AFRICAN JOURNAL OF FETOMATERNAL MEDICINE

Original Article

Intravenous Acetaminophen in a Faith-Based Hospital in Nigeria: A Randomized Trial of a Labor Analgesic.

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Abstract

Background: The undesirable maternal and neonatal side effects of opioid analgesics, and less ready availability and affordability of epidural analgesia in resource poor settings has necessitated the search for a safe, efficacious, affordable and readily available labor analgesic. **Aim:** To determine the efficacy, safety and acceptability of intravenous acetaminophen as an intra-partum analgesic. **Methods:** A randomized controlled double-blinded study involving 162 consenting pregnant women in labor, assigned to two groups, each receiving either 900mg of intravenous acetaminophen or an equal volume of normal saline. The Numeric Rating Scale and Likert scale were used to measure the degree of pain experienced and the level of acceptability. Data was analyzed using IBM SPSS Statistics for Windows, version 24.0. The student's T-test, Chi-square test ($\chi 2$), Hazard ratio and Mann-Whitney U test were used to test associations with level of statistical significance set at $p < 0.05$. **Results:** At 15, 60-, 120-, 180- and 240-minutes post-administration of medications, there was a statistically observed significant difference between the pain scores of women in the two groups ($t = 3.71$, 7.58, 9.45, 9.48, and 9.18 respectively, $p < 0.001$). The participants in the acetaminophen group had better pain relief than those in the placebo group (Hazard ratio = 0.51; 95% CI: 0.35 – 0.73; $p < 0.001$). There was no significant difference between the two groups in terms of side effects of administered agents. The difference between the maternal level of acceptability of acetaminophen and placebo as labor analgesia was found to be statistically significant ($\chi 2 = 72.981$, $p < 0.001$). **Conclusions:** In poor resource settings, intravenous acetaminophen is an effective alternative labor analgesic agent with no adverse maternal and neonatal side effects.

Keywords: Acceptability, Intravenous Acetaminophen, Labor analgesia, Pain Relief.

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Introduction

Recent advances in medical science have increased the options available for obstetric analgesia for women in labor, however inequalities still exist regarding availability especially in low resource settings.[1,2] Labor pain is often severe and an unpleasant experience which may be associated with uncooperative attitudes, psychological disturbances and irrational behaviour leading to maternal and fetal side effects.[3,4]

Labor pain activates the sympathetic nervous system, resulting in an increase in plasma catecholamine concentrations and a decrease in uterine blood flow which can lead to serious compromise of fetal well-being.[5] There are visceral and somatic components of labor pain, with the

visceral stimulation occurring in the latent or early active phase as the cervix and lower uterine segment dilates while the somatic stimulation occurs late and is caused by distension of the pelvic floor, perineum and vagina.[3,5,6] The pain impulses are transmitted via the visceral afferent nerve fibres to the spinal cord at the level of T10 – L1 and via the pudendal nerves to spinal segment S2-S4.[3,7]

Previous history of traumatic birth can predispose to tokophobia and research estimates 6-10% of women have a pathological disabling fear of childbirth, commonly the fear of having an episiotomy, fear of having no control on the situation and fear of pain.[8] About 9-11% of non-gravid women report fear of childbirth sufficient to postpone or avoid pregnancy.[9] With regular and consistent use of appropriate labor analgesia universally, it is postulated that there will be a significant reduction in tokophobia resulting from previous traumatic births. Pain is a complex, subjective and perceptual phenomenon dependent on many factors, and in research is frequently assessed using the Numeric Rating Scale (NRS).[10]

Labor analgesia could be in the form of pharmacologic or non-pharmacologic therapy.[6] Non-pharmacological pain therapy includes massage, breathing exercises, emotional support, transcutaneous electric nerve stimulation (TENS), acupuncture, hydrotherapy and aromatherapy while pharmacologic therapy comprises of systemic analgesia, inhalational analgesia, neuraxial blocks and other regional anaesthesia.[5,6,11] Opioid analgesics are common effective pain medications in labor, however its use have been associated with undesirable maternal and neonatal side effects such as drowsiness, sedation and respiratory depression in the mother, and neonatal respiratory depression.[5,6] Though epidural analgesia is the gold standard for labor analgesia, the paucity of skilled personnel and cost implication of the procedure limits its availability and use in low resource settings.[1,12] The challenges with the use of opioid analgesics and epidural analgesia in resource poor settings has necessitated the search for a safe, efficacious, affordable and readily available form of labor analgesia.[6]

