**Original Research Article**

**Efficacy Of Paracetamol in The Relief of Pain in Advanced Labour: A Randomized Double Blinded Placebo Controlled Study**

**ABSTRACT**

***Introduction:*** Thelabour process is associated with pain and may be the most painful experience many women will encounter in their lifetime. Out of all the methods available for pain relief in labour, parenteral opioids are the most popular in developing countries. However, its use is associated with some maternal and neonatal side effects. Paracetamol is a non-opioid analgesic with a lesser incidence of side effects that has been tried in labour pain management.

**Objective:** The aim of this study was to determine the efficacy of paracetamol in the relief of pain in advanced labour.

***Methodology:*** Atotal of 140 pregnant women admitted in advanced labour (6-7cm cervical dilation) were randomised into two equal groups. The control group had a single intravenous dose of 6 ml of water for injections administered slowly, while the experimental group had a single intravenous dose of 6 ml (900 mg) of paracetamol given slowly. Pain was assessed with the Visual Analogue Scale (VAS) just before receiving the study drug and at 30 min, 1 and 2 hours after administration of the drug. Data were coded and entered into Statistical Package for the Social Sciences (SPSS) version for analysis.

***Results:*** The pain relief experienced in the paracetamol group was significantly higher than the Placebo group (Mean Difference [mm]: 32.41±2.33, 35.84±2.33, 18.15±2.08 at 30mins, 1 hour, 2 hours after administration of paracetamol and placebo respectively).

***Conclusions:*** Intravenous paracetamol is an effective analgesia in the advanced first stage of labour when compared with placebo. Paracetamol could be an alternative analgesia in the advanced stage of labour in low-resourced settings with limited options.

**Keywords: Labour, Pain, Paracetamol, Analgesia, Relief**

**1. INTRODUCTION**

One of life's most excruciatingly painful events is labour (Thomson et al., 2018). The pain experienced during labour results from variety of factors. As the cervix dilates, it stretches, creating discomfort. At the same time, the myometrium faces ischemia, which leads to a buildup of lactate, contributing further to the sensation of pain. Additionally, as labour progresses into its advanced first stage and moves into the second stage, there's a significant stretch occurring in the vaginal and perineal areas, adding another layer to the challenging experience of childbirth (Thomson et al., 2018; Allameh et al., 2012).

Although the pain of labour is a normal phenomenon, if not addressed, it can cause a significant degree of respiratory alkalosis with a left shift of the mother oxyhaemoglobin dissociation curve, therefore limiting oxygen delivery to the foetus (Lapinsky, 2015). Concern, anxiety, psychological issues, a delayed attachment, and perhaps hostility towards the carer are additional consequences of unrelieved birth pains (Aimakhu et al., 2017).

To mitigate pain in humans, analgesia was introduced. Of importance is the obstetric analgesia, which has evolved over the past years, including both non-pharmacological and pharmacological techniques (Tournaire & Theau-Yonneau, 2007). Paracetamol is an example of a non-opioid drug that has pain-relieving, fever-lowering, and inflammation-reducing effects, with or without a sedative effect (Omotayo et al., 2018). Intravenous paracetamol has been proven to be an effective, affordable, and safe analgesic agent that needs no special monitoringin numerous studies(Omotayo et al., 2018; Toğrul et al., 2011; Anter et al., 2022).

For labour pain, the efficacy of paracetamol has been established by varying authors to produce a satisfactory labour analgesia, positively influences the progress of labour, reduces the probability of caesarean section, eases maternal stress and improves maternal and perinatal outcomes (Aimakhu et al., 2017; Abdollahi et al., 2014; Elbohoty et al., 2012). However, there are limited data that compared paracetamol with placebo to be sure that the pain relief experienced by the parturient is not from the placebo effect.

This study sought to evaluate the effectiveness of intravenous paracetamol relative to placebo in alleviating pain during the advanced first stage of labour. If proven to be an effective analgesic during delivery, paracetamol, due to its inexpensive cost and simplicity of administration, together with minimal monitoring needs, could serve as a valuable option for obstetric analgesia in developing nations.

**2. METHODS**

**2.1 Study Design and Study Population:** This is a randomized double-blind placebo-controlled trial among parturient that were admitted into the labour ward with a diagnosis of the active phase of labour (between 6-7cm) at an estimated gestational age of 37 weeks to 41 weeks + 6 days in Ekiti State University Teaching Hospital Ado-Ekiti (EKSUTH).

