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Opioid-Free Versus Opioid-Based Post Caesarean Section Analgesia among Preeclamptics on Magnesium Sulphate: A Randomised Clinical Trial.

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ABSTRACT

Background: Despite the benefit of multimodal analgesia in avoiding opioid side effects, opioid administration is still associated with dose dependent opioid tolerance, dependence and addiction in some patients. This limitation has led to the current drive towards opioid-free multimodal analgesia which entails combination of non-opioid and adjuvant analgesics on a regular scheduled basis, with the use of opioids limited only to rescue analgesia. Magnesium sulphate being an adjuvant analgesic can be a suitable component of opioid-free analgesia, especially in preeclamptic women on magnesium sulphate undergoing a caesarean section.

Aim: To determine the effectiveness and safety of combining intravenous paracetamol and rectal diclofenac as a preventive, opioid-free multimodal analgesia regimen for management of acute post-operative pain in preeclamptic women on parenteral magnesium sulphate undergoing caesarean section.

Methods: Ethical approval was obtained from the research ethics committee of Federal Medical Centre, Yenagoa. The study was a non-inferiority randomized clinical trial. One hundred preeclamptic women undergoing caesarean section who gave consent and met the eligibility criteria was enrolled into the study. Sampling method was convenience sampling. Randomization was carried out by using WINPEPI. There were two groups with 50 participants in group A (experimental arm) and 50 participants in group B (control arm). Experimental arm received postoperative intravenous paracetamol, intramuscular placebo and rectal diclofenac for 24 hours. Control arm received postoperative intramuscular pentazocine, intravenous paracetamol and rectal diclofenac for 24 hours. Rescue analgesia (intramuscular pethidine) was administered to women in this study outside the established analgesic regimen for both arms of the study if needed. Variables assessed include post-operative pain intensity at 4, 8, 1 2 and 24 hours using Numerical Rating Scale, number of women who used post-operative pethidine as rescue analgesia, number and nature of adverse drug reactions were assessed and compared. Mean Difference in pain intensity and dose of opioid used were explored using Student t test, while Chi-square test compared the nature of adverse drug reaction in the 2 groups. Statistical significance was pValue <0.05.

Results: In the experimental and control arms, pain scores at 4, 8, 12 and 24 hours were 3.02±1.15 vs 3.12±1.42, 2.61±1.78 vs 2.74±1.67, 2.30 ± 1.52 vs 2.50 ± 1.61 and 2.12 ± 1.39 vs 2.41 ± 1.50 respectively, with no significant difference. Request for rescue opioid analgesic was significantly higher in the experimental arms. The mean time to first pethidine use was similar between groups (p = 0.765). The differences in adverse effect showed no statistical significance between both arms.

Conclusion: Preventive, opioid-free, multimodal analgesia using intravenous paracetamol, plus rectal diclofenac among preeclamptic on magnesium sulphate significantly reduced post-operative opioid consumption and it is as effective and safe as the routine opioid-based analgesia used in this study.

Keywords: Magnesium sulphate, Preeclampsia, Caesarean section, Acute post-operative pain, Opioid free analgesia

INTRODUCTION

Caesarean delivery is the most frequently performed surgery in several countries and its incidence has increased, underlining the need to discuss cesarean delivery management (Julia et al., 2022; Demelash, 2022; Macones et al., 2019). Discomfort is the most frequent issue following surgery. Pain is a sensory and emotional experience that is influenced by physiological, sensory, affective, cognitive, sociocultural, and behavioral aspects (Demelash, 2022; Ibrahim et al., 2022). Although pain is an inevitable component of the healing process after surgery, if not managed properly, can have negative effects.

Untreated postoperative pain can result in clinical and psychological changes that impair quality of life while raising morbidity and death (Demelash, 2022; Ibrahim et al., 2022).

