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Research

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A randomised controlled trial comparing intramuscular tramadol with intramuscular paracetamol labor analgesia in low-resource settings

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Abstract

Introduction: *labour pain affects maternal psychology and may affect the course of the labour event. Neuraxial analgesia remains a luxury in developing nations hence the search for an effective alternative. The study aims to assess the efficacy of intramuscular Paracetamol versus Tramadol in pain management during normal labour.* ***Methods:*** *a double-blind randomized control was done involving one hundred and forty-one participants. They were randomized into two groups; the study group (women in Paracetamol group - group A) received 600mg of intramuscular Paracetamol while the control group (women in Tramadol group - group B) received 100mg of intramuscular Tramadol. The efficacy of Paracetamol or Tramadol in achieving labour analgesia was assessed using the visual analogue scale as the primary outcome. Maternal satisfaction with labour care was the secondary outcome, assessed using the Likert scale. Data were analyzed using SPSS version 25.* ***Results:*** *labour pain was significantly higher in women in the Tramadol group compared to women in the Paracetamol group from 2 - 4 hours after drug administration (p= 0.05). Rescue analgesia was more in women in the Tramadol group compared to the Paracetamol group (RR = 0.53 95%CI 0.24-0.86; p = 0.01). The mean duration of labour was significantly higher in women in the Tramadol group (446.7 ± 126.3 minutes) compared with women in the Paracetamol group (376.1 ± 122.8 minutes). Labour was augmented more in women in the Tramadol group than women in the Paracetamol group (RR = 0.29, 95%CI 0.14 - 0.65; p = 0.002). Women in the Paracetamol group were associated with significantly lesser side effects: nausea (RR = 0.31, 95%CI = 0.16 - 0.61, p < 0.001); vomiting (RR = 0.07, 95%CI = 0.01 – 0.56, p < 0.001). Maternal satisfaction of labour analgesia was significantly higher in the Paracetamol group than in the Tramadol group (RR = 7.45 95%CI 2.34 - 23.69; p < 0.001).* ***Conclusion:*** *our study shows that 600 mg intramuscular Paracetamol provided better pain relief in labour when compared with 100 mg intramuscular Tramadol. Paracetamol use has a better side effect profile.*

Introduction

Pain is regarded as an unpleasant, subjective, sensory, and emotional experience associated with real or potential tissue damage [1]. Labour pain is among the most excruciating pain experienced by women and affects maternal psychology and the course of labour causing apprehension, anxiety, and stress [2]. It is a complex, subjective and multi-faceted physiological phenomenon [2]. Pain during the first stage of labour arises from cervical dilatation that occurs following uterine muscle contractions, resulting in uterine muscle wall ischaemia with subsequent lactate accumulation [2-4]. Also, during the late first stage of labour, and the second stage, pain is caused by stretching of the vagina, perineum, and compression of the pelvic structures [2,3]. The associated increase in sympathetic action leads to increased maternal oxygen consumption, respiratory alkalosis, and metabolic acidosis which could lead to decreased oxygen transfer to the fetus [2,3]. It is therefore important to relieve labour pain to reduce maternal distress and improve maternal and perinatal outcomes [2,3]. As a component of the active management of labour proposed by O´Driscoll in 1969 [5], pain relief in labour has evolved over the years; from non-pharmacological techniques to pharmacological methods which include the use of nitrous oxide, non-opioid analgesics like Paracetamol, opioids such as pethidine, Tramadol and regional analgesia such as the use of epidural analgesia [3,6-8]. In some cultures, women are taught that labour pain is natural and the ability to accept and endure labour pain is a sign of womanhood [9]. However, the American College of Obstetricians and Gynaecologists rightly observed that labour is associated with severe pain for many women and that under no circumstance should a woman be allowed to bear the pain which is amenable to safe intervention while under the care of a physician [10].

Ideal labour analgesia should have potent analgesic efficacy with negligible side effects, rapid onset of action, be affordable, should not hinder labour progress, and should be readily available for use with ease of administration [11,12]. Regional analgesia is the gold standard and is routinely used in modern obstetric analgesia in developed countries, with 50-90% use in high-income countries [2,4,6,13]. However, most of the modern obstetric analgesia practices involve the participation of expert anaesthesiologists, costly equipment and continuous electronic monitoring. These are not available in routine obstetric practice in developing countries where the majority of obstetric services are in the hands of midwives, trained nurses and non-specialist doctors [2,4]. In such a situation, a method with minimum technicality is required.