Acetaminophen is one of the most frequently used analgesic and antipyretic medications worldwide, available over the counter, both in mono- and multi-component preparations and a few studies have reported the efficacy of acetaminophen for pain control in labor, using various dosages(1).[13] The need to prevent such excruciating pain in women with affordable and readily available analgesics is paramount in obstetrics care and the search for the lowest effective safe dose of parenteral acetaminophen and acceptability as a labor analgesia formed the basis for this study. Therefore, this study was designed to determine the efficacy, safety, and acceptability of intravenous acetaminophen as an intra-partum analgesic.

Materials And Methods

The study was carried out at the Our Lady of Apostle (O.L.A.) Catholic Hospital, Oluyoro Oke-Offa, Ibadan, Oyo State, Nigeria. The hospital was established in 1952 and is the largest private hospital in Ibadan, providing primary and secondary health care to patients in Ibadan, Oyo State and from other states in Nigeria. It is an accredited establishment for postgraduate training of specialist doctors in Family Medicine and Obstetrics and Gynaecology and serves as a rural posting facility for other specialties. The department of Obstetrics and Gynaecology is manned by two consultants and six postgraduate doctors at various levels of training, midwives, public health nurses and is supported by functional radiological, laboratory, blood banking, pediatric and anesthetist services.

This was a randomized controlled double-blinded study involving consenting 162 pregnant women in labor, assigned to the study or control group. Participants were recruited from the Antenatal Clinic (ANC) of O.L.A. Catholic Hospital, Ibadan during health talks and counselling sessions.

Pregnant women in established labor with cervical dilatation of at least 4cm and not more than 6cm**, s**ingleton viable fetus, cephalic presentation and spontaneous onset of labor at term were included in the study while those who were unbooked for ANC, had medical and obstetric disorders in pregnancy, previous caesarean section (CS), pre-labor rupture of membranes, women on induction of labor and history of allergy to acetaminophen were excluded from this study.

The sample size was determined using the formula, $n = 2\sigma^2\{[\varepsilon_{1-\alpha/2} + \varepsilon_{1-\beta}]/\Delta_A\}^2$, for a two-tailed hypothesis testing with the assumption of one treatment group and one control group of equal size.[14] Previous similar studies were used to determine a suitable standard deviation from which calculation was made of the pooled variance(σ^2), and as well, a clinically acceptable difference of means between the 2 treatment groups.[15,16] The calculated minimum sample size after adding 10% for attrition was 81 in each group.

Consecutive sampling technique was used for the selection of the women in the labor ward who had volunteered to participate in the study during the ANC. Randomization was done using a computer-generated sequence of random numbers allotted to either the study group or placebo group using Groups A and B. The hospital pharmacists constituted identical looking vials pre-labelled as A or B, either of which contained equal volumes of 900mg intravenous acetaminophen (diluted to 20mls with water for injection) or the placebo/control agent which was 20mls of intravenous normal saline. The prepared agent was given to participants in the active phase of labor at a cervical dilatation of 4cm to 6cm. This was double-blinded research with the participants, the investigators, the attending midwives and research assistants all blinded.