**2.2 Inclusion And Exclusion Criteria:** Participants were parturient, aged 18–35 years, with spontaneous onset of labour at term (37–41 weeks + 6 days gestation), cervical dilatation of 6-7 cm and a single live foetus in cephalic presentation with consent to participate in the study. Excluded from the study were parturient with multiple pregnancy, previous uterine scar, cervical dilation ≤ 5 and ≥ 8cm at admission, chronic or pregnancy-induced medical conditions, presence of any contraindication to vaginal delivery, foetal distress, congenital malformations, intrauterine growth restriction, intrauterine foetal death, allergy to paracetamol, breech presentation, use of any other kind of analgesia before study and non-consenting patient.

**2.3 Sample Size Determination:** The sample size was determined using data from the previous study (Kaur et al., 2019). The formula for sample size calculation for comparative study when the endpoint is quantitative and continuous variables was used (Charan & Biswas, 2013), giving a sample size of 70 in each arm of the study.

**2.4 Randomization and measurement:** The participants were randomized into two arms of the study using blocked randomization table from computer generated random numbers.The control group had a single intravenous dose of 6 ml of sterilised water for injections given slowly under an aseptic condition while the experimental group had a single intravenous dose of 6 ml (900 mg) of paracetamol given slowly under an aseptic condition.

The Visual Analogue Scale (VAS) was used to measure pain. "No pain" and "the worst pain" are the boundaries of the 100-mm VAS pain intensity scale. It was evaluated right before the study medication was administered. The on-duty research assistant assisted the patient in marking the pain score on the VAS once the parturient indicated it on the study proforma. At 30 minutes, 1 hour, and 2 hours following medication delivery, the VAS rating was conducted again.

**2.5 Data collection:** Each participant's study proforma included the following parameters, among others: baseline information such as her age, parity, and estimated gestational age; time; and cervical dilatation at admission. Using the VAS, pain was measured. Participants used a 100-mm VAS to rate their level of pain, with "no pain" and "the worst pain" as the boundaries, immediately before taking the study medication and 30 minutes, one hour, and two hours following. Pain following drug injection; neonatal condition before birth; nausea, vomiting, diarrhoea, dyspepsia, and other side effects during the early stage of labour.

**2.6 Method of Data Analysis:** Data obtained were coded and entered into IBM SPSS Statistics for Windows, version 26. Continuous variables were presented as mean ± standard deviation (SD), and categorical data were presented as frequency tables and percentages. Student’s t-test and Chi-square test were used as appropriate to determine statistical significance. Results were considered statistically significant when P< 0.05.

**3. RESULTS**

**Table 1: Sociodemographic data of the parturient in the two groups**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **CHARACTERISTICS** | **Paracetamol**  **Group n=69** | **Placebo**  **Group n=68** | **Mean difference** | **P value** |
| **MEAN AGE±SD (YEARS)** | 27.4±4.47 | 28.6±4.03 | 1.17±0.72 | 0.117 |
| **MEAN PARITY** | 0.71±1.04 | 0.71±1.04 | 0.00±0.18 | 1.000 |
| **MARITAL STATUS** | | | **Χ2** |  |
| Single | 8(11.6%) | 8(11.8%) | 0.001 | 1.000 |
| Married | 61(88.4%) | 60(88.2%) |  |  |
| **TRIBE** | | | | |
| Yoruba | 61(88.4%) | 56(88.2%) | 1.091 | 0.583 |
| Igbo | 6(8.7%) | 8(11.8%) |  |  |
| Others | 2(2.9%) | 4(5.9%) |  |  |
| **RELIGION** | | | | |
| Christianity | 60(87.0%) | 62(91.2%) | 0.677 | 0.412 |
| Islam | 9(13.0%) | 6(8.8%) |  |  |
| **EDUCATION** | | | | |
| Primary | 4(5.8%) | 4(5.9%) | 0.158 | 0.931 |
| Secondary | 19(24.6%) | 19(27.9%) |  |  |
| Tertiary | 48(69.6%) | 45(66.2%) |  |  |
| **OCCUPATION** | | | | |
| Skilled | 24(34.8%) | 21(30.9%) | 0.141 | 0.932 |
| Unskilled | 33(47.8%) | 35(51.4%) |  |  |
| Unemployed | 12(17.4%) | 12(17.6%) |  |  |