Many labour suites in developing countries use parenteral opioids. This is because these drugs are cheaper than neuraxial analgesia, simple to use, and readily available. While Pethidine is the most used opioid for obstetric analgesia throughout the world, it, however, has some unimpressive adverse effects which range from nausea, vomiting, sedation, maternal and fetal respiratory depression, and delayed gastric emptying [8,14]. Due to these side effects, an increasing number of delivery suites are shifting towards the use of parenteral Tramadol as a means of labour analgesia [4]. Tramadol is a synthetic analogue of codeine and a weak opioid agonist [15,16]. It binds 'u' opiate receptors and inhibits norepinephrine and serotonin uptake [15-18] The onset of the analgesic effect of intramuscular Tramadol is rapid and the effect lasts for 4-6 hours [19]. It has also been found to have analogous analgesic efficacy to pethidine but with a less sedative effect on the mother and less neonatal respiratory depression [4,19]. There are concerns that it may still cause some of the above side effects although to a lesser degree than pethidine [19,20]. These concerns have led to an exploration of an alternative non-opioid for maternal pain relief in labour.

Paracetamol is one of the world´s most widely used analgesics [21]. The actual mechanism of action remains to be elucidated but is probably a centrally acting drug that inhibits prostaglandin synthesis. It is a weak COX-1 and COX-2 inhibitor in the peripheral tissues but recent evidence suggests that it may inhibit a third enzyme COX-3 in the central nervous system [21,22]. Paracetamol is used in the management of pain in diverse scenarios and is effective with little or no side effects [21]. It is used in the management of pain associated with abortions, post-operative pain following caesarean deliveries, and perineal pain following childbirth and has proved efficacious in relieving such pains [23-26]. It is cheap, readily available, easily administered, with a high safety profile, and without the need for highly trained manpower [21]. With the above background, this study aims to compare the efficacy of intramuscular Paracetamol with that of intramuscular Tramadol in pain relief amongst parturients in spontaneous labour at Alex Ekwueme Federal University Teaching Hospital, Abakaliki.

Methods

Study design: this was a double-blind randomized control study conducted in the Labour ward of the Department of Obstetrics and Gynaecology of Alex Ekwueme Federal University Teaching Hospital, Abakaliki (AEFUTHA). The participant was recruited between 1st of May and 1st October 2020.

Study setting and background: AEFUTHA is a tertiary hospital in Ebonyi state, Nigeria with Abakaliki as the state capital. The Department of Obstetrics and Gynaecology is one of the clinical departments in the hospital. There are 52 obstetric bed spaces including antenatal and postnatal wards. The department has five teams which are sub-divided into two units each. Each unit is manned by at least two consultants. Resident doctors are distributed to all the units. The department runs antenatal clinics managed by consultants and resident doctors, assisted by midwives and other health workers. Antenatal

clients are booked daily from Monday to Friday and are assigned by the matrons to consultants according to the units/teams running the antenatal clinic each day. During the antenatal booking and on the clinic days, some dedicated midwives teach pregnant women about labour, and pain care in labour. The average antenatal booking is 4200 clients per annum, while the total antenatal clinic attendance averages 21,000 per annum, with an average annual delivery rate of 3,100. The department has established protocols for the management of women in labour.

Booked pregnant women in labour are admitted into the labour ward and their antenatal folders are reviewed for any important notes or necessary lines of action. Thereafter, a history of the labour and physical examination is carried out to confirm labour. Once labour has been confirmed, active management of labour is instituted and events of labour are monitored using a partograph. Pain relief in labour is achieved with the aid of opioid analgesia with Tramadol being commonly used. The unbooked patients are usually admitted initially into the accident and emergency ward where history and physical examination are carried out to confirm labour. Once labour has been confirmed, they are transferred immediately to the labour ward for adequate monitoring of labour events.

Study population: the patients were selected once they came into early active labour (cervical dilatation of 4-6cm). Parturients were counselled at the antenatal clinic to present once they start having the signs and symptoms of labour. They were educated about labour analgesia during the antenatal clinic period and they were further educated about this particular work by the Chief researcher and research assistants as group teaching at the antenatal classes. Once in labour and a diagnosis of active labour was made, those who met the inclusion criteria and consented were recruited into the study. The details of the study were further explained before informed consent was obtained.

Inclusion criteria: patients included in this study were consenting booked pregnant women in the spontaneous onset of labour with term (≥37 weeks) singleton fetus, in cephalic presentation and no contraindication to vaginal delivery.

Exclusion criteria: women excluded were parturients with multiple gestation, histories of narcotics dependency, antepartum haemorrhage, depression, liver disease, renal disease and allergy to Acetaminophen/Tramadol. Other women excluded included those diagnosed with fetal distress, intrauterine fetal growth retardation and women scheduled for induction of labour or undergoing trial of labour after caesarean section.