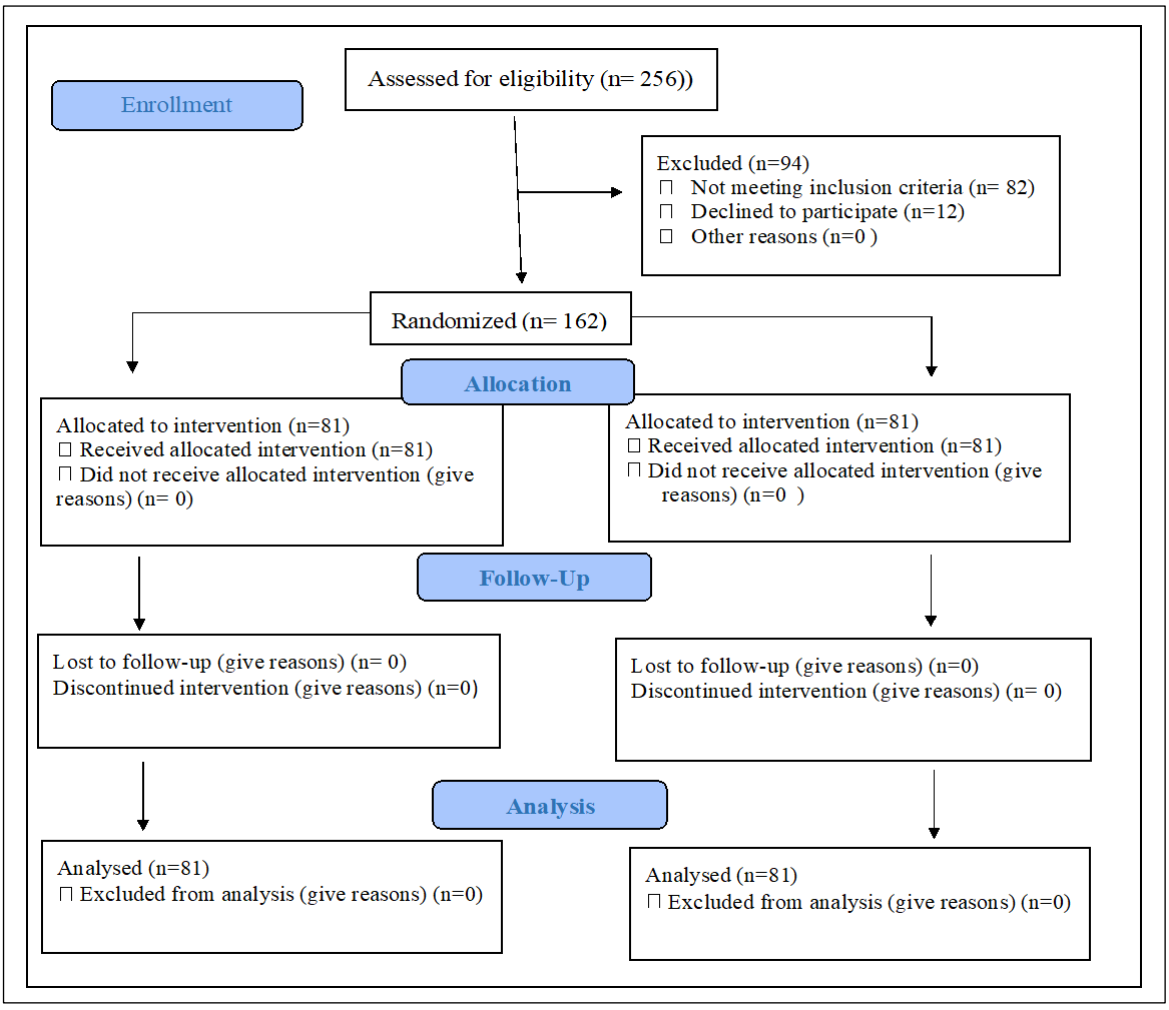

Fig 1. Participant Flow Diagram.

Data was collected using closed-ended questionnaires developed by the researcher from the literature and rating scales. The NRS, which is a segmented numeric version of the visual analogue score (VAS) in which a respondent selects a whole number (0 to 10 integers) that best reflects the intensity of their pain, was used for the measurement of the degree of labor pain experienced by women in the two groups.[17] The 5-point Likert scale was used for assessing the level of acceptability of acetaminophen as a labor analgesic.[18,19] The pain scores were measured at baseline, then at 15 minutes, 30 minutes, 60 minutes, and hourly thereafter till full cervical dilatation or first demand for rescue analgesia.

When a participant in any of the two groups demanded rescue analgesia, the time of first demand was recorded and intramuscular (I.M,) pentazocine 30mg was given provided cervical dilatation had not exceeded 6cm. The efficacy of the administered agent to supply adequate analgesia as measured by a change in pain intensity score using the various time intervals was documented. The time interval between recruitment dose and rescue dose of analgesia was also noted for each group

The level of acceptability was assessed 24 hours post-delivery using the 5-point Likert scale. Any adverse effect of the drug on the mother, fetus or neonate was also recorded. The differential effect of administered labor analgesia and participants' response based on different confounding variables were also recorded for subsequent analysis.