Post-caesarean section pain, resulting from surgical tissue injury, is an important source of patient dissatisfaction and needs to be addressed aggressively for mothers to functionally recover quickly for optimization of the early stages of mother-child interaction (Azanu et al., 2022; Roofthooft et al., 2021). Inadequately controlled acute post-CS pain is associated with long hospital stay, increased costs and incidence of chronic pain (Azanu et al., 2022). Effective pain management is a benchmark for adequate health care and with CS being the most common surgical procedure conducted in the world, healthcare providers must achieve adequate post-CS pain control as early as possible.[5,6] There is no 'gold standard' for post-CS pain management. Factors such as the use of general anaesthesia, under treatment with opioid analgesics fueled by fear of addiction or respiratory depression, the ability to request for more pain relief, pain threshold, religion and anxiety are known to influence acute postoperative pain following CS (Azanu et al., 2022; Roofthooft et al., 2021).

Traditionally, opioid analgesics have been the mainstay of analgesic management of acute postoperative pain due to their effectiveness (Yim & Parsa, 2018; Koekpe et al., 2018). However, liberal administration of opioid analgesics to achieve optimum pain control is associated with various side effects including respiratory depression, sedation, postoperative nausea and vomiting, constipation, ileus, pruritus, urinary retention, opioid-induced hyperalgesia (OIH), opioid tolerance, dependence and addiction (Allison & Russell, 2021; World Health Organization, 1986; Mullman et al., 2020; Smith et al., 2019). These limitations have led to the introduction of use of multimodal analgesia which combines the use of 2 or more analgesics, with different mechanisms of action, to achieve effective analgesia, to reduce opioid use and the side effects of component analgesic drugs especially opioid.

The sequelae associated with opioid abuse is currently of public health importance, hence the move towards avoidance of opioids. This is currently driving multimodal analgesia towards a combination of non-opioid and adjuvant analgesics (Federal Ministry of Health et al., 2018; Lee et al., 2018; Fiore et al., 2019; Uros et al., 2021; Kim, 2019; Johnson, 2019). Opioid-free postoperative analgesia; a multimodal analgesia technique that combines non-opioid and adjuvant analgesics on a regular scheduled basis, with the use of opioids limited to rescue analgesia only if required, has a potential to tackle the fast rising and spreading opioid crises (Fiore et al., 2019). The aim of this study is to determine the effectiveness and safety of combining intravenous paracetamol and rectal diclofenac with parenteral magnesium sulphate, as a preventive, opioid-free multimodal analgesia regimen for management of acute post-operative pain in preeclamptic women undergoing caesarean section.

MATERIAL AND METHODS

A single-center, non-inferiority, randomized controlled trial (RCT). Randomization was into two equal arms. Participants were preeclamptic women undergoing Caesarean section at the Federal Medical Center Yenagoa, Bayelsa State, Nigeria. All procedures followed the 2013 Helsinki Declaration. The research ethics committee, Federal Medical Center Yenagoa approved the trial protocol. Each participant gave written informed consent to participate. Exclusion criteria included preeclamptic women with active peptic ulcer disease, active liver disease, hepatic failure, renal failure, previous history of ischemic heart disease/myocardial infarction, heart failure, venous thrombosis, stroke, hypersensitivity to pentazocine, paracetamol, diclofenac or magnesium sulphate, history of non-medical use (abuse) of opioids and can neither communicate in English nor Pidgin English.

INTERVENTION

After preloading, all the women received spinal anaesthesia with 2 ml [10 mg] of hyperbaric 0.5% bupivacaine into the subarachnoid space, and patients laid supine immediately. This fixed dose of bupivacaine was used instead of height and weight-adjusted dose to make the protocol easy to follow for the anaesthetist. It is backed by evidence from a randomized controlled trial showing that a fixed dose of 10 mg of hyperbaric 0.5% bupivacaine had similar results to height and weight-adjusted dose in spinal anaesthesia for caesarean section (Alam et al., 2018).