Sample size calculation: the sample size calculation was according to the randomized control trial formula of a two-sided study [8]:

$$N = [(Z\alpha + Z\beta)^2 (p1q1 + p2q2)]/X^2$$

Zα= standard normal deviate corresponding to 5% level of significance = 1.96; Zβ= standard normal deviate corresponding to a power of 80% ≤ 0.842; p1= proportion of subjects in the treatment group (Paracetamol) who were expected to exhibit the outcome interest; p2= proportion of subjects in the control group (Tramadol) who were expected to exhibit the outcome of interest. q1= 1-p1; q2= 1-p2; x= the difference the investigation wishes to detect; therefore, N= [(1.96 + 0.842)2 (0.51 x 0.49) + (0.49 + 0.51)]/$(0.25)^2$; N= 63. With an attrition rate of 10%, the calculated sample size was multiplied by a factor 1/(1-NR) [27]; where NR is the non-response proportion. (1/1-0.1) x 63= 70. Thereby giving each arm of the study 70 and total participants being 140.

Study procedure: all the eligible women who had spontaneous active phase labour were randomized. A proforma form was filled at the time of admission into the labour ward, antenatal records of the patients were reviewed, and history taking and physical examination were done. The socio-demographic data and obstetric data of the patients were collated with the proforma. Each

patient was further educated about the trial drugs and the visual analogue scale (VAS) system for the assessment of pain at enrollment. As shown in Figure 1 above, VAS is a continuous scale comprised of a horizontal or vertical line, 10cm (100mm) in length, anchored by 2-word descriptors at each end (no pain at one end and worst pain at the other end) [16], It is self-completed by the respondent (takes less than 1 minute to complete) who were asked to place a line perpendicular to the VAS line at the point that represented their pain intensity. The patient's mark on the line represented the perception of her current pain state. Using a ruler, the score was determined by measuring the distance in millimetres on the 10cm line between the "no pain" anchor and the patient's mark, providing a range of scores between 0-100. A higher score indicates greater pain intensity. The following cut points on the pain VAS were used: no pain
(0-4mm), mild pain (5-44mm), moderate pain (45-74mm), and severe pain (75-100mm) [28]. The marked part is then measured and represents the actual score

Eligible women who presented to the labour ward were consecutively recruited into the study until the required sample size was obtained. The initial VAS scores were assessed before randomization. Patients who met the criteria for selection were asked to pick a number with a replacement from a black cellophane bag. This number corresponded to an envelope located within a box in the labour ward. The corresponding envelope was opened and the analgesia corresponding to the letter (A or B) in the numbered envelope was administered. The initial analgesia was picked from a pool in a dedicated refrigerator for this research and handed over to the nurse on duty who then administered the medication. Both the researcher and patient were unaware of the medication given which was only open to the hospital pharmacist who performed the blinding of medications. Patients in the study group A received intramuscular Paracetamol 600mg in the gluteal muscle while the control group (group B) received 100 mg of intramuscular Tramadol in the gluteal muscle. Rescue or repeat analgesia was given when patients demanded it, however, this was another analgesia other than the one from the initial pool. However, if parturients did not demand analgesia, repeat analgesia from the initial pool was only given after 4 hours from the initial dose for patients who were still in labour and who were adjudged to need further doses. Labour pain was assessed at intervals following the initial administration of analgesia (15 minutes, 1, 2, 3, and 4 hours after). Maternal side effects were recorded. The duration of the active phase labour was obtained. The neonatal outcome was assessed by the APGAR scoring system and the need for admission into the neonatal intensive care unit. This was done by the resident neonatologists who were always present at deliveries The parturients' overall satisfaction with the analgesia was assessed after 24 hours using the Likert scale.

Procedure for randomization and blinding: the study population was randomized using computer-generated random numbers using the software Research Randomiser®. Using this software seventy numbers (70) were randomly generated from a pool of 140 numbers and these numbers were assigned to group A by the pharmacist. The remaining seventy were automatically assigned to group B. These numbers were inscribed on a piece of paper with the inscription group A or group B and were placed in the respective envelopes and sealed. These envelopes also had numbers inscribed boldly on them from 1 to 140 corresponding to the numbers within the envelope. All 140 envelopes were placed in a secured box in the labour ward. Separately, numbers 1 to 140 were written on freshly cut-out cardboard papers and shuffled thoroughly, and these were placed in a separate box within the labour ward. As parturients presented in the labour ward and having met the inclusion criteria, they were asked to pick a card from the box containing the cardboard papers with replacement. After picking the card, the corresponding envelope was searched to determine the group (A or B). Each number inscribed on the envelope was coded with a particular drug: either Paracetamol or Tramadol.