The sociodemographic data of the parturient in the two groups were shown in Table 1. The sociodemographic characteristics were comparable between the two groups. The age group ranged from 19 – 35 years in both groups with the mean age in the paracetamol group being 27.4±4.47 years while that of the placebo group was 28.6±4.03. The mean parity in the paracetamol group was 0.71±1.04 and in the placebo group was 0.71±1.04. There was no statistically significant difference in the distribution of the patients by their marital status among the two groups (X2 = 0.001, p = 1.000) with the bulk of the parturient recruited being married; 61(88.4%) and 60(88.2%) in the paracetamol and placebo groups, respectively. Most of the women in the study group were Yoruba; 61(88.4%) and 56(88.2%) in the paracetamol and placebo groups, respectively. All the women practised either Christianity (60(87.0%) in the study group, and 62(91.2%) in the control group) or Islam (9(13.0%) in the study group and 6(8.8%) in the control group). Most of the women in both groups had tertiary levels of education; 48(69.6%) & 45(66.2%) in the paracetamol and placebo groups, respectively. About 24(34.8%) women in the paracetamol group were skilled and 21(30.9%) in the placebo group, while 33(47.8%) and 35(51.4%) women were unskilled in the paracetamol and placebo groups, respectively. Others were unemployed.

**Table 2: Labour characteristics of parturient**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Variables** | **Paracetamol** | **Placebo** | **Mean difference** | **95% C.I**\* | **P value** |
| **Mean Duration of Labour±SD(hrs)** | 4.11±1.15 | 3.96±1.31 | 0.15±0.21 | -0.26 ̶ -0.56 | 0.486 |
| **Cervical dilatation at recruitment(cm**) | **Paracetamol** | **Placebo** | **Χ2** | | **P value** |
| 6.00 | 57(82.6%) | 58(85.3%) | 0.221 | | 0.641 |
| 7.00 | 12(17.4%) | 10(14.7%) |  | |  |
| **AUGMENTATION** | **Paracetamol** | **Placebo** | **Χ2** | | **P value** |
| YES | 49(71.0%) | 42(61.8%) | 1.172 | | 0.284 |
| NO | 20(29.0%) | 26(38.2%) |  | |  |
| **Mode of delivery** | **Paracetamol** | **Placebo** | **Χ2** | | **P value** |
| SVD | 57(82.6%) | 59(86.8%) | 2.033 | | 0.366 |
| IVD | 2(2.9%) | 0(0.00%) |  | |  |
| CS | 10(14.5%) | 9(13.2%) |  | |  |

\*C.I: Confidence Interval

Table 2 presents the labour characteristics of the parturients. The mean duration of labour in the study group was 4.11±1.15hours and 3.96±1.31hours in the placebo group. The difference in the mean duration of labour was not statistically significant (p=0.486). The bulk of the parturients were recruited at cervical dilatation of 6cm; 57(82.6%) and 58(85.3%) in the study and control group respectively. The difference was not statistically significant (X2 = 0.221, p = 0.641). About 49(71.0%) of the women in the paracetamol group and 42(61.8%) women in the placebo group had augmentation of labour. The difference was not statistically significant (X2 = 1.172, p = 0.284). The majority of the women had spontaneous vaginal delivery (SVD), in the paracetamol group, 57(82.6%) women had SVD while 59(86.8%) had SVD in the placebo group. Similarly, the caesarean section rate in both groups was comparable. The difference in the mode of delivery between both groups was not statistically significant (X2 = 2.033, p = 0.366).

**Table 3: Comparison of visual analogue scale scores between paracetamol and placebo group following drug administration**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **VAS (mm)** | **Paracetamol** | **Placebo** | **Mean difference** | **T test** | **95% CI** | **P value** |
| VAS at 0min | 78.57±14.37 | 79.00±12.50 | 0.43±2.28 | -0.188 | -4.93 ̶ 4.07 | 0.852 |
| VAS at 30mins | 46.16±15.63 | 78.57±11.58 | 32.41±2.33 | -9.523 | -36.99 ̶ -27.78 | **0.001\*** |
| VAS at 1 hour | 48.45±16.86 | 84.29±9.72 | 35.84±2.33 | -7.801 | -39.75 ̶ -31.54 | **0.001\*** |
| VAS at 2 hours | 70.42±15.38 | 88.57±8.22 | 18.15±2.08 | -6.170 | -22.74 ̶ -13 54 | **0.001\*** |

***\* Statistically significant***

Table 3 compares the Visual Analogue Scale (VAS) scores between both groups following drug administration. The VAS scores in both groups were comparable at 0 mins (before drug administration); 78.57±14.37mm and 79.00±12.50mm in the paracetamol and placebo group respectively (t= -0.188, p= 0.852). However, mean VAS after 30 mins, 1&2 hours were 46.16±15.63mm, 48.45±16.86mm, 70.42±15.38mm and 78.57±11.58mm, 84.29±9.72mm, 88.57±8.22mm in the paracetamol and placebo group, respectively. All were statistically significant (p= 0.001).