Experimental group received a combination of parenteral magnesium sulphate (ANCALIMA®- LIFESCIENCES LTD, India) according to Pritchard regimen as follows: 4g of a 20% solution of magnesium sulphate as an intravenous bolus slowly over 10 minutes and 10g of 50% solution intramuscularly (5g into each buttock) as loading dose preoperatively. Thereafter, 5g of 50% solution of magnesium sulphate into alternate buttocks every 4 hours was given for 24 hours. Post-operatively; immediately after wound dressing and patient cleaning, 100 mg of suppository diclofenac (LOFENAC®- BLISS GVS PHARMA LTD, India) was administered and continued 12-hourly, intravenous paracetamol (Drugamol®-DRUGFIELD PHARMACEUTICALS LTD, Nigeria) 1g 6-hourly and intramuscular placebo 30 mg (45 mg if patient is > 70 kg) was administered 6-hourly over 24 hours post-operatively.

Control group (routine opioid-based regimen active control) received a combination of parenteral magnesium sulphate (ANCALIMA®- LIFESCIENCES LTD, India) according to Pritchard regimen, as follows: 4g of a 20% solution of magnesium sulphate as an intravenous bolus slowly over 10 minutes and 10g of 50% solution intramuscularly (5g into each buttock) as loading dose preoperatively. Thereafter, 5g of 50% solution of magnesium sulphate into alternate buttocks every 4 hours was given for 24 hours. Post-operatively; immediately after wound dressing and patient cleaning, 100 mg of suppository diclofenac (LOFENAC®- BLISS GVS PHARMA LTD, India) was administered and continued 12-hourly, intramuscular pentazocine (ZOPENT®- GREENLIFE PHARMACEUTICALS LTD, Nigeria) 30 mg (45 mg if patient is > 70 kg) was administered 6-hourly, intravenous paracetamol (Drugamol®-DRUGFIELD PHARMACEUTICALS LTD, Nigeria) 1g 6-hourly was commenced, all over 24 hours post-operatively.

Rescue analgesia was administered to women in this study outside the established analgesic regimen for both arms of the study if needed. It was administered only on patients' expression of moderate to severe pain or following an assessment of moderate to severe pain by ward nurses/research

assistants, despite the planned analgesic regimen for both arms of the study. One hundred milligrams of intramuscular pethidine (MARTINDALE PHARMA, BAMPTON ROAD, HAROLD HILL, ROMFORD, RM3 8UG, UK) was used as rescue analgesia during the first 24 hours after caesarean section in both arms of the study.

PRIMARY OUTCOME MEASURE

The primary outcome measure was post-operative pain scores following caesarean section at 4-, 8-, 12- and 24-hours post-operative using the Numerical Rating Scale (NRS) for pain

SECONDARY OUTCOME MEASURES

The secondary outcome measures were the need to use pethidine as rescue analgesia during the first 24 hours post-operative and presence of women with post-operative adverse drug reactions including respiratory depression, constipation, ileus, pruritus, urinary retention and any other adverse event during the first 24 hours postoperative.

SAMPLE SIZE DETERMINATION

Sample size was determined using the formula for sample size determination for non-inferiority clinical trials with a continuous outcome (Flight & Julious, 2016).

$$n = \frac{2(Z_{1-\alpha} + Z_{1-\beta})^2 \; X \; SD^2}{d^2}$$

Where n = minimum sample size.

$Z_{1-\alpha =}$ is the standard normal deviate giving a confidence level of 95% and a level of significance (α) of 5% = 1.96.

$Z_{1-\beta}$ = the standard normal deviate at a power of 80%, = 0.842

SD = the standard deviation of the pain intensity after caesarean section (primary outcome measure) in a study done in Brazil and reported as 2.2 (Juan et al., 2020), and

d (non-inferiority limit) = 1.3, being MCID for acute post-caesarean section pain as derived from a previous study (Cepeda et al., 2003).

$$n = \frac{2(1.96 + 0.842)^2 \; X \; 2.2^2}{1.3^2}$$

$$n = \frac{2(2.80)^2 \; X \; 4.84}{1.69}$$

$$n = \frac{2 \; X \; 7.84 \; X \; 4.84}{1.69}$$

$$n = \; 44.9$$

$$n \approx 45$$

Using an attrition rate of 10%, this minimum sample size was increased by 5 (10% of 45). Fifty women were thus selected into each arm of this study, giving a total sample size of 100.

