**Original Research Article**

**COMPARSION BETWEEN ADJUCNTIVE SUBLINGUAL MISOPROSTOL VERSUS OXYTOCIN ALONE IN THE REDUCTION OF INTRAOPERATIVE BLOOD LOSS DURING CAESAREAN SECTION**

**ABSTRACT**

**Background:** Oxytocin use in tropical developing countries for the reduction blood loss at caesarean section has being met with the challenge of ineffectiveness due to poor transportation, inadequate storage and drug adulteration. Therefore, there is a need for an effective, temperature stable, adjunctive uterotonic with a lesser risk of adulteration such as misoprostol.

**Methodology:** The study aimed at evaluating the effectiveness of adjunctive sublingual misoprostol in reducing intraoperative blood loss at caesarean section. One hundred and fifty-two pregnant women at term who had indications for caesarean section and have risk factors for primary postpartum haemorrhage as well as met the eligibility criteria were randomized equally into the Misoprostol study arm and Placebo study arm. The Misoprostol study group received 400-ug of sublingual misoprostol. Both study arms received 30 IU intravenous oxytocin. The main outcome measure was the estimated intraoperative blood loss. A *P-*value < .05 was considered statistically significant.

**Results:** The blood loss at abdominal birth, was lower in the misoprostol study group when compared to the placebo study group (664.0 ± 285.2 ml vs 677.9 ± 430.3 ml), but this was not statistically significant (*P* = .80). The reduction in the packed cell volume after caesarean birth in the misoprostol trial arm of the study was lesser than that obtained in the placebo study group, but it too was not statistically significant, (3.8± 2.9 vs 4.4 ± 3.1, *P* = .18).

**Conclusion:** Adjunctive sublingual 400 ug misoprostol didn’t considerably reduce caesarean haemorrhage.

*Keywords: Caesarean, haemorrhage, misoprostol, oxytocin*.

**1. INTRODUCTION**

Postpartum haemorrhage is the foremost cause of maternal morbidity and mortality in developing countries especially in the Sub-Saharan Africa (Tunclap et al.; 2015). Caesarean section, a commonly performed operation, is associated with a higher amount blood loss when compared with vaginal delivery (Week & Neilson; 2015).When blood loss at caesarean section is not curtailed, maternal morbidity and possible maternal mortality can occur. Postpartum haemorrhage rate is increasing rapidly globally, and this is also seen in developing countries (Maswine & Buchmann, 2017). All means necessary to reduce this rate will be a welcomed development since this obstetric emergency is the bane of most societies in undeveloped nations.

The underlying cause of primary postpartum haemorrhage common to most risk factors is uterine atony (Ononge et al.; 2016). Once uterine atony is prevented, then excessive blood loss at caesarean sections vis-à-vis primary postpartum haemorrhage is forestalled. There are various uterotonic used for the prevention of excessive blood loss at caesarean deliveries, and they work by ensuring good uterine contraction after delivery (WHO, 2018).

Oxytocin is the uterotonic of choice for the prevention of postpartum haemorrhage as recommended by the World Health Organization (WHO, 2018).However, oxytocin effectiveness for the reduction of blood loss at caesarean section, and thus primary postpartum haemorrhage prophylaxis in the tropics is marred with poor storage and transportation (Adanikan et al.; 2013).There is therefore a need to give an additional uterotonic to oxytocin to ensure that an effectual blood loss control intra-operatively is achieved.

Misoprostol is not affected by tropical temperature, it is cost effective especially as it relates to the cost of refrigeration when compared to other oxytocic (Adanikan et al.; 2013). Misoprostol can be used an adjunctive uterotonic to oxytocin for the reduction of blood loss at caesarean deliveries, and by extension primary postpartum haemorrhage (Adanikan et al.; 2013).

There are some studies (Ugwu et al.; 2014, Akpan et al.; 2021, Sood & Sanjay, 2012)that have x-rayed the effectiveness and safety of adding misoprostol to oxytocin regimen for the prevention of primary postpartum haemorrhage with various methodological approaches. There are other studies in this category (Rekha & Lathak, 2014; Agarwal & Thakar, 2022; Sallam & Shady, 2018).