Concealment: concealment was done in sequentially numbered opaque sealed envelopes as stated above. These numbers (1-140) were inscribed on these opaque envelopes and a piece of paper with the inscription A or B was placed inside the respective envelopes and sealed. The hospital pharmacist did the randomization and concealment. All the envelopes were placed in a box in the labour room while the trial drugs were packaged in 2 separate Ziploc bags and kept in the dedicated refrigerator for the research, and this was made accessible to all the members of the research team.

Primary outcome measure: the efficacy of Paracetamol or Tramadol in achieving labour analgesia using the visual analogue scale.

Secondary outcome measures: i) the total duration of the labour event; ii) presence of adverse maternal or foetal outcome; iii) need for additional analgesia; iv) maternal satisfaction.

Statistical analysis: data were collated, tabulated, and then statistically analysed using a statistical package for Social Science (IBM SPSS) software (version 22, Chicago II, USA). Continuous variables were presented as mean and standard deviation (mean ± 2SD), while categorical variables were presented as numbers and proportions. The Chi-square test (χ^2) for matched paired studies was used for comparison between groups for categorical variables while the student t-test was used for comparison between groups for continuous variables. A difference with a P-value <0.05 was considered statistically significant

Ethical clearance: ethical clearance was obtained from the Health Research and Ethics Committee of AEFUTHA (FETHA/REC/VOL 2/2019/190). The study was registered with the Pan African Clinical Trial (PACTR202203615684194). A signed consent form was obtained from each parturient before recruitment into the study. The study objectives, procedure, and full implications of participation were discussed with the participants before their consent was obtained. The participants were made to understand that declining to participate in the study or withdrawing from the study would have no consequences to obtaining care.

Results

During the study period, 142 women were assessed for eligibility; one hundred and forty-one participants were randomized for the study with 71 respondents in Group A (Paracetamol group) and 70 in Group B (Tramadol group). None was lost in follow up and the data obtained were analyzed as shown in Figure 2. The participant´s characteristics are represented in Table 1. There is no significant different in socio-demographic and maternal characteristics of the participant. The treatment outcomes of the two study groups in relation to their VAS scores is shown in Table 2. On admission, there was no statistically significant difference in the VAS mean scores between group A with Paracetamol (64.9 ± 15.6) and group B with Tramadol (69.1 ± 12.8) (p = 0.089). At 2 hours post administration of treatment, Group B had a higher mean score (65.2 ± 15.1) compared with Group A (57.9 ± 19.4) and the difference in means was statistically significant (p = 0.014). After 3 hours, there remained a difference in the VAS mean scores between Group A (53.5 ± 17.9) and Group B (65.6 ± 15.6) which was statistically significant (p < 0.001). At 4 hours post administration of treatment, Group B still had a higher mean score (66.2 ± 16.9) when compared with Group A (54.9 ± 18.1), and the difference in their means scores was statistically significant (p < 0.001).

The first stage, the mean duration of labour was longer in group B (404.5 ± 125.2 minutes) when compared with group A (342.6 ± 119.5 minutes) is shown in Table 3. This difference in the means was statistically significant (p = 0.003). At the second stage, group B had a longer mean duration of labour (39.7 ± 17.8 minutes) compared with group A (33.6 ± 17.8 minutes), although, the difference in the means was not statistically significant (0.053). At the third stage, the mean duration of labour remained longer in group B (6.6 ± 2.7 minutes)

compared with group A (6.0 ± 2.8 minutes), but the difference was not statistically significant (p = 0.253). In total, the mean duration of labour was higher in Group B (446.7 ± 126.3 minutes) than in Group A (376.1 ± 122.8 minutes). The difference in their means was statistically significant (p = 0.001).

A higher proportion of participants in group B (Tramadol, 31.9%) were given Rescue Analgesia when compared with group A (Paracetamol, 19.7%), and the difference in proportion was statistically significant (RR = 0.53, 95%CI = 0.24 - 0.86, p = 0.010). A higher proportion of participants in group B (40.6%) had labour augmentation compared with group A (16.9%) and the difference was statistically significant (RR = 0.29, 95%CI = 0.14 - 0.65, p = 0.002). There was no statistically significant difference in the proportions of the newborns´ Apgar scores at the first minute (RR = 2.23, 95%CI = 0.97 - 5.09, p = 0.055) and at the fifth minute (RR = 2.04, 95%CI = 1.73 - 2.42, p = 0.493). Majority of the participants in group B (40.6%) compared with group A (12.7%) had nausea (RR = 0.31, 95%CI = 0.16 - 0.61, p < 0.001) (Table 4).