RECRUITMENT

Patients were enrolled into the study in order of appearance, based on their eligibility and willingness to participate in the study (convenience sampling). All women being prepared for induction of labour were met by the researcher or trained assistant in the antenatal ward or labour ward. Exclusion criteria were identified through relevant information obtained from case folders and history obtained from the women. To obtain an informed consent, the researcher or a trained assistant explained the aim and processes of the study and its benefits to eligible women in simple and clear terms, and an assurance of safety was given. Participants signed the consent form for the study only after they have expressed an understanding of the study and showed willingness to participate.

RANDOMIZATION AND ALLOCATION CONCEALMENT MECHANISM

Allocation sequence generation

Using the WINPEPI software for randomization, a random and balanced allocation of numbers 1 to 100 to letters A and B was conducted. Intervention arm A was designated the experimental group and intervention arm B was designated the control group. The women were allocated to receive either a preventive opioid-free multimodal analgesia regimen in the intervention arm A (experimental) or a routine post-operative, opioid-based multimodal analgesia regimen in the intervention arm B (control).

Allocation concealment mechanism

Identical, sealed, sequentially arranged and opaque envelopes had cards inscribed with letter A or B concealed within them according to the randomly assigned letter to each number from 1 to 100. These envelopes were labelled outwardly using serial numbers from 1 to 100.

Implementation

As each eligible woman is received into the theatre for a caesarean section, a research assistant picks an envelope according to the sequence. The number inscribed on the card in the envelope was announced and shown to the researcher, anaesthetist and peri-operative nurse (A = experimental arm and B = control arm). The serial number / identification number on the envelope selected was attached to the case folder, operation note and other documents for the study.

Blinding

The participants, researcher, research assistants, nurses who administered the post-operative analgesics and assess the post-operative pain intensity of the women and those responsible for data entry were all blinded in this study except the pharmacist preparing the drugs. All the trial documents were concealed in an opaque envelope on the ward.

Data collection methods

The primary and secondary outcome measures were obtained using a purpose designed proforma.

Data management

SPSS spreadsheet was used for data management. Data entry from paper data collection instruments into the SPSS spreadsheet was done weekly.

Data Monitoring

Full compliance with the trial monitoring mechanism of the study Centre was ensured.

DATA ANALYSIS

An intention-to-treat (ITT) analysis will be employed. Statistical analysis of the data obtained from the study was done using Statistical Package for Social Sciences (SPSS) version 25. Frequencies and percentages of categorical data was determined. Mean and standard deviation of continuous numerical data, median, mode and range of discrete numerical data was determined. Continuous data was assessed for normality using the Shapiro-Wilk test. Comparisons between experimental and control groups was done using Chi-square test of proportions for categorical data, Student ‘t’ test for normally distributed continuous data and Mann-Whitney U test for non-normally distributed continuous data. A clinically relevant difference in mean pain score of NRS < 1.3 was used to determine non-inferiority of experimental group to control group. A p-value < 0.05 will be considered significant statistically.

RESULTS

Three hundred and sixty-seven women booked for caesarean section at the Obstetrics and Gynaecology department of Federal Medical Centre, Yenagoa, during the study period and one hundred and eight of them were identified as potential participants presenting with preeclampsia. However, six of these women were excluded due to at least one of the exclusion criteria and two women declined to participate in the study.

One hundred women were ultimately enrolled in the study and randomly assigned to one of two study arms in a 1:1 ratio. The two arms consisted of an experimental group (Arm A) and a control group (Arm B). In the experimental group (Arm A), 50 women were assigned to receive the intervention and were assessed for primary and secondary outcome measures. In the control group (Arm B), all 50 women assigned to the control group (Arm B) received the intended intervention and were assessed for primary and secondary outcome measures. Consequently, data from all 100 enrolled women were included in the final analysis.