This study would help develop a prophylactic uterotonic protocol for the reduction of blood loss at caesarean section vis-à-vis prevention of primary postpartum haemorrhage at caesarean deliveries done in tropical developing countries. The study findings would lend support/strengthen or refute the stand point that adjunctively administered misoprostol to oxytocin regimen for the reduction of blood loss at caesarean section is a necessity in Sub-Saharan region of Africa and other tropical climes.

The study was aimed evaluating the effectiveness and safety of adjunctive sublingual misoprostol in reducing intraoperative blood loss during caesarean section. The outcome measures were to determine and compare the estimated intraoperative blood loss during caesarean section in the misoprostol- oxytocin combination study arm and in the oxytocin alone study arm; as well as to determine and compare the reduction in packed cell volume after caesarean section between the study arms.

**2. METHODOLOGY**

**2.1 Study site**

This study was carried out at the Obstetrics and Gynaecology department of the Federal Medical Centre, Yenagoa, Bayelsa State, Nigeria. The hospital is the foremost tertiary hospital in Bayelsa and receives patients from primary, secondary, tertiary and private hospitals in the state.

**2.2 Study design**

The study was a randomised controlled trial (superiority design). It was carried out from 1st March to 30th December 2024.

**2.3 Inclusion criteria**

Included in this trial were pregnant women at term (37+0 weeks to 41+6 weeks gestational age) for elective or non-elective caesarean sections and who had risk factor for primary postpartum haemorrhage.

**2.4 Exclusion criteria**

Women excluded from the study were those with: caesarean sections for dire emergencies (umbilical cord prolapse, suspected fetal distress and active antepartum haemorrhage), caesarean section done under general anaesthesia, previous caesarean sections or other uterine surgeries, and allergy to misoprostol use. Also, excluded were women with known history of hepatic, renal and haematological disorders, fever (temperature ≥ 37.50c), pre-operative anaemia (pre-operative haematocrit level < 30 %) and eclampsia.

**2.5 Sample size**

A sample size of 152 was gotten using the formula for calculating sample size for a superiority randomized controlled trial; as shown below:

 $n=\frac{2 X (Z\_{α}+ Z\_{в} )^{2} σ^{2}}{( μ\_{1}- μ\_{2 } - ẟ)^{2}}$

Where ‘n’ is the minimum sample size needed for the study, $Z\_{α}$ is the standard normal deviate at 95 % confidence level taken as 1.96 for a two-tail study, $Z\_{в}$ is the power of the study and power of 80 % (0.84) would be adopted for this study, $σ^{2}$ is the standard deviation of the mean in blood loss from a previous study (Ugwu et al.; 2014). An attrition rate of 20 % was put into consideration in arriving at the sample size. Eligible participants that were greater than or equals to 18 years of age at the point of obtaining informed written consent for abdominal birth (at the labour ward for emergency/urgent cases or at the antenatal ward for elective cases), were educated about the study.

The random allocation of the participants in this study was done using the WIN PEPI software. The WIN PEPI software was used to allocate numbers 1 to 152 randomly into two equal groups (A and B), hence generating a randomization list. After obtaining an informed consent from a participant, the participant was allocated to either group “A” or group “B”.

Firstly, every participant was requested by the researcher/research assistant(s) to pick a tag bearing a number from a box (Research ballot box). The box contained tags numbered from 1 to 152. Once a numbered tag was picked, that tag was not be replaced till the end of the research.

The researcher/research assistant(s) gave the numbered tag to a research clerk(s) (circulating theatre nurses) who in turn looked at the randomization list generated using the WIN PEPI software, and allocated the participants to either study group (‘A’ or ‘B’) corresponding to the number on the tag the participants had randomly picked.

**2.6 BLINDING**

Misoprostol tablets and the inactive tablets (placebo) were manufactured by a hospital’s pharmacist. The placebo tablets contained a starch base only, while the active tablets contained 200 ug of misoprostol each.

Both the active and inactive tablets had the same size, colour and smell. The misoprostol tablets and placebo tablets were packed in envelopes, which were sealed and labelled by the pharmacist.