A higher proportion of participants in the Tramadol group (15.9%) was very unsatisfied compared with those in the Paracetamol group (7.0%), but the difference was not statistically significant (RR = 0.44, 95%CI = 0.16 - 1.21, p = 0.098). A total of 37.7% of participants in the Tramadol group was unsatisfied when compared with 16.9% in the Paracetamol group and the difference was statistically significant (RR = 0.45, 95%CI = 0.25 - 0.82, p = 0.006). Comparable proportions of participants in both groups, 43.7% to 42.0%, were neutral about maternal satisfaction and the difference was not statistically significant (RR = 1.04, 95%CI = 0.71 - 1.52, p = 0.841). Lastly, 32.4% of participants in the Paracetamol Group compared with 4.3% in the Tramadol Group was satisfied and the difference was statistically significant (RR = 7.45, 95%CI = 2.34 - 23.69, p < 0.001) (Table 5).

Discussion

The labour process is a painful event that needs to be relieved to help improve maternal satisfaction of childbirth experience [29]. Neuraxial analgesia remains a luxury in developing nations hence the search for an effective alternative. The study is aimed at determining the efficacy of intramuscular Paracetamol versus Tramadol in pain management during spontaneous labour. This randomized study indicates that 600mg of intramuscular Paracetamol is more effective in reducing pain during labour when compared with 100mg of intramuscular Tramadol. This was observed with significantly more VAS mean scores 1-4 hours after drug administration among participants who received Tramadol compared with those who received Paracetamol.

This superiority may be due to the anti-prostaglandin effect of Paracetamol on the uterus as it is a weak COX-1 and COX-2 inhibitor in the peripheral tissues but recent evidence suggests that it may inhibit a third enzyme COX-3 in the central nervous system. Tramadol which is a weak opioid, however, has no direct effect on peripheral receptors but the u receptors in the central nervous system. The result is consistent with studies done in Ibadan and India which indicate that Paracetamol is more effective in reducing pain during labour when compared with Tramadol [2,4]. Tramadol though an effective opioid as studies have shown, however, may have had a higher pain score in this study from 2 hours and onward may be due to its slower onset of action as compared to Paracetamol. Tramadol has a peak effect from about 2-4 hours after administration, unlike Paracetamol whose onset of action commences at about 32 minutes after administration and could even be as early as 8 minutes when given intravenously. This may show why the intervention group had a reduced VAS score at an earlier time compared to the control group. Our finding is in keeping with earlier studies [8,9].

In the present study, the duration of labour was significantly longer among the Tramadol group compared with the Paracetamol group. This was also similar to the study in Ibadan, Nigeria, and that done by Lallar *et al.* [2,4]. The total duration of labour was reduced in patients who received Paracetamol as compared to Tramadol. Tramadol causes sedation leading to lesser mobility of women in labor, which could lengthen the labor as shown in a Cochrane review by Berta M *et al.* [30]. Walking and upright positions in the first stage of labour reduce the length of labour [30].

In the course of this study, some participants in both groups needed rescue analgesia with significant differences between the groups. This may further buttress the analgesic efficacy of Paracetamol. The proportion of women who needed repeat/rescue analgesia was higher in the tramadol group. This may be compared with the VAS pain score which was also higher with the Tramadol group showing that this group of women had more pain despite having Tramadol and required extra pain relief to combat this pain. However, this finding was not supported by studies in Egypt and India, which recorded no significant difference in the proportions of women requiring further analgesia between the Paracetamol and Tramadol groups [31]. There was a need for labour augmentation in both groups in this study, although a more significant number had this need among the Tramadol group. This may cause an assumption that oxytocin infusion may probably have been the reason for the increased pain in the women in the Tramadol group. However, Aimhaku *et al.* in Ibadan did not find a difference in labour augmentation between Paracetamol and Tramadol groups and even with this finding, Tramadol was noted to have a higher VAS score showing that augmentation may not be a reason for the higher VAS score in Tramadol group in the present study [4]. In this study, the mode of delivery did not differ significantly between both groups. This was comparable to studies in Nigeria, Egypt, and India which did not record any difference in the mode of delivery following the choice of analgesic in labour [2,4,31,32].

Concerning neonatal outcomes after analgesia, Apgar scores of neonates at the first and fifth minute were not significantly different between the Paracetamol and Tramadol groups, as both drugs show favourable neonatal outcomes. This is in tandem with earlier reports in Nigeria, Egypt, and India [2,4,31]. The comparable 1- and 5-minute Apgar scores in both groups, despite a difference in the duration of labour, may indicate the absence of both serious neonatal adverse effects and an effect of labour duration on neonatal outcome. More participants in the Tramadol group had nausea and vomiting when compared with the Paracetamol group and this was significant. Studies in India also reported a higher proportion of women with nausea and vomiting in the Tramadol group [2,4,32] No other adverse effect was noted in both trial drugs and thus it is safe to adduce that both drugs can be used safely in labour.