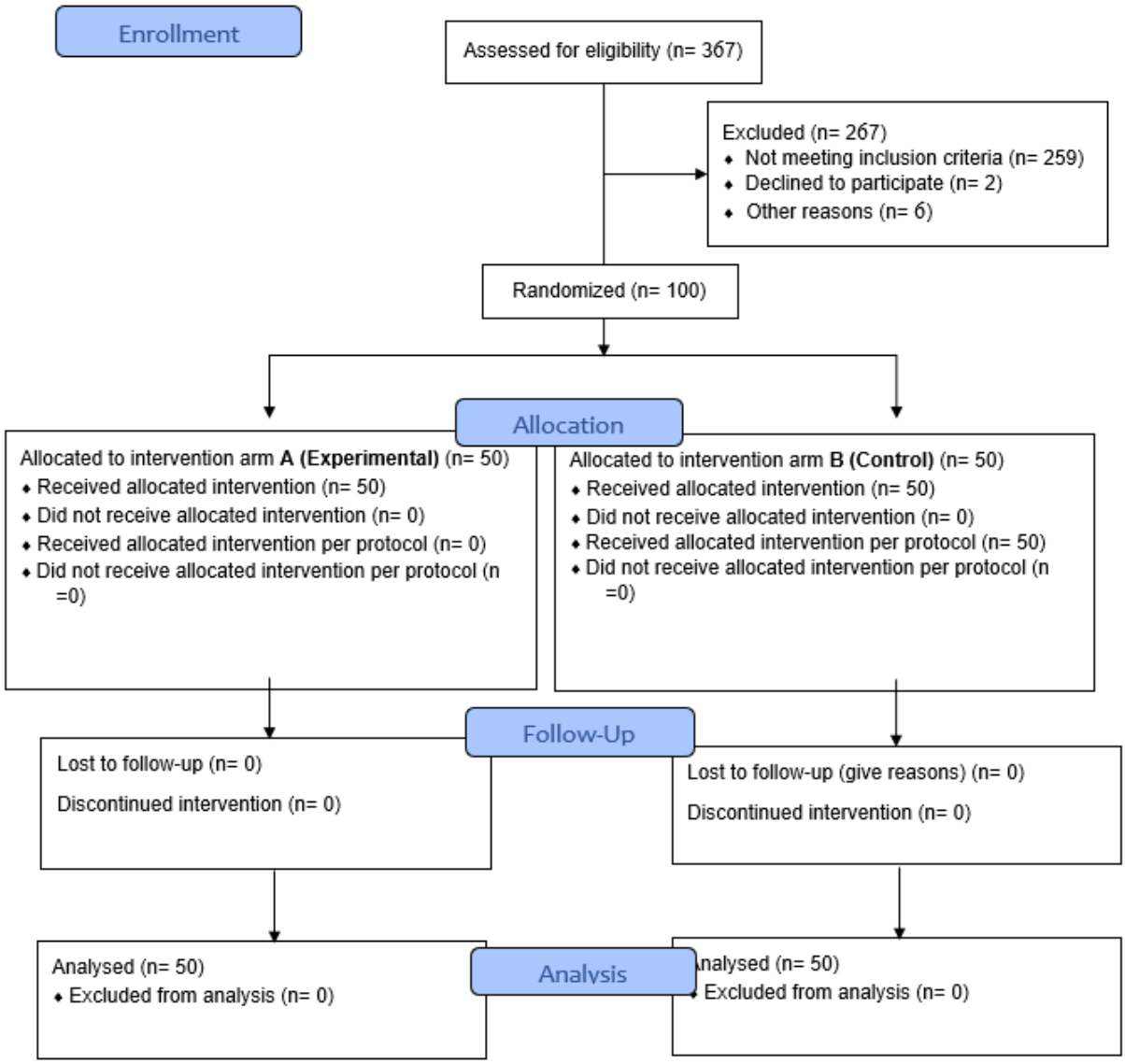

Figure 1: Study Flow Diagram

Table 1: Sociodemographic data of participants

Variable	Treatment Arm A		Treatment Arm B		Significance Test	p-value
	Freq (N=50)	%	Freq (N=50)	%		
Age (years)						
• 20-24	1	2.0	0	0.0	4.35[a]	0.210
• 25-29	13	26.0	17	34.0		
• 30-34	23	46.0	15	30.0		
• 35-39	13	26.0	18	36.0		
Mean age ± SD	31.92 ± 3.60 yrs		30.76 ± 4.05 yrs		1.12[b]	0.254
Mean weight ± SD	83.84 ± 12.41 kg		78.64 ± 9.32 kg		2.82[b]	0.063