Each envelope packed by the pharmacist contained three (3) active tablets (containing misoprostol) or three (3) placebo tablets.

Only the circulating theatre nurses held the randomization lists until the end of the trial. Their sole activity was to allocate participants to their randomly picked study groups.

In this research, each study participant received two sublingually administered tablets, either misoprostol tablets if in the misoprostol study group or placebo tablets if in the placebo study group.

**2.7 Data collection**

The caesarean sections were performed by at least a second year senior registrar, following standard lower uterine segment technique in order to avoid the bias of surgical skill.

At point of opening the parietal peritoneum at caesarean section, the anaesthetic nurse sublingually administered two tablets to the study participants, 400 ug misoprostol tablets to the misoprostol study arm or two placebo tablets (which contained a starch base) to the placebo study arm. The anaesthetist in charge of the surgery administered to all study participants, at the time of the clamping of the umbilical cord, 10 IU of intravenous bolus of oxytocin, followed by an infusion of 20 IU of oxytocin in 500 ml of normal saline at a rate of twenty drops per minute, which ran over eight hours. The oxytocin ampoules used in the study were of the same brand and batch. The misoprostol tablets and placebo (containing starch base) tablets were produced in indistinguishable forms.

The outcome measures were the estimated intraoperative blood loss and the drop in haematocrit levels after caesarean section.

Intraoperative blood loss was estimated using the volumetric and gravimetric methods. For the volumetric method, standard calibrated suction bottles were used. While for the gravimetric method; the weight gain of the abdominal mops, delivery mats, theatre drapes, theatre gowns, and vaginal gauzes were utilised.

The *Mettler PB 153* weighing scale which had a sensitivity of 0.001g was used to weigh the intraoperatively used surgical gowns, surgical towels, drapes gauzes and delivery mats, so as to calculate the amount of blood absorbed by these items. The dry weights of a vaginal gauze, an abdominal mop, a theatre gown, a theatre drape and a delivery mat used in the study were 7 g, 16 g, 129 g, 129 g and 85 g, respectively. Part of the estimated blood loss at surgery was calculated by summing the wet weights of the above items and subtracting from the total gotten, their summative dry weights. Thus, part of the blood loss intra-operatively was estimated from the used abdominal mops’ weight gain or vaginal gauzes’ or theatre drapes’ or theatre gowns’ or delivery mats’ weight gain. A weight gain of 1 g of any of the items was equivalent to 1 ml of blood contained within the weighed item. It was assumed that 1 ml of blood weighs approximately 1 g (Schorn et al.; 2010)

Two millilitres of blood was taken from each study participant by the researcher/ research assistant(s), and then put into heparinized bottles, and carried to the haematology laboratory of the Federal Medical Centre, Yenagoa. The blood samples were analysed by the researcher/ research assistants /laboratory assistant using the micro-haematocrit centrifuge (low spin, TT 645B, 12,000 revolutions per minute), and read off a micro-haematocrit reader. After every twentieth analysed blood sample, the twentieth blood sample was sent to the Research Laboratory of the same facility and analysed for its haematocrit level by a different laboratory assistant using the haematocrit centrifuge (T-15, 12,000 revolutions per minute), and read off a micro-haematocrit reader. The researcher and research assistants were trained by a haematologist of the department of haematology, Federal Medical Centre, Yenagoa on how to analyse the participants’ blood samples for their haematocrit level.

**2.7 Data analysis**

All data extracted were subjected to statistical analysis using the IBM SPSS version 25.0. Categorical variables were summarized in frequencies and proportions and presented in figures and tables. Continuous variables were summarized in mean/standard deviations. The intention-to-treat (ITT) principle of analyzing randomized controlled trials (RCT) was deployed in analyzing the data from the study. Chi-square test and t-test were used as appropriate. A *P*-value < .05 was considered statistically significant.

**3. RESULTS**

One hundred and ninety-eight pregnant women were screened for the trial, out of which 152 pregnant women (76.8 %) who met the eligibility criteria were recruited. Equal number of them (76) were allocated randomly to both the Misoprostol study arm (Study arm “A”) and the Placebo arm (Study arm “B”).