Data from the data collection forms were analyzed using IBM SPSS Statistics for Windows version 24.0.IBM Corp Chicago. Frequency tables and charts were generated, and tests of association were done using Chi square test, T–test, Hazard ratio and Mann-Whitney U test. The statistical level of statistical significance was set at $p < 0.05$. Prior to commencement of this research, ethical approval was sought and obtained from the Hospital Research Ethics Committee of O.L.A. Catholic Hospital, Ibadan (OCH/EC/20/05). The ethical principles of research were adhered to in this study.

Results

Two hundred and fifty-six women in labor were assessed for eligibility, out of which 82 did not meet the inclusion criteria, and 12 declined to participate. Hence, 162 women who met the eligibility criteria and who gave written informed consent were randomized into two groups of 81 each, namely the acetaminophen (treatment) and normal saline (placebo) groups. This is shown in Figure 1.

Majority, one hundred and thirteen (69.7%), one hundred and ten (67.9%), one hundred and fifty-six (96.33%), one hundred and twelve (69.1%) and one hundred and five (64.8%) participants, had tertiary level of education, were Yoruba, were married, of the Christian faith and multigravida, respectively. There were no statistically significant differences in the socio-demographic and obstetrics characteristics following randomization. This is shown in Table 1.

Table 1: Sociodemographic and Obstetrics Characteristics of the study participants

Variable	Acetaminophen Group	Placebo Group	Total	$\chi 2$	p
	n (%)	n (%)	n (%)		
Age group(years)					
20-24	5(6.2)	4(4.9)	9(5.6)	0.282	0.964
25-29	25(30.9)	23(28.4)	48(29.6)		
30-34	37(45.7)	39(48.2)	76(46.9)		
≥35	14(17.2)	15(18.5)	29(17.9)		
Highest Level of Education					
Primary	1(1.23)	2(2.5)	3(1.9)	4.535	0.104
Secondary	29(35.81)	17(21.0)	46(28.4)		
Tertiary	51(62.96)	62(76.5)	113(69.7)		
Ethnicity					
Yoruba	54(66.6)	56(69.1)	110(67.9)	0.130	0.937
Ibo	19(23.5)	18(22.3)	37(22.8)		
Others	8(9.9)	7(8.6)	15(9.3)		
Marital Status					
Married	79(97.5)	77(95.1)	156(96.3)	0.173	*0.677
Single	2(2.5)	4(4.9)	6(3.7)		
Religion					
Islam	27(33.3)	23(28.4)	50(30.9)	0.463	0.496
Christian	54(66.7)	58(71.6)	112(69.1)		
Occupation					
Professional	14(17.3)	7(8.6)	21(13.0)	6.327	0.388
Trading	18(22.3)	24(29.6)	42(25.9)		
Artisan	33(40.7)	29(35.8)	62(38.3)		
Civil Servant	4(4.9)	2(2.5)	6(3.7)		
Teacher	7(8.6)	10(12.4)	17(10.5)		
Housewife	5(6.2)	9(11.1)	14(8.6)		
Parity					
1-2	38(46.9)	52(64.2)	90(55.6)	5.444	0.066
3-4	37(45.7)	23(28.4)	60(37.0)		
>4	6(7.4)	6(7.4)	12(7.4)		
Gravidity					
Primigravida	23(28.4)	34(42.0)	57(35.2)	3.275	0.070
Multigravida	58(71.6)	47(58.0)	105(64.8)		

The mean pain scores using the NRS in the acetaminophen group at baseline, 15, 60, 120, 180 and 240 minutes were 9.64 ± 0.68, 8.22 ± 0.88, 6.90 ± 1.03, 5.98 ± 1.20, 5.48 ± 1.25 and 5.41 ± 1.31 respectively while for the placebo group were 9.43 ± 1.17, 8.80 ± 1.10, 8.28 ± 1.28, 7.90 ± 1.38, 7.60 ± 1.51 and 7.53 ± 1.46 respectively. There was no statistically significant difference in the pain scores of the women in the two groups at baseline (t = -1.40, p = 0.165) but there was a statistically observed difference between the pain scores of women in the two groups at 15, 60, 120, 180 and 240 minutes (t = 3.71, 7.58, 9.45, 9.48, and 9.18 respectively, p < 0.001). This is shown in Figure.2.