Ethnicity						
• Igbo	22	44.0	19	38.0	2.56[a]	0.287
• Ijaw	22	44.0	21	42.0		
• Others	6	12.0	10	20.0		
Parity						
• Nulliparous	7	14.0	10	20.0	3.01[a]	0.215
• Primiparous	10	20.0	7	14.0		
• Multiparous	33	66.0	33	66.0		

[a] Chi-square test, [b]Student's t Test, *Statistically significant

The socio-demographic data of participants revealed comparable characteristics between Treatment Arms A and B. The mean age was slightly higher in Arm A (31.92 ± 3.60 years) than in Arm B (30.76 ± 4.05 years), with no significant difference (p = 0.254). Arm A participants had a higher mean weight (83.84 ± 12.41 kg) than Arm B which is not statistically significant (78.64 ± 9.32 kg, p = 0.063). Ethnicity and parity distributions were similar across groups, with Igbo and Ijaw being the predominant ethnicities, and most participants being multiparous. There were no significant differences in age categories, ethnicity, or parity between the groups.

Table 2: Clinical data of participants

Variable	**Treatment Arm A**		**Treatment Arm B**		**X^2**	**p-value**
	Freq (N = 50)	**%**	**Freq (N = 50)**	**%**		
Previous CS						
• No	26	52.0	28	56.0	0.48	0.487
• Yes	24	48.0	22	44.0		
	N = 24		**N = 22**			
Number of previous CS						
• 1	17	70.8	13	59.1	0.64	0.423
• 2	7	29.2	9	40.9		

The clinical data showed no significant differences between Treatment Arms A and B regarding previous cesarean sections (CS). A similar proportion of participants in Arm A (48.0%) and Arm B (44.0%) had a history of CS (p = 0.487). Among those with a previous CS, the majority in both groups had undergone only one prior CS (70.8% in Arm A vs. 59.1% in Arm B), with no significant difference in the number of previous CS between the arms (p = 0.423).

Table 3: Post-operative pain scores following caesarean section

Variable	**Treatment Arm A**	**Treatment Arm B**	**Mean Difference**	**t-test**	**p-value**
	Mean ± SD	**Mean ± SD**			
4 hours post-op	3.02 ± 1.15	3.12 ± 1.42	0.10	0.65	0.518
8 hours post-op	2.61 ± 1.78	2.74 ± 1.67	0.13	0.35	0.728
12 hours post-op	2.30 ± 1.52	2.50 ± 1.61	0.20	0.58	0.564
24 hours post-op	2.12 ± 1.39	2.41 ± 1.50	0.29	1.08	0.281

The post-operative pain scores following caesarean section were comparable between Treatment Arms A and B at all-time points. At 4-, 8-, 12- and 24-hours post-operation, the mean pain scores showed no significant differences, with p-values of 0.518, 0.728, 0.564 and 0.281, respectively. Both groups experienced a gradual decrease in pain scores over time, indicating similar pain management effectiveness.

Table 4: Request, Frequency and Time to first use of Rescue Analgesia

Variable	Treatment Arm A		Treatment Arm B		Significance Test	p-value
	Freq (N = 50)	%	Freq (N = 50)	%		
Request for Rescue Analgesia						
• **Request**	45	90.0	2	4.0	82.11a	0.001*
• **No request**	5	10.0	48	96.0		
Frequency of pethidine use						
• **Not used**	3	6.0	48	96.0	82.12a	0.001*
• **Once**	36	72.0	2	4.0		
• **Twice**	11	22.0	0	0.0		
• **Four times**	0	0.0	0	0.0		
Time to first use	139.80 ± 102.43 mins		146.20 ± 75.90 mins		0.30b	0.765

[a]Chi-square test, [b]Student's t Test, *Statistically significant

Rescue analgesia was requested by 90% of participants in Arm A, but only 4% in Arm B (p = 0.001). Regarding the frequency of pethidine use, Treatment Arm B exclusively reported four-time usage, while Arm A had varying patterns (72% used it once, 22% twice, and 6% not at all). The mean time to first pethidine use was similar between groups (p = 0.765).