**Table 4. Comparison of the vas scores before paracetamol administration with vas scores at intervals following paracetamol administration**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **VAS (mm)** | **Mean** | **Mean difference** | **T test** | **95%CI** | **P value** |
| VAS at 0min vs 30 mins | 78.57±14.37 vs46.16±15.63 | 32.41±9.27 | 19.986 | 29.93 ̶ 34.35 | **0.001\*** |
| VAS at 0min vs 1 hour | 78.57±14.37vs62.15±16.86 | 30.12±10.16 | 10.343 | 27.93 ̶ 32.35 | **0.001\*** |
| VAS at 0min vs 2 hours | 78.57±14.37vs70.42±15.38 | 8.15±15.05 | 1.588 | -5.73 ̶ 11.45 | 0.124 |

\* ***Significance level p < 0.05***

The VAS scores before paracetamol administration were compared with the VAS scores at intervals following paracetamol administration in Table 4. The mean pain reduction at 30 mins& 1 hour after paracetamol administration was 32.41±9.27mm and 30.12±10.16mm, both were significant statistically with p=0.001. The mean pain reduction at 2 hours following drug administration further decreased to 8.15±15.05mm. However, this difference was statistically insignificant (t= 1.588, p=0.124).

**Table 5. Comparison of the vas scores before placebo administration with vas scores at intervals following placebo administration**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **VAS (mm)** | **Mean** | **Mean Difference** | **T test** | **95%CI** | **P value** |
| VAS at 0 min vs 30 mins | 79±12.50 vs 78.57±11.58 | 0.43± 8.71 | 0.412 | -1.65 ̶ 2.51 | 0.681 |
| VAS at 0 min vs 1 hour | 79±12.50 vs 84.29±9.72 | 5.29± 10.35 | -4.272 | -7.75 ̶ -2.82 | **0.001\*** |
| VAS at 0 min vs 2 hours | 79±12.50 vs 88.57±8.22 | 9.57±10.9 | -7.329 | -12.18 ̶ -6.97 | **0.001\*** |

\* ***Significance level p < 0.05***

Table 5 compared the VAS scores before the administration of placebo with the VAS scores at intervals following placebo administration. At 30 mins following placebo administration, the VAS scores slightly increased with a mean difference of 0.43± 8.71mm, (t= 0.412, p=0.681). However, at 1 and 2 hours after, there was a significant increase in the VAS scores with mean differences of 5.29± 10.35mm and 9.57±10.9mm respectively, p=0.001.

**Table 6. Comparison of the vas scores before intervention with vas scores at intervals following paracetamol and placebo administration**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **VAS (mm)** | **Mean** | **Mean**  **Difference** | **T test** | **95% CI** | **P value** |
| VAS at 0min vs 30 mins | 78.79±13.42 vs 62.36±17.64 | 16.43±14.11 | 9.465 | 13.93 ̶ 18.65 | 0.001\* |
| VAS at 0 min vs 1 hour | 78.79±13.42 vs 66.37±16.46 | 12.42±15.22 | 2.776 | 10.18 ̶ 14.96 | 0.013\* |
| VAS at 0 min vs 2 hours | 78.79±13.42 vs 79.5±13.87 | 0.71±14.51 | -0.737 | -3.58 ̶ 4.29 | 0.082 |

\* ***Significance level p < 0.05***

Table 6 further compared the VAS scores before the administration of both paracetamol and placebo with the VAS scores at intervals following paracetamol and placebo administration. The mean pain reduction after 30 mins and 1 hour were 16.43±14.11mm, (t= 9.465, p=0.001) and 12.42±15.22mm (t= 2.776, p= 0.013) while the mean difference in VAS scores at 2 hours was 0.71±14.51mm, (t= -0.737, p=0.082).

**4. DISCUSSION**

This randomized, double-blind, placebo-controlled study was carried out among parturient in the advanced active phase of labour to compare the efficacy of intravenous paracetamol and placebo in providing pain relief during labour in low resource settings. There were no statistically significant differences observed between the two groups in terms of their sociodemographic characteristics in this study. This shows that the randomization was properly done and the variables, that could affect pain perception, and maternal and foetal outcomes, were comparable in both groups. Thus, the observed differences in the pain perception, maternal and foetal outcomes were mainly due to the different agents administered in the two groups.

