Original Article

Comparison of intramuscular paracetamol and intramuscular pethidine as analgesic in the first stage of labor

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ABSTRACT

Background: In general, opioid use as labor analgesic has been associated with some maternal and neonatal side effects including maternal sleepiness and reduced neonatal Apgar score among other side effects. In view of this, many mothers have been undergoing labor without analgesia. The search for safer and effective alternative has continued over the years.

Objective: The study was aimed at comparing the efficacy and side effect profile of intramuscular paracetamol and intramuscular pethidine as analgesia in labor.

Study Design: This study is a prospective randomized double-blind comparative study.

Materials and Methods: Two groups of 54 consenting parturients each were recruited following a computer-generated randomization pattern. Parturients in one group had 600 mg of intramuscular paracetamol and the other 50 mg intramuscular pethidine, and mean pain reduction at 30 min, 1, 2, 3, and 4 h was obtained using a visual analog scale in both groups and compared. Demographