotonics were all shown to be considerably reduced within the carbetocin group. They concluded that carbetocin is a better alternative to conventional oxytocin for preventing PPH in women with at least two PPH variables, with fewer hemodynamic abnormalities and adverse effects [14].

Another study randomly assigned 100 women who delivered vaginally and had experienced atonic PPH to receive either 100 mc g IM carbetocin or 10 IU IM oxytocin. The quantity of

bleeding and the requirement for additional uterotonics were all shown to be considerably reduced in the carbetocin group [15].

Boucher et al. recently published research in which they found that the carbetocin group needed substantially less uterine massage and other uterotonics, which matched our findings. They administered carbetocin 100 µg IM or oxytocin 10 IU iv oxytocin infusion over 2 hours to 160 women with at least one risk factor for PPH who delivered delivery vaginally [16].

Carbetocin 100 g has all the earmarks of being as effective as oxytocin in decreasing PPH, according to Boucher et al [16], Elbohoty et al [17], Widmer et al [18], and Fenix et al [19]. Similarly, adding sublingual misoprostol to oxytocin improves the efficacy of oxytocin as compared to IV carbetocin in terms of determined blood loss in our study.

Evidence suggests that Prior oxytocin exposure appears to desensitize oxytocin receptors, leading to poor oxytocin-induced uterine contractility [20].

In 2010, Winikoff et al. published the results of a single trial that compared the effectiveness of misoprostol vs. traditional uterotonics in the absence of oxytocin prophylaxis [21]. In this study, 978 women were treated for PPH at four hospitals in Ecuador, Egypt, and Vietnam. Participants were randomly assigned to receive either 800-g sublingual misoprostol (n = 488) or 40 IU intravenous oxytocin (n = 490). Misoprostol, while being less effective than oxytocin, was able to stop active bleeding in 90% of women. As a result, the researchers concluded that it was effective enough to be utilized as a first-line treatment for PPH in the absence of oxytocin.

Blum et al. (2010) evaluate the effects of misoprostol and conventional uterotonics after delivery of 10 IU oxytocin prophylaxis in one of two studies [22]. PPH was treated in a total of 807 women. Participants were given either 800 g sublingual misoprostol (n = 407) or 40 IU intravenous oxytocin (n = 402) at random. When used for the management of PPH owing to uterine atony, the authors found that misoprostol is clinically comparable to oxytocin in women who had received oxytocin prophylaxis during the third stage of labor.

Lokugamage et al. presented the results of research looking at the effects of misoprostol after oxytocin prophylaxis in 2001. When given to 64 women with PPH, they found that 800 g rectal misoprostol had a substantial benefit over a combination of Syntometrine IM plus Syntocinon IV for PPH therapy [23]. In favor of misoprostol, there was a 28.1 percent difference in the rate of bleeding cessation within 20 minutes ($p = 0.01$).

Despite continuing efforts, less competent health personnel attend births in low-resource countries, which can lower maternal mortality; as a result, the maternal death rate in developing countries remains high [1].

Preventing and treating PPH is particularly difficult in areas where most deliveries take place at patients' homes or in tiny clinics, and when obstetric care is limited [3]. Without skilled delivery attendants, sublingual misoprostol with oxytocin might be a one-of-a-kind combo, and it could potentially be the only medical option for treating PPH after births [17]. Misoprostol does not need to be kept at a certain temperature; thus, it can be used in the absence of skilled labor and delivery personnel or when injectable oxytocic is unavailable [10].

The findings of this trial, in agreement with other trials [23-27], add to the body of data on the

safety of misoprostol for PPH therapy. In this trial, no serious side effects or safety issues were observed among women who used misoprostol for treatment as well as prevention.

There were several limitations to the study. First, the generalizability of our findings may be restricted since this was a single-center study with a small number of women with PPH.

The comprehensive data collection that took place over a two-and-a-half-year period to document the use of carbetocin versus oxytocin plus misoprostol and oxytocin alone for the treatment of PPH is a significant strength of this study.

The randomized trial was sufficiently powered to evaluate the effects of intravenous TA with oral misoprostol vs intravenous carbetocin on the amount of blood loss, which was one of the study's merits.

The simplicity with which sublingual misoprostol and IV TA can reduce postpartum blood loss by a clinically significant amount is another highlight of the research.

Clinical implications

This study demonstrates that utilizing oxytocin in conjunction with sublingual misoprostol and IV carbetocin alone lowers the occurrence of severe PPH and the need for further uterotonics when compared to using oxytocin alone. Compared to carbetocin, adjuvant sublingual misoprostol improves oxytocin's effectiveness. Misoprostol appeared to reduce blood loss more successfully when used in conjunction with oxytocin as secondary prophylaxis of postpartum hemorrhage.

Conclusion

Oxytocin plus misoprostol is more effective than oxytocin and carbetocin in the management of post-partum blood loss >500 ml after vaginal delivery. Adjuvant sublingual misoprostol increases oxytocin's efficiency in comparison to carbetocin. When administered in conjunction with oxytocin as a supplementary prophylactic for postpartum hemorrhage, misoprostol seems to increase the efficacy of oxytocin to lessen blood loss more successfully.