Study findings show that maternal satisfaction was significantly higher in the Paracetamol group than in the Tramadol group. Aimhaku *et al.* also reported a statistically significant difference in patients´ satisfaction between Paracetamol and Tramadol use as labour analgesia [4] which is similar to another report in Kano, Nigeria [8]. This shows that Paracetamol was equally as satisfying as commonly used opioids in labour. This satisfaction may not be unconnected to the fact that more women in the intervention group had VAS scores, and were freely mobile as they were less sedated and requested less analgesia. Our study has some limitations that must be borne in mind when interpreting our findings. Our findings may not be a true reflection of the participants in the study area as our study is hospital-based. Despite the meticulous assessment of the participants´ parameters and pain scores, there could still be inter and intra-observer errors. Social desirability bias might affect labour pain assessment. Some parturients might report lower pain scores to avoid being mocked after delivery while women with higher pain thresholds will report lesser pain.

Conclusion

The findings from this study shows that 600 mg intramuscular Paracetamol provided better pain relief in labour when compared with 100 mg intramuscular Tramadol. In addition, Paracetamol has fewer maternal adverse effects than Tramadol. However, the neonatal outcomes of both drugs were essentially similar. Despite the study limitations, paracetamol is recommended as analgesic of choice when compared to Tramadol as labour analgesia. This is due to its simple formulation, fewer maternal side effects, and its availability in poor resource settings.

What is known about this topic

- *The childbirth process is painful event requiring its alleviation;*
- *Neuraxial analgesia is the recommended form of labour analgesia;*
- *In sub-Saharan Africa, neuraxial labour analgesia is a luxury necessitating the use of opioids in labour pain management.*

What this study adds

- *Our study highlighted that intramuscular 600mg Paracetamol has a good analgesic effect compared to intramuscular 100mg Tramadol;*
- *Intramuscular 600mg Paracetamol has a better side effect profile compared to intramuscular 100mg Tramadol;*
- *Labour analgesia with intramuscular Paracetamol is an alternative to the use of opioids during labour in resource-poor centers like sub-Saharan Africa.*

Competing interests

The authors declare no competing interests.

Authors' contributions

Conception and study design: Ikenna Chidi Ebere and Chidebe Christian Anikwe. Data collection: Ikenna Chidi Ebere, and Chidebe Christian Anikwe. Data analysis and interpretation: Ikenna Chidi Ebere, Osita Samuel Umeononihu, Nnenna Assumpta Nweke, Ayodele Adegbite Olaleye and Chidebe Christian Anikwe. Manuscript drafting: Ikenna Chidi Ebere, Ayodele Obianuju Okwuosa, Osita Samuel Umeononihu and Richard Lawrence Ewah. Manuscript revision: All authors. Guarantor of the study: Ikenna Chidi Ebere and Chidebe Christian Anikwe. All authors have read and approved the final version of the manuscript.

Tables and figures

Table 1: sociodemographic characteristics of the participants

Table 2: comparison of pain scores (VAS) at intervals during labour

Table 3: duration of labour among the study groups

Table 4: labour, maternal and perinatal outcomes, and adverse effects among study groups