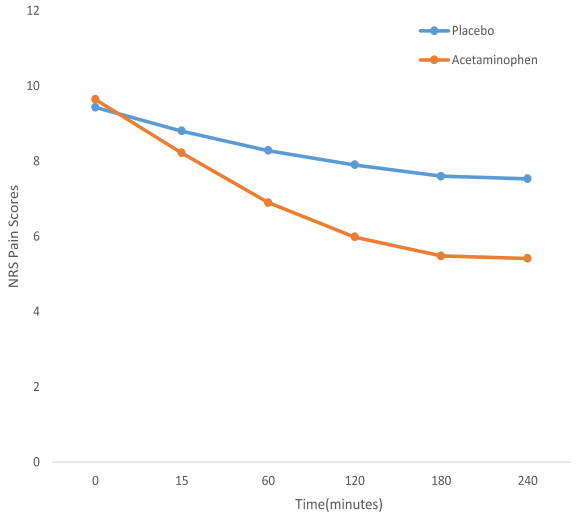

Figure 2: Comparison of NRS Pain Scores between the Acetaminophen and Placebo group

The median time and interquartile range of first demand for rescue analgesia in the acetaminophen and placebo groups was 80 (300) and 120 (120) minutes respectively. The Hazard ratios in the acetaminophen and placebo groups were 0.51 and 1.00 respectively and this was found to be statistically significant (p<0.001, 95% CI 0.35-0.73). This is shown in Table 2.

Table 2: Comparison of pain perception based on hazard ratios of time of demand for rescue analgesia among the study groups

	Acetaminophen Group Median (IQR)	Placebo Group Median (IQR)	U	p
Time of demand for first rescue analgesia (minutes)	180(300.0)	120(120.0)	2977.0	0.304
Hazard ratio	Acetaminophen	Placebo	95% CI	p
	0.51	1.00	0.35-0.73	<0.001

Thirty-eight (46.9%) participants found acetaminophen fully acceptable as a labor analgesia compared to 3 (3.7%) in the placebo. The difference between the maternal level of acceptability was found to be statistically significant ($\chi 2$ = 72.981, p < 0.001). This is shown in Table 3.

Table 4 shows the maternal and fetal side effects among the two groups. There was no statistically observed significant difference in the observed effects between these two groups of women.

Table 3. Maternal Level of Acceptability

Variables	Acetaminophen Group n (%)	Placebo Group n (%)	Total N (%)	$\chi 2$	p
Acceptability					
Fully acceptable	38(46.9)	3(3.7)	41(25.3)	65.792	<0.001
Partially acceptable	21(25.9)	6(7.4)	27(16.7)		
Undecided	6(7.4)	12(14.8)	18(11.1)		
Not fully acceptable	5(6.2)	22(27.2)	27(16.7)		
Not acceptable at all	11(13.6)	38(46.9)	49(30.2)		

Table 4: Maternal and fetal side effects among the acetaminophen and placebo groups