Table 5: Adverse effects of analgesia regimen in the Treatment arms A and B

Variable	Treatment Arm A		Treatment Arm B		X^2	p-value
	Freq (50)	%	Freq (50)	%		
Vomiting						
• **Present**	1	2.0	1	2.0	0.000	1.000
• **Absent**	49	98.0	49	98.0		

Adverse effects of the analgesia regimens showed vomiting was reported by 2% of participants in both arms, with no significant difference (p = 1.000). Other post-operative adverse drug reactions including respiratory depression, constipation, ileus, pruritus, urinary retention and any other adverse event during the first 24 hours postoperative was not present.

DISCUSSION

This study found that women receiving preventive, opioid-free, multimodal analgesia reported lower mean pain scores at 4, 8, 12 and 24 hours post-operatively, but the use of post-operative opioid analgesic was not completely eliminated. Though, post-operative pain and post-operative opioid analgesic consumption was reduced without significant side effects. These results are consistent with a previous study by Makinde (Makinde et al., 2022) although carried out among non-preeclamptic women. The study found a significant reduction in mean opioid analgesic consumption among women who received a preventive, opioid-free, multimodal analgesia regimen consisting of intravenous paracetamol, plus postoperative rectal diclofenac, compared to the control group (54.10 ± 20.78 mg vs 162.90 ± 27.80 mg). This was in keeping with the findings of Uros (Uros et al., 2021) that reported a reduction in total opioid consumption in the opioid-free group. These results are consistent with findings from the Cleveland Clinic, USA, where introducing opioid-free post-operative analgesia for caesarean section patients led to a significant 70% reduction in opioid use within the first month (Johnson, 2019). Similarly, Kirk Medicine at the University of Southern California reported a 45-60% decrease in post-operative opioid usage by limiting or avoiding opioid use (Kim, 2019). The reason for this observation may be due to the non-opioid analgesics combining additive or synergistic analgesia to provide effective pain management and minimizing opioid-related side effects, such as nausea, vomiting, and constipation, which can contribute to increased pain scores. However opioid consumption was not completely eliminated as some patients may experience breakthrough pain that requires opioid analgesics. Some patients may also have high expectations for pain relief or experience anxiety related to pain, leading to requests for opioid analgesics.

This study also revealed that rescue medication in the form of intramuscular pethidine was administered less frequently in the control arm than women that received preventive, opioid-free, multimodal analgesia. Li (Li et al., 2022) observed a similar result where rescue analgesia was frequently administered among the experimental group than control group. However, the result contrast to finding from a study done by Adebisi (Adebisi et al., 2024) where intramuscular pentazocine as rescue analgesia was administered less frequently in the experimental group than the control group (57 vs. 70, p=0.024 which constitutes 60.6% and 76.1%). Melese (Melese et al., 2019) also in their study found rescue analgesia administered less frequently in the control arm than women in the experimental arm. In this present study, the mean time (in minutes) to the first dose of rescue analgesia was similar between the experimental and control group (139.80 ± 102.43 vs. 146.20 ± 75.90 p=0.765). This report differs with a study by Adebisi (Adebisi et al., 2024) where the mean time in minutes to the first dose of rescue medication was found to be longer in the experimental group compared to the control group (386.0±222.9 vs. 314.6±179.5, p=0.048). This may be due to women receiving opioid-based analgesia developing tolerance, reducing the intensity of pain and the need for rescue medication. They may have better pain control and provide better management of breakthrough pain, reducing the need for rescue medication, hence regular monitoring and adjustment of pain management strategies can help minimize the need for rescue medication.