**3.1 SOCIO-DEMOGRAPHIC/ MATERNAL CHARACTERISTICS OF PARTICIPANTS**

As depicted in Table 1, about three out of every ten participants were in the 30 - 34 years or the 35 -39 years age range, (31.6%) and (32.9 %) respectively. Approximately 18.4 % and 10.5 % of the women were in the 25 - 29 years and 20 - 24 years age ranges, respectively. The mean ages for all the study participants was 32.59 ± 5.97 years. There was no analytically appreciable difference between the trial arms in terms of their age (*P* = .69).

About 46.1% of participants were nulliparous parous. This formed a significant proportion of the study participants, followed by the multiparae (33.6 %), and then the primiparae (15.1 %). There was no analytical considerable dissimilarity between the trial arms as regards the participants’ parity (*P* = .80).

**Table 1: Socio-demographic/maternal characteristics of participants**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Characteristics** | **Total****N = 152 (%)** | **Study Groups** | **Test Statistics****(*P*-Value)** |
|  | **Sublingual Misoprostol****N = 76 (%)** | **Sublingual Placebo****N = 76 (%)** |
|  | **Age group** |  |  |  |  |
|  | 20 -24 years | 16 (10.5) | 7 (9.2) | 9 (11.8) | 2.20 (.69) |
|  | 25 - 29 years | 28 (18.4) | 13 (17.1) | 15 (19.7) |
|  | 30 - 34 years | 48 (31.6) | 28 (36.8) | 20 (26.3) |  |
|  | 35 - 39 years | 50 (32.9) | 24 (31.6) | 26 (34.2) |  |
|  | > 40 years | 10 (6.6) | 4 (5.3) | 6 (7.9) |  |
|  |  **Age in years – Mean ± SD** | 32.59 ± 5.97 | 32.22± 5.28 | 32.17 ± 5.77 |  |
|  |  |  |  |  |  |
|  | **Parity** |  |  |  |  |
|  | Nulliparous | 70 (46.1) | 36 (47.4) | 34 (44.7) | 0.96 (.80) |
|  | Primiparous | 23 (15.1) | 10 (13.2) | 13 (17.1) |
|  | Multiparous | 51 (33.6) | 25 (32.9) | 26 (34.2) |  |
|  | Grandmultiparous | 8 (5.3) | 5 (6.6) | 3 (3.9) |  |
|  | **Parity – Median (Range)** | 1.0 (1.0 – 4.0) | 1 (1.0 – 4.0)  | 1 (1.0 – 4.0) |  |
|  |  |  |  |  |  |
|  | **Gestational Age** |  |  |  |  |
|  | 37 weeks | 56 (36.8) | 27 (35.5) | 29 (38.2) | 0.50 (.97) |
|  | 38 weeks | 46 (30.3) | 22 (28.9) | 24 (31.6) |
|  | 39 weeks | 15 (9.9) | 8 (10.5) | 7 (9.2) |  |
|  | 40 weeks | 18 (11.8) | 10 (13.2) | 8 (10.5) |  |
|  | 41 weeks | 17 (11.2) | 9 (11.8) | 8 (10.5) |  |
|  | **Gestational Age in weeks \_ Mean ± SD** | 38.3 ± 1.36 | 38.3 ± 1.36 | 38.3 ± 1.36 |  |
|  |  |  |  |  |  |
|  | **Type of CS** |  |  |  |  |
|  | Elective CS | 50 (32.9) | 25 (32.9) | 25 (32.9) | 2.43 (.29) |
|  | Urgent CS | 84 (55.3) | 45 (59.2) | 39 (51.3) |
|  | Emergency CS | 18 (11.8) | 6 (7.2) | 12 (15.8) |  |
|  |  |  |  |  |  |
|  | **Cadre of Surgeon** |  |  |  |  |
|  | Consultant | 60 (39.5) | 32 (42.1) | 28 (36.8) | 0.44 (.50) |
|  | Senior Registrar | 92 (60.5) | 44 (57.9) | 48 (63.2) |

 CS- Caesarean section

On considering the type of caesarean birth performed for the study participants, both trial groups were similar (*P* = .29). An appreciable proportion of the study participants had urgent caesarean delivery (55.3 %). That is, more than half of the total number of study participants underwent this category of abdominal delivery. Elective abdominal birth constituted slightly above one-third of the caesarean cases (32.9%). Emergency caesarean delivery category recorded, 11.8 % of the caesarean operations. This meant that slightly above one out of ten study participants had emergency abdominal birth.