Maternal	Acetaminophen Group n (%)	Placebo Group n (%)	Total N (%)	$\chi 2$	p
Nausea					
Yes	14(17.3)	10(12.3)	24(14.8)	0.783	0.376
No	67(82.7)	71(87.7)	138(85.2)		
Vomiting					
Yes	22(27.2)	20(24.7)	42(25.9)	0.129	0.720
No	59(72.8)	61(75.3)	120(74.1)		
Drowsiness					
Yes	1(1.2)	0(0.0)	1(0.6)	-	-
No	80(98.8)	81(100.0)	161(99.4)		
Respiration Depression					
Yes	0(0.0)	0(0.0)	0(0.0)	-	-
No	81(100.0)	81(100.0)	162(100.0)		
Delayed Gastric Emptying					
Yes	0(0.0)	0(0.0)	0(0.0)	-	-
No	81(100.0)	81(100.0)	162(100.0)		
Dizziness					
Yes	0(0.0)	0(0.0)	0(0.0)	-	-
No	81(100.0)	81(100.0)	162(100.0)		
Blurry Vision					
Yes	0(0.0)	0(0.0)	0(0.0)	-	-
No	81(100.0)	81(100.0)	162(100.0)		
Dry Mouth					
Yes	0(0.0)	0(0.0)	0(0.0)	-	-
No	81(100.0)	81(100.0)	162(100.0)		
Fetal Admitted to SCBU					
Yes	8(9.9)	4(4.9)	12(7.4)	1.44	0.230
No	73(90.1)	77(95.1)	150(92.6)		

Discussion

The socio-demographic characteristics in this study is similar to other previous studies in Nigeria except for the educational level and tribe.[20-22] Some studies in Northern Nigeria had more participants with lower levels of education and likewise most participants in this study were Yorubas which is the most prevalent tribe in southwest Nigeria where the study was done.[15,22] Regarding the influence of socio-demographic characteristics on pain, previous studies have reported that women with higher level of education express higher level of pain when in labor and this may be due to their exposure to educational materials that changes their orientation .[22-24] Also, culture influences pain perception during childbirth due to the belief that it is cowardly and shameful to express the intensity of pain so the lower pain scores recorded may not be a true reflection of the severity of labor pain however this study was done in southwest Nigeria where majority perceive labor pain as severe and desire effective methods of pain relief.[24,25]

In this study, women who received acetaminophen had better labor pain relief from the 15 minutes up to the 4th hour post-administration with the highest occurring between 3rd and 4th hour. The mean pain reduction scores were higher than those obtained in previous similar studies which occurred prior to 2-hours post-administration.[21,22] The observed pain scores at the 2nd and 3rd hours post-administration were also slightly lower than the scores obtained by Aimakhu et al. and Omotayo et al. over the same period and this may be due to the higher dose of acetaminophen used in this study and the intravenous route of administration which has been attributed to the greater bioavailability of the medication.[21,22,26] Even though these pain scores obtained in this study are moderate, they were statistically significantly less than the placebo group so demonstrating the added benefit of intravenous acetaminophen which is similar to other studies.[15,16,21,22]

Furthermore, the practice in the study site for women in labor is to allow the intake of oral fluids to prevent dehydration and maternal exhaustion however this may promote vomiting if narcotics are used as documented in other studies.[26,27] This may be the reason for the hesitation in the liberal use of opioids for labor pain relief in this study site until it is demanded. Also, parturients are allowed to have companionship by relatives in labor and this has been shown to help patients cope better and reduce their demand for analgesia.[28,29] Other considerations in the choice of opioid analgesics are the fear of neonatal respiratory depression especially when used shortly before delivery and the less ready availability and affordability of epidural analgesia which has been showed from previous studies as an ideal analgesia.[26]

The Hazard ratio concept, used in this study for a better comparative statistical analysis of the time of first demand for rescue analgesia by participants in both groups, describes the outcome of therapeutic trials where the question is to what extent treatment can shorten duration of illness.[30] Our study found the hazard ratios of 0.51 and 1 for the acetaminophen and placebo group respectively, and this implied that the acetaminophen receiving group were about 0.51 times as exposed to the hazard of labor pain meaning that women in the placebo group were 1.96 times more likely to demand for rescue analgesia. This further corroborates the analgesic effectiveness of intravenous acetaminophen as labor analgesia.

In this study, women in the acetaminophen group had a higher level of satisfaction with pain relief and this was also statistically significant. This is similar to documented findings of other studies, though the study done in northern Nigeria used a higher dosage of acetaminophen probably due the fact that women in northern Nigeria have a higher pain threshold and had a slightly higher level of satisfaction.[20,22]

The side effects observed in this study were mainly nausea and vomiting and there was no statistically significant difference between the two groups. These side effects might have been due to the physiological responses to the effect of labor, and not to any of the administered agents. The absence of other side effects following administration of parenteral acetaminophen is similar to findings in other studies and this is a major advantage over the opioids which has been known to cause dizziness in the mother and respiratory depression in the neonate.[21,22] In addition, there is no statistically significant difference between the number of admissions to the Special Care Baby Unit (SCBU) between the two groups. This is similar to findings in some previous studies in Nigeria.[20,22] Hence, acetaminophen administration does not appear to influence the number of admissions to SCBU.