The duration of labour is similar in both groups. This is similar to the observation made by Kaur et al. (2019)in a previous study where analgesic efficacy of 1000mg of intravenous Acetaminophen was compared to 100mls of normal saline in 100 parturient in early first stage of labour, the VAS was used to assess pain intensity and duration of labour in each group also recorded, the mean drug to delivery interval were found to be comparable. Studies done by Omotayo et al. (2018) and Elbohoty et al. (2012), that compared paracetamol with pethidine in 108 and 102 parturient respectively in the first stage of labour also showed no statistical difference in the mean duration of labour in both groups. However, findings from a study from Aimakhu et al. (2017) differed from this where a reduction in the duration of labour with the use of paracetamol was observed when it was compared with tramadol in the first stage of labour.

In this present study, an equal proportion of women in paracetamol and placebo groups in this study had a caesarean section. This is similar to the observation made in a study done in Ibadan, Nigeria by Aimakhu et al. (2017), 600mg of intramuscular paracetamol was compared with 100mg of tramadol in active phase of labour, pain intensity was assessed using the Numerical Rating Scale, mode of delivery was recorded and it was found that equal proportion of the parturient had caesarean section. Additionally, the two groups' parturients' mean VAS scores for labour pain perception at recruitment were comparable. This suggests that prior to the drug's administration, participants' pain thresholds and perceptions were similar in both groups. Nonetheless, there was a statistically significant difference in how each group perceived pain following the drug's administration during labour; this is demonstrated by the fact that the Paracetamol group's VAS scores decreased while the Placebo group's VAS scores increased. This finding indicates that intravenous paracetamol is a better intrapartum analgesic than a placebo. Elbohoty et al. (2012) also reported that the analgesic efficacy of intravenous paracetamol is comparable to that of intravenous pethidine, VAS was used to assess pain in the first stage of labour.

In this study, the analgesic effect of paracetamol lasted for at least 1 h, as seen by the significant drop in the VAS scores at 30 mins, and 1 hour in comparison to the VAS scores before paracetamol administration. At 2 hours, there was a decrease in the mean difference from the pre-treatment VAS score in the paracetamol group, this indicates diminished clinical effect. This finding is comparable to results of Aimakhu et al. (2017). There was a reduction in pain scores at 30 minutes in the placebo group; this was followed by a rise in the VAS scores at 1 and 2 hours. This initial decline in pain scores experienced by these women who were given a Placebo could be due to the psychological effect of the injection on them. This is because pain has both sensory and emotional components. Lowe (1996) explained that Labour and birth involve intense physical, emotional, psychological, social, cultural, and spiritual rudiments that may be critical to each woman’s experience. Also, Colloca & Grillon (2014) explained that placebo analgesia makes individuals experience pain reduction merely by the expectation of a benefit. This expectation facilitates a mechanism in the brain and spinal cord, which leads to the release of substances that inhibit pain.

**5. CONCLUSION**

This study concluded by demonstrating the effectiveness of intravenous paracetamol in managing pain during advanced labour. There aren't many unpleasant side effects. These results demonstrate that, in both primigravida and multigravida women in the advanced stages of labour, intravenous paracetamol is an effective intrapartum analgesia that has no negative effects on the foetal outcome. It is affordable, easily accessible, and safe for both mother and child. As a result, it is a viable choice for labour analgesia, particularly in environments with limited resources. The results of this study suggest that intravenous paracetamol can be administered as a safe and effective analgesic in low-resource settings during the advanced first stage of labour.

**6. LIMITATIONS OF THIS STUDY**

It was conducted in a single centre. The results from the study may as well not be generalizable. A larger multi-centre study will be ideal for validating the results of the study. The method used in assessing pain may not be accurate because it is subjective. Also, a study design in which the drugs will be manufactured and packaged by the pharmaceutical company in the same format is preferable because this will ensure that the person who opens the drug administers it.

**DISCLAIMER (ARTIFICIAL INTELLIGENCE)**

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

**ETHICAL APPROVAL AND CONSENT**

Ethical approval for the study was obtained from the Ethics and Research Committee of the Ekiti State University Teaching Hospital, Ado Ekiti, Ekiti State, with the protocol number: A67/2022/04/006. The study was also registered with the Pan African Clinical Trials Registry with the identification number: PACTR202308835750161. The purpose and conduct of the study were explained to all the potential participants. The willing patients signed an informed consent form. All information, including history, physical examination findings, and results obtained from the patients, was kept strictly confidential. All precautions were taken to reduce the possible complications that may arise from the research. The study design and conduct followed relevant ethical requirements, following local, national, and regional guidelines relating to the conduct of non-interventional biomedical studies in human subjects.

**COMPETING INTERESTS DISCLAIMER:**

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

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