For the cadre of the lead surgeon who performed the caesarean operation for the study participants, there was also no analytically appreciable difference on comparing the study arms (*P* = .50). About six out of every ten lead surgeons in the study were senior registrars (60.5 %).

**3.2 BLOOD LOSS ESTIMATION IN THE MISOPROSTOL AND PLACEBO GROUPS**

Table 2 shows the amount of blood loss in the two study arms. There was no analytically considerable dissimilarity between the study arms in terms of the duration of surgery and the preoperative packed cell volume. The prime endpoint measurable variable of interest, the amount of blood loss at abdominal birth, was lower in the misoprostol study group when compared to the placebo study group (664.0 ± 285.2 ml vs 677.9 ± 430.3 ml), but this was not statistically significant (*P* = .80).

In addition, there was no analytical dissimilarity between the sublingual misoprostol study arm and the sublingual placebo study arm, as regards the 48-hours postoperative packed cell volume (30.2 ± 3.6 vs 30.9 ± 4.8, *P* = .23). Also worthy of note is that, the reduction in the packed cell volume in the misoprostol trial arm of the study after caesarean birth was lesser than that obtained in the placebo study group, but it also was not statistically significant, (3.8± 2.9 vs 4.4 ± 3.1, *P* = .18).

**Table 2: Blood loss estimation in the misoprostol and placebo groups**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Characteristics** | **Mean ± SD**  | **Mean difference****(95% CI)**  | **Student’s t-test (*P*Value)** |
|  | **Blood loss at surgery** |  |  |  |
|  | Total population | 670.9 ± 364.0 |  |  |
|  | Sublingual Misoprostol | 664.0 ± 285.2 | 13.95 (-95.93 – 123.83) | 0.25 (.80) |
|  | Sublingual Placebo | 677.9 ± 430.3 |  |  |
|  |  |  |  |  |
|  | **Pre-Operative PCV** |  |  |  |
|  | Total population | 34.9 ± 4.1 |  |  |
|  | Sublingual Misoprostol | 33.9 ± 3.0 | 0.52 (-1.73 – 0.33) | 1.34 (.18) |
|  | Sublingual Placebo | 34.6 ± 3.9 |  |  |
|  |  |  |  |  |
|  | **48-hour post-operative PCV** |  |
|  | Total population  | 30.5 ± 4.2 |  |  |
|  | Sublingual Misoprostol | 30.2 ± 3.6 | 0.76 (-0.49 – 2.03) | 1.20 (.23) |
|  | Sublingual Placebo | 30.9 ± 4.8 |  |  |
|  |  |  |  |  |
|  | **Difference in PCV** |  |  |  |
|  | Total population | 4.4 ± 3.9 |  |  |
|  | Sublingual Misoprostol | 3.8 ± 2.9 | 0.60 (-0.29 – 1.49) | 1.33 (.18) |
|  | Sublingual Placebo | 4.4 ± 3.1 |  |  |
|  |  |  |  |  |
|  | **Duration of Surgery** |  |  |  |
|  | Total population | 68.4 ± 21.1 |  |  |
|  | Sublingual Misoprostol | 67.4 ± 21.6 | 2.08 (-8.43 – 4.27) | 0.65 (.52) |
|  | Sublingual Placebo | 69.5 ± 20.6 |  |  |

 SD – Standard deviation; CI – Confidence Interval, PCV- Packed cell volume

**4. DISCUSSION**

Misoprostol has been found to be a useful adjunct to oxytocin in lowering the amount of bleeding associated with caesarean birth, and thus prevents primary postpartum haemorrhage (Nayak et al.; 2017).