Table 5: maternal satisfaction in both study groups

Figure 1: pictorial representation of visual analogue scale

Figure 2: consort flow diagram

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Table 1: sociodemographic characteristics of the participants			
Variable	**Paracetamol (N=71) n(%)**	**Tramadol (N=70) n (%)**	**p-value**
Age (years)			
≤ 19	2 (2.8)	1 (1.4)	
20 - 26	23 (32.4)	15 (21.7)	
27 - 33	30 (42.3)	34 (47.8)	
34 - 40	15 (21.1)	19 (27.5)	
> 40	1 (1.4)	1 (1.4)	
Mean age ± SD (years)	28.9 ± 5.3	30.3 ± 5.2	0.116
Gestational age (weeks)			
37 - 38	33 (46.5)	37 (52.2)	
39 - 40	34 (47.9)	30 (43.5)	
41 - 42	4 (5.6)	3 (4.3)	
Mean GA ± SD (weeks)	38.9 ± 1.1	38.8 ± 1.1	0.520
Parity			
0	19 (26.8)	16 (21.7)	
1	17 (23.9)	12 (17.4)	
2 - 4	27 (39.4)	33 (47.8)	
≥ 5	7 (9.9)	9 (13.0)	
Mean parity ± SD	1.9 ± 1.8	2.1 ± 1.8	0.512
Marital status			
Single	4 (5.6)	1 (1.4)	0.366
Married	67 (94.4)	69 (98.6)	
Educational attainment			
No formal education	1 (1.4)	2 (2.9)	0.936
Primary	8 (11.3)	8 (11.6)	
Secondary	21 (29.6)	22 (30.4)	
Tertiary	41 (57.7)	38 (55.1	
Husband's occupation			
Unskilled	7 (9.9)	6 (8.7)	0.941
Semi-skilled	25 (35.2)	27 (37.7)	
Skilled	39 (54.9)	37 (53.6)	
Social class			
1	39 (54.9)	35 (49.3)	0.461
2	2 (2.8)	7 (10.1)	
3	19 (26.8)	18 (26.1)	
4	6 (8.5)	4 (5.8)	
5	5 (7.0)	6 (8.7)	
Religion			
Christianity	66 (93.0)	67 (95.7)	0.573
Islam	4 (5.6)	3 (4.3)	
Others	1 (1.4)	0 (0)	
Mean cervical dilatation on admission ± SD	5.0 ± 0.8	5.0 ± 0.8	0.913
Abbreviations: SD: standard deviation, GA: gestational age			

Table 2: comparison of pain scores (VAS) at intervals during labour			
VAS score	**Paracetamol (N=71) Mean ± SD**	**Tramadol (N=70) Mean ± SD**	**p-value**
On admission	64.9 ± 15.6	69.1 ± 12.8	0.089
After administration			
15 minutes	65.0 ± 16.5	67.6 ± 14.7	0.327
1 hour	59.9 ± 18.1	65.0 ± 15.4	0.074
2 hours	57.9 ± 19.4	65.2 ± 15.1	0.014
3 hours	53.5 ± 17.9	65.6 ± 15.6	< 0.001
4 hours	54.9 ± 18.1	66.2 ± 16.9	< 0.001
SD: standard deviation			

Table 3: duration of labour among the study groups			
Stage of labour	**Paracetamol (N=71) Mean± SD (minutes)**	**Tramadol (N=70) Mean ± SD (minutes)**	**p-value**
First stage	342.6 ± 119.5	404.5 ± 125.2	0.003
Second stage	33.6 ± 17.8	39.7 ± 17.8	0.053
Third stage	6.0 ± 2.8	6.6 ± 2.7	0.253
Total duration of labour	376.1 ± 122.8	446.7 ± 126.3	0.001

Table 4: labour, maternal and perinatal outcomes, and adverse effects among study groups				
Variable	**Paracetamol (N=71) n (%)**	**Tramadol (N=70) n (%)**	**RR (95% CI)**	**p-value**
Rescue analgesia given	14 (19.7)	22 (31.9)	0.53(0.24-0.86)	0.010
Labour augmentation	12 (16.9)	28 (40.6)	0.29(0.14-0.65)	0.002
Mode of delivery				
Vaginal delivery	64 (90.1)	64 (91.3)	1.15(0.37-3.61)	0.813
Caesarean section	7 (9.9)	6 (8.7)		
Apgar score at first minute				
< 7	11 (15.5)	20 (29.0)	2.23(0.97-5.09)	0.055
≥ 7	60 (84.5)	50 (71.0)		
Apgar score at fifth minute				
< 7	0 (0)	1 (1.4)	2.04(1.73-2.42)	0.493
≥ 7	71 (100)	69 (98.6)		
Drug side effects				
Nausea	9 (12.7)	28 (40.6)	0.31(0.16-0.61)	<0.001
Vomiting	1 (1.4)	13 (18.8)	0.07(0.01-0.56)	<0.001
Headache	0 (0)	1 (1.4)	-	0.493
Sedation/immobility	0 (0)	5 (7.2)	-	0.027
Fetal bradycardia	1 (1.4)	1 (1.4)	0.97(0.06-15.2)	0.745

Table 5: maternal satisfaction in both study groups				
Level of satisfaction	**Paracetamol (N=71) n (%)**	**Tramadol (N=70) n (%)**	**RR (95%CI)**	**p-value**
Very unsatisfied	5 (7.0)	11 (15.9)	0.44(0.16-1.21)	0.098
Unsatisfied	12 (16.9)	26 (37.7)	0.45(0.25-0.82)	0.006
Neutral	31 (43.7)	30 (42.0)	1.04(0.71-1.52)	0.841
Satisfied	23 (32.4)	3 (4.3)	7.45(2.34-23.69	<0.001
Very satisfied	0 (0.0)	0 (0.0)	-	-

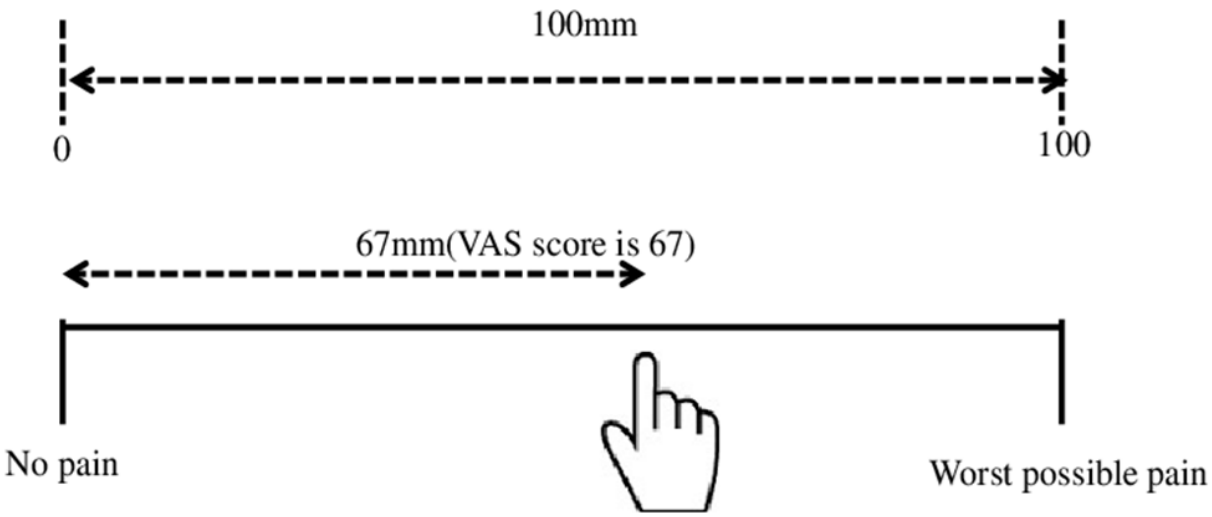

Figure 1: pictorial representation of visual analogue scale

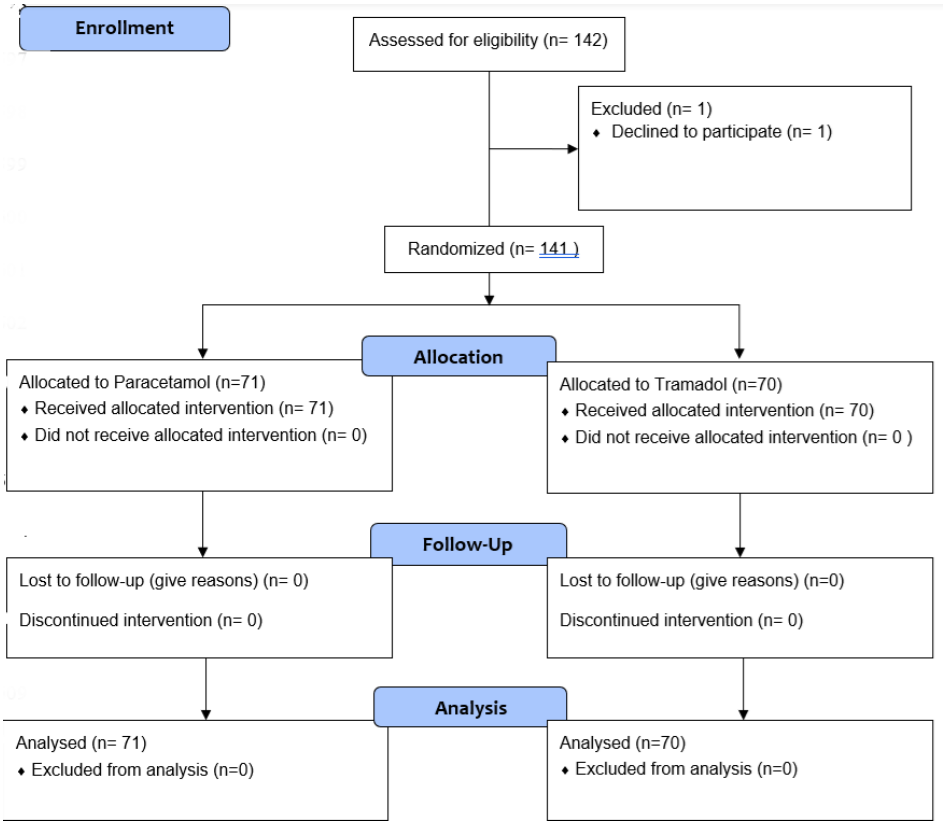

Figure 2: consort flow diagram