The strength of this study is the randomization which ensured that the sociodemographic characteristics of participants were similar in the two groups, the pre-labor counselling which allowed for better understanding of the information rather than if counselling was done solely in the active phase of labor. The double-blind nature of the study helped to reduce bias and this study was conducted in a secondary tier hospital that is closer to the community and more likely to reflect the effects on the general population.

Limitations of the Study

The limitations in this study included the challenging nature of assessment of labor pain using the NRS to some participants, and the intravenous route of administration of the medications which may have caused discomfort and pain and invariably affect the pain scores. Also, pain perception is subjective and may be influenced by previous experiences and culture of the parturients.

Conclusion

In conclusion, this study has shown that 900mg of intravenous acetaminophen has modest efficacy as a labor analgesic agent and that its use in labor is safe to the mother and fetus. Furthermore, it can be said to have a reasonable level of acceptability among parturients, thereby making it useful in places where there is unavailability of the more acceptable obstetrics analgesics. We recommend its use in resource poor settings where there is no facility, funds or expertise for standard labor analgesia and in advanced active phase to avoid the side effects associated with opioid use. There is the need for further research to explore other routes of administration of acetaminophen such as the oral and rectal route for their possible labor analgesic efficacy.

Acknowledgement/Funding

We acknowledge the contributions of the participants who consented to this study knowing that the findings may contribute towards improving the care for women in labor and the midwives for their cooperation during the period of this study. This study was self-sponsored.

Conflicts Of Interest

There are no conflicts of interest to declare.

References

1. Lam KK, Leung MKM, Irwin MG. Labour analgesia: Update and literature review. Hong Kong Medical Journal. 2020;26(5):413–20.
2. Mousa O, Abdelhafez AA, Abdelraheim AR, Yousef AM et al. Perceptions and practice of labor pain-relief methods among health professionals conducting delivery in Minia maternity units in Egypt. Obstet Gynecol Int. 2018; 12:1–7.
3. Labor S, Maguire S. The pain of labour. Rev Pain. 2008;2(2):15–9.
4. Whitburn LY, Jones LE, Davey MA, Small R. The meaning of labour pain: How the social environment and other contextual factors shape women's experiences. BMC Pregnancy Childbirth. 2017;17(1):1–10.
5. Wong CA. Advances in labor analgesia. Int J Womens Health [Internet]. 2009; 1:139–54.
6. Czech I, Fuchs P, Fuchs A, Lorek M et al. Pharmacological and non-pharmacological methods of labour pain relief—establishment of effectiveness and comparison. Int J Environ Res Public Health. 2018;15(12):1–11.
7. Alkatout I, Wedel T, Pape J, Possover M et al. Review: Pelvic nerves - From anatomy and physiology to clinical applications. Transl Neurosci. 2021;12(1):362–78.
8. Demšar K, Svetina M, Verdenik I, Tul N et al. Tokophobia (fear of childbirth): Prevalence and risk factors. J Perinat Med. 2018;46(2):151–4.
9. Rondung E, Thomtén J, Sundin Ö. Psychological perspectives on fear of childbirth. J Anxiety Disord. 2016; 44:80–91.
10. Kim TK. Practical statistics in pain research. Korean Journal of Pain. 2017;30(4):243–9.
11. Zha Y, Gong X, Yang C, Deng D et al. Epidural analgesia during labor and its optimal initiation time-points: A real-world study on 400 Chinese nulliparas. Medicine. 2021;100(9):1–8.
12. Ezeonu PO, Anozie OB, Onu FA, Esike CU et al. Perceptions and practice of epidural analgesia among women attending antenatal clinic in FETHA. Int J Womens Health. 2017; 9:905–11.
13. Ayoub SS. Paracetamol (acetaminophen): A familiar drug with an unexplained mechanism of action. Temperature. 2021;8(4):351–71.
14. Zhong B. How to calculate sample size in randomized controlled trial? J Thorac Dis. 2009;1(1):1–4.
15. Ekweani JC, Adesiyun AG, Ogboli-Nwasor E, Avidime S. A comparative study of intramuscular acetaminophen versus intramuscular pentazocine as labour analgesia in Zaria Northwestern Nigeria. J West Afr Coll Surg. 2014;4(3):35–53.
16. Zutshi V, Usha Rani K, Marwah S, Patel M. Efficacy of intravenous infusion of acetaminophen for intrapartum