The onset of action of misoprostol is very critical to making sure that blood loss at delivery is kept at a minimum. Misoprostol when given sublingually has an onset of action of 11-minutes while other routes takes longer, except for the oral route where the onset of action is 8-minutes (Tang et al.; 2007).Therefore, knowing about this timing will aid in guiding the appropriate time to administer the uterotonic at caesarean deliveries. Giving misoprostol too early at caesarean section (for example just after spinal anaesthesia) in patients with previous abdominal surgeries (caesarean section inclusive) may predispose the parturients to uterine rupture on the theatre table. This is so if the time needed to gaining access to the uterus is prolonged or lengthened by the presence of intraabdominal adhesions from previous abdominal surgeries.

In this study, the most of the participants were aged 30 to 39 years. This finding is similar to that the study by Akpan et al.; 2021.This occurrence may be probably due to late onset marriages occurring in the region of the country where these researches were conducted. Persistence economic woes and a need for women to further their education have been noticed to be contributors to delayed marriages in the region. However, in contrast to this present study, Ugwu et al.; 2014 study showed that a significant number of participants were aged 25-29 years. A possible explanation for this disparity may be due to early marriages or betrothal culture in predominantly Islamic Ibadan where the Ugwu et al; 2014 study was carried out. This participants’ age disparity finding was also noticed in the works of other researchers in India and Egypt, in which it was seen than most of participants were less than 30 years of age (Maged et al.; 2019, Karya et al,; 2021). Again, in these countries, early marriages are said to be common occurrences because of cultural/ religious practices.

A majority of the participants in this research were of low parity. This finding is in keeping with that of other studies (Akpan et al.; 2021, Agarwal & Thakar, 2022, Nayak et al.; 2017).A possible reason may be that, in the locality where this study was done, the nulliparous and primiparous women, unlike the multiparae, tend to book for antenatal care. There is a common belief, and from primary researcher’s observations, that multiparous women in Southern Nigeria, especially grandmultiparous women, feel “experienced” concerning the events of pregnancy and labour. Therefore, they do not make themselves available for hospitalised care. Contraception may also play a role in this present work having low parity participants.

More than half of the total number of the cadre of surgeons in this study were the senior registrars, while the rest were consultants. This was so because, most of the emergency or urgent surgeries occurred during the call hours at night when most consultants were not physically on duty to perform the cases themselves. However, this statistical difference in the proportion of attending chief surgeon at the caesarean operation was not significant in the study. This result was no different from studies by Ugwu et al; 2014 and Maged et al.; 2019.

The intraoperative blood loss in this study also showed that there was smaller amount of bleeding in the misoprostol (intervention) arm than in the placebo study arm; nonetheless, this difference was not statistically significant. This finding agreed with a study by Mirteimouri et al; 2020.However, this finding of no statistically significant difference between the study arms is in contrast with studies by Sood et al; 2012, Sallam & Shady, 2018) where there was considerable dissimilarity between misoprostol study group and standard group, in favour of the former as a good adjunctive uterotonic. This incongruity may be explained by the use of a smaller sample size in their investigations (Ugwu et al.; 2014, Rekha & Lathak; 2014, Agarwal & Thakar, 2022),and the use of formulae for caesarean blood loss assessment, rather than a direct quantification of blood loss (Agarwal & Thakar, 2022)or no clearly stated method for blood loss quantification (Sood & Sanjay, 2012; Rekha & Lathak; 2014). It should be noted that, Sood et al.; 2012 studyused a larger sample size (sample size of 174) when compared to this present trial (sample size of 152), and had a statistical significant reduction in caesarean blood loss in the misoprostol arm of their study. This difference in finding of statistical significant difference as compared to this present work may due to inclusion of participants with previous caesarean birth in Sood et al.; 2012 work.