Opioid use can lead to a range of adverse effects. These include nausea and vomiting, slow heart rate (bradycardia), and respiratory depression (Fiore et al., 2019; Kamel & Shoukry, 2022). In this present study there was reduced occurrence of side effects in both groups with no significant difference between both groups. The decrease in side effects in both opioid and non-opioid groups may be attributed to a combination of factors, including optimization of dosing regimens, improved patient selection, enhanced patient education, and improved pain assessment and monitoring. Haesun (Haesun et al., 2020) in their study found a significant reduction in postoperative occurrence of opioid-related side effects especially postoperative nausea and vomiting. Daoust (Daoust et al., 2020) in a prospective study showed that opioid side effects are highly prevalent during short-term acute pain treatments. Furthermore, they observed a dose-response relationship for constipation and showed that certain types of opioids are associated with increased incidences of nausea/vomiting and dizziness.

Despite more frequent opioid dosing in the control arm, the combined preventive analgesic effect of intravenous paracetamol and rectal diclofenac may have contributed to lower postoperative pain scores and significantly reduced opioid consumption in the experimental arm. The study aimed to establish non-inferiority of the experimental group compared to the control group. With a non-inferiority limit set at a mean pain score difference of <1.3, the results showed mean differences of 0.10, 0.13, 0.20 and 0.29 at 4, 8, 12 and 24 hours, respectively. This indicates that the experimental group was not inferior to the control group in terms of pain management effectiveness.

STRENGTHS AND LIMITATIONS:

The study used primary data, which gave precise information. The randomized clinical trial design of this study gives a high level of evidence and also reduces bias. Bias was reduced by randomization, blinding, use of standardized methods for data collection and analysis, as well as data quality control.

The limitation includes; the subjective nature of pain perception, expression, and assessment made it challenging to compare pain intensity between participants. Pain assessment relied heavily on self-reported pain intensity, which, although recorded verbatim, may be influenced by individual differences. To mitigate potential biases, research assistants received training from a consultant anaesthetist on pain assessment, emphasizing the importance of accepting participants' self-reported pain experiences without skepticism. Additionally, this study's findings may not be generalizable to other populations, as it was conducted exclusively among preeclamptic women undergoing caesarean sections at a single hospital, the Federal Medical Centre Yenagoa, Bayelsa State.

CONCLUSION

In conclusion, this study demonstrates that non opioid multimodal analgesia is as effective as opioid based analgesia in managing post caesarean section pain in preeclamptic on magnesium sulphate and offers a pathway to reduced opioid consumption as it significantly reduced post-operative opioid consumption in this study.

RECOMMENDATIONS

Based on the findings of this study, it is recommended that a preventive, opioid-free, multimodal analgesia regimen consisting of perioperative paracetamol, with postoperative rectal diclofenac, be adopted for managing acute postoperative pain among preeclamptic on magnesium sulphate following caesarean sections at the Federal Medical Centre Yenagoa, Bayelsa State.

To further validate and generalize these findings, larger, multicenter studies using a similar protocol are suggested. Such studies could also investigate the optimal timing for administering a single dose of opioid analgesic within this regimen, potentially enhancing its effectiveness.

AUTHOR CONTRIBUTIONS

Idea/Concept: Atemie Gordon, Jeremiah Israel, Olakunle I Makinde; Design: Atemie Gordon, Jeremiah Israel, Olakunle I Makinde; Control/Supervision: Atemie Gordon, Warisuo S. Ariwelo, Porbeni-Fumudoh B. Offiong; Data Collection and/or Processing: Atemie Gordon, Warisuo S. Ariwelo, Porbeni-Fumudoh B. Offiong, Amadi-Oyioma M Chigesilem; Analysis and/or Interpretation: Atemie Gordon, Sintei Erigheyefa, Feghabo J Ebiegberi; Literature Review: Atemie Gordon, Amadi-Oyioma M Chigesilem, Sintei Erigheyefa, Feghabo J Ebiegberi; Writing the Article: Atemie Gordon; Critical Review:

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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ETHICAL APPROVAL

Ethical approval was obtained from the ethical committee of the Federal Medical Centre, Yenagoa, Bayelsa State.

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