Authors' contributions:

NS, AT,and HS were involved in patient care during and after the operation and prepare, draft and approved the final manuscript.

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Study registration:

It was a clinically registered randomized, double-blind, clinical trial (ClinicalTrials.gov: NCT03870503)

Disclosure of Interests:

Authors declare no conflict of interests.

Ethical approval:

The ethical review board approved the study by a grant number of (Aswu/280/7/18).

Informed consent:

Informed consent was received from the patient for the publication of this case report.

Data sharing:

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available as it could compromise the privacy of the patient.

Abbreviations:

PPH: Postpartum hemorrhag

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Table 1. Baseline Characteristics of pregnant women in the study groups.

Parameters	Group I (n = 45)	Group II (n = 45)	Group III (n = 45)	Significance
Age (year)	29.5 ± 2.42	29.6 ± 2.68	29.83 ± 2.85	0.854
Weight (kg)	69.25 ± 7.76	69.43 ± 7.18	69.4 ± 7.77	0.994
Height (cm)	162.45 ± 4.19	163.58 ± 4.38	163.52 ± 4.6	0.436
BMI	26.2 ± 2.55	25.96 ± 2.74	25.94 ± 2.71	0.888
Parity (median) (Minimum – maximum)	3 (0 – 4)	2 (0 – 5)	3 (0 – 5)	0.866
Gestational age (weeks)	38.4 ± 1.45	38.55 ± 1.34	37.5 ± 1.22	0.878
Initial Hemoglobin	10.97 ± 0.624	10.98 ± 0.623	10.83 ± 0.622	0.905
Duration of first stage (h)	9.78 ± 2.91	9.81 ± 2.06	9.92 ± 1.06	0.965
Duration of second stage (mins)	64.72 ± 16.12	63.72 ± 17.13	63.72 ± 13.16	
Duration of third stage (mins)	4.42 ± 1.2	4.73 ± 2.3	4.23 ± 1.3	
birth weight (g)	3176 ± 376.64	3182 ± 35.21	3182 ± 35.25	

BMI (body mass index), CS (Cesarean Section), CPD (cephalopelvic disproportion)

 # Variables are presented as mean and standard deviation, median (minimum – maximum) and number (percentage).

Table 2. Post-delivery variables in the three groups.

Blood loss	**Group I (n = 45)**	**Group II (n =45)**	**Group III (n = 45)**	**Significance**
Amount of bleeding (ml)	811 ± 525.66	722 ± 312.77	910 ± 389.17	0.007* 0.03* / 0.04* / 0.0001*
PPH >1000 ml (%)	**6 (13.3 %)**	**5 (11.1%)**	**11 (24.4 %)**	0.0001* 0.326 / 0.0001*/ 0.0001*
Temperature	**36.91 ± 0.07**	**37.45 ± 0.64**	**36.95 ± 0.43**	**0.0001*** **0.0001*/0.12/ 0.0001***
Pulse(30minutafter delivery)	**94.46 ± 7.5**	**93.99 ± 9.7**	**96.99 ± 9.7**	**0.692** **0.721/ 0.692/ 0.126**
Hb 24 h after delivery(g/dl)	9.98 ± 2.71	8.98 ± 4.21	9.93 ± 3.27	0.0001* 0.0001* / 0.221 / 0.0001*
SBP (30minutafter delivery)	119.09 ± 3.67	**116.04± 7.23**	**103.04± 6.12**	0.0001* 0.193 / 0.0001*/ 0.0001*
DBP (30minutafter delivery)	86.32 ± 3.36	81.41 ± 5.15	73.41 ± 4.48	0.0001* 0.026* / 0.026* / 0.0001*

*** Statistically Significant Difference (Group I Versus Group II / Group I Versus Group III / Group II Versus Group III). # Variables are presented as mean and standard deviation, and number (percentage).**

Table 3. adjuvant interventions and side effect measurements.

Variables	Group I (n = 45)	Group II (n = 45)	Group III (n = 45)	Significance
Additional Uterotonics (%)	7(15.5)	6 (13.3 %)	12(26.6)	0.0001* 0.261 / 0.0001*/ 0.0001*
Bakri balloon (%)	1(2.2)	1(2.2)	3(6.6)	0.132
B lynch stitch (%)	1(2.2)	1(2.2)	2(2.2)	0.536
Uterine artery ligation (%)	--	--	1(7.5)	-----
Hysterectomy (%)	--	--	--	----
Need Blood Transfusion (%)	8(50)	7 (12.5)	13 (7.5)	0.0001* 0.214 / 0.0001*/ 0.0001*
Tachycardia (>100 b/min)	9(20)	10(22.2)	15(33.3)	0.0001* 0.672 / 0.0001*/ 0.0001*
Fever (%)	-----	3(6.6)	------	--------
Nausea (%)	2 (4.4)	3(6.6)	3(6.6)	0.906
Vomiting (%)	1(2.2)	1(2.2)	2 (4.4)	1.000
Diarrhea (%)	1(2.2)	1(2.2)	3(6.6)	0.620

***Statistically Significant Difference (Group I Versus Group II / Group I Versus Group III / Group II Versus Group III). # Variables are presented as mean and standard deviation and number (percentage).**

Figure 1. Consort flowchart showing enrollment of participants.