analgesia. Journal of Clinical and Diagnostic Research. 2016;10(8):18–21.
17. Hawker GA, Mian S, Kendzerska T, French M. Measures of Pain. Arthritis Care Res (Hoboken). 2011;63(11):240–52.
18. Safikhani S, Gries KS, Trudeau JJ, Reasner D et al. Response scale selection in adult pain measures: Results from a literature review. J Patient Rep Outcomes. 2018;2(1):1–9.
19. Hulsbosch LP, Nyklíček I, Potharst ES, Boekhorst MG et al. Development of the Labor Pain Relief Attitude Questionnaire for pregnant women (LPRAQ-p). BMC Pregnancy Childbirth. 2020;20(1):1–12.
20. Muhammad Z, Abdulrahman A, Tukur J, Shuaibu S. A Randomized controlled trial of intramuscular pentazocine compared to intravenous paracetamol for pain relief in labor at Aminu Kano Teaching Hospital, Kano. Trop J Obstet Gynaecol. 2017;34(2):116–23.
21. Omotayo RS, Faturoti SO, Ehinmitan RR, Alao FO. Comparison of intramuscular paracetamol and intramuscular pethidine as analgesic in the first stage of labor. Trop J Obstet Gynaecol. 2018;35(3):348–57.
22. Aimakhu C, Saanu O, Olayemi O. Pain relief in labor: A randomized controlled trial comparing intramuscular tramadol with intramuscular paracetamol at the University College Hospital, Ibadan, Nigeria. Trop J Obstet Gynaecol. 2017;34(2):91-98.
Akadri AA, Odelola OI. Labour pain perception: Experiences of Nigerian mothers. Pan African Medical Journal. 2018;30(288):1–7.
23. Aduloju O. Pain perception among parturients at a University Teaching Hospital, South-Western Nigeria. Nigerian Medical Journal. 2013;54(4):211-216.
24. Obuna J, Umeora O. Perception of labor pain and utilization of obstetrics analgesia by Igbo women in southeast Nigeria. Journal of Obstetrics Anaesthesia Critical Care. 2014;4(1):18–22.
25. Jin JF, Zhu LL, Chen M, Xu HM et al. The optimal choice of medication administration route regarding intravenous, intramuscular, and subcutaneous injection. Patient Prefer Adherence. 2015; 9:923–42.
26. Aziato L, Kyei AA, Deku G. Experiences of midwives on pharmacological and non-pharmacological labour pain management in Ghana. Reprod Health. 2017;14(128):1-8.
27. Khresheh P. Support in the first stage of labour from a female relative: the first step in improving the quality of maternity services. Midwifery. 2010; 26(6): 21-24.
28. Rogers W, Hutchison K, Skea ZC, Campbell MK. Strengthening the ethical assessment of placebo-controlled surgical trials: three proposals. BMC Med Ethics. 2014;15(78):1–10.
29. Spruance SL, Reid JE, Grace M, Samore M. Hazard ratio in clinical trials. Antimicrob Agents Chemother. 2004;48(8):2787–92.

Author's contribution.

The study was conceived and designed by Mobolaji Philip Oyeyiola (MPO), Olayinka Oladunjoye Ogunbode (OOO), Adetola Morenikeji Ogunbode (AMO) and Ayodele Olatunji Arowojolu (AOA). MPO participated in the recruitment of study participants under the supervision of OOO and AOA. MPO, OOO and AMO were involved in the data entry, analysis and interpretation of the result. MPO, OOO, AMO and AOA were involved in the writing of the draft manuscript, editing and approval of the manuscript.