Having a large sample size in studies improves the accuracy of a study’s findings, and validates the tests of significance used in the research (Andrade et al.; 2020).Again, accuracy in quantifying the amount of blood loss is very critical in ensuring validity of a study’s findings. The volumetric method in combination with the gravimetric methods for assessing the amount of blood loss at surgeries have been found to reduce measurement bias from studies (Gerdessen et al.; 2021). The study by Agarwal & Thakar, 2022used the Bourke and Smith formula for intraoperative blood loss estimation. The formula has approximations, therefore, it is not so accurate in calculating the amount of blood loss at surgery. Again, this present research used a combination of volumetric and the gravimetric methods in quantifying caesarean section blood loss, and both methods have been found to be reasonably more accurate than other methods (Gerdessen et al.; 2021).

In this research, addition of misoprostol to oxytocin caused a decline in packed cell volume following abdominal birth; but, there was no statistically significant difference between the study groups. This finding is in concordance with some trials (Ugwu et al.; 2014, Sallam & Shady, 2018).However, this is in disparity with some other similar studies’ findings (Sood & Sanjay, 2012; Rekha & Lathak, 2014, Agarwal & Thakar, 2022).In these later studies, misoprostol statistically appreciably reduced blood loss at surgical birth. This disparity may be due to assessing the packed cell volume less than 48-hours post-surgery (Rekha & Lathak, 2014, Nayak et al.; 2017)or the use of different equipment for haematocrit assessment or the use of automated haematocrit machine (Sood & Sanjay, 2012, Agarwal & Thakar, 2022). The micro-haematocrit readers used in this present trial was not automated. Assessing haematocrit less than 48- hours post-surgery would not give a true picture of the patient’s haemoglobin level, because of continued blood loss from the operation site, infusion of post-operative fluids (dextrose or normal saline), which causes further haemodilution, especially if a subarachnoid block had been used; inflammatory reaction of the body to surgical trauma and time taken for blood to re-equilibrate in the various body’s compartment (Aworinde et al.; 2018). It has been found out that it takes 24-hours for blood to re-equilibrate in the body after acute haemorrhage (Khalfaouni et al.; 2017).37 Accordingly, the best next time to assess haematocrit is 48-hours after surgery. The present study ensured that a 48-hours period of packed cell volume evaluation was used.

Different instruments have different calibrations, and this may influence results obtained from using various equipment, even if they were meant to evaluate a particular parameter. In this current investigative research, the micro-haematocrit centrifuge (low spin, TT 645B, 12,000 revolutions per minute), and T-15 haematocrit centrifuge with 12,000 revolutions per minute were used.

Evaluating the reduction in packed cell volume or haematocrit following caesarean delivery is an indirect means of assessing intraoperative blood loss. This present study’s indirect intraoperative blood loss assessment findings tallied with the direct quantification of caesarean section blood loss.

**5. CONCLUSION**

Sublingually administered adjunctive misoprostol at a dose of 400 ug did not appreciably curtail caesarean delivery bleeding.

**DISCLAIMER (ARTIFICIAL INTELLIGENCE)**

Authors hereby declare that NO generated AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

**CONSENT**

Written informed consent was secured from all participants after explaining the aim and objectives of the study, procedure and potential risks.

**ETHICAL APPROVAL**

All authors declare that the study was approved by the ethical committee of the Federal Medical Centre, Yenagoa with application form number – FMCY/REC/ECC/2022/JULY/477.

**COMPETING INTERESTS DISCLAIMER:**

Authors have declared that they have no known competing financial interests OR non-financial interests OR personal relationships that could have appeared to influence the work reported in this paper.

**REFERENCES**

Adanikan, A.l; Oriji, E; Adanikin, P.O; et al. (2013). Comparative study of rectal misoprostol to oxytocin infusion in preventing postpartum haemorrhage after caesarean section. Nepal Journal of Obstetrics and Gynaecology 1. 8(2):34-37.

Agarwal, S & Thakar N.D (2022). Sublingual misoprostol to reduce blood loss at caesarean delivery. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 11(1):95-99.

Akpan, U; Asibong, U; Arogundade, K; et al. (2021). Effectiveness of Pre-operative Rectal Misoprostol in Reducing Blood Loss during Caesarean section for Placenta Previa and Manual Removal of Retained Placenta: A Parallel Placebo-Controlled Study. Open Access Macedonian Journal of Medical Sciences. 9(B):161-166.

Andrade C. (2020). Sample size and its importance in Research. Indian Journal of Psychological Medicine. 42 (1):102-103.

Aworinde, O.O; Olufemi-Aworinde, K.J; Ogunlaja, O.A; et al. (2018). Optimal timing of post-operative haematocrit check in obstetric and gynecological surgeries. Research Journal of Health Sciences. 6(1):35-42.

Gerdessen, L; Meybohm, P; Choorapoikayil, S; et al. (2021). Comparison of common perioperative blood loss estimation techniques: a systematic review and meta-analysis. Journal of Clinical Monitoring and Computing. 35(2):245-248.

Karya, U; Maheshwari, S & Rani, A. (2021). Uterotonic effect of rectal misoprostol of intraoperative and postoperative blood loss in caesarean delivery. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 10(4):1415-1420.

Khalfaouni, M.Y, Godaritarne, C & Wilkinson, M.C.P. (2017). Optimal Timing for Hemoglobin Concentration Determination after Total Knee Arthroplasty: Day 1 versus Day 2. Knee Surgery Related Research. 29(1):52-56.

Maged, A; Fawzi, T; Shalaby, M; et al. (2019). A randomised controlled trial of the safety and efficacy of preoperative rectal misoprostol on preoperative and postoperative blood loss at elective caesarean delivery. International Journal of Gynaecology and Obstetrics. 147:102-107.

Maswine, S & Buchmann, E. (2017). A systematic review of maternal near miss and mortality due to postpartum haemorrhage. International Journal of Gynecology and Obstetrics. 137:1-7.

Mirteimouri, M; Akhlaghi, F & Jalali B.R. (2020). Effect of sublingual misoprostol in combination with oxytocin in reducing blood loss during and after caesarean delivery: a randomised clinical trial. Tehran University Medical Journal. 78(6): 357-365.

Nayak, L; Pradhank, K & Mishra S. (2017). Role of 400 ug intraoperative sublingual misoprostol for reduction of caesarean section blood loss. Journal of Evidence Based Medicine and Healthcare. 4(10), 573-577.

Ononge, S; Mirembe, F; Wandabwa, J; et al. (2016). Incidence and risk factors for postpartum haemorrhage in Uganda. Reproductive Health. 13(1):1-7.

Rekha, P & Latha, K. (2014). Sublingual misoprostol to reduce blood loss at Caesarean section. International Journal of Modern Research and Reviews. 2(10):444-446.

Sallam, H.F & Shady, N.W. (2018). Adjunctive sublingual misoprostol for secondary prevention of postpartum haemorrhage during caesarean delivery: double blind placebo randomized controlled trial. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 7(2):495-502.

Schorn, M.N. (2010). Measurement of blood loss: Review of the literature. Journal of Midwifery Women’s Health. 55: 20-27.

Sood, A.K & Sanjay, S. (2012). Sublingual Misoprostol to Reduce Blood Loss at Caesarean Delivery. The Journal of Obstetrics and Gynecology of India. 62(2):162-167.

Tang, O.S, Gemzell-Danielsson, K & Ho, P.C. (2007). Misoprostol: Pharmacokinetic profiles, effect on the uterus and side effects. International Journal of Gynecology and Obstetrics. 99(2): s160-s167.

Tunclap, O; Were, W.M; Maclennan, C; et al. (2015). Quality of care for pregnant women and newborn -the WHO vision. British Journal of Obstetrics and Gynaecology,122 (8):1045-1049.

Ugwu, I.A; Enabor, O.O; Adeyemi, A.B; et al. (2014). Sublingual misoprostol to decrease blood loss after caesarean delivery. A randomized controlled trial. Journal of Obstetrics and Gynaecology. 34:407-411.

Weeks A.D & Neilson J.P. (2015). Rethinking our approach to postpartum haemorrhage and uterotonics. British Medical Journal, 351-356.

WHO. (2018). Recommendation: Uterotonics for the prevention of postpartum haemorrhage. World Health Organization, Geneva: World Health Organization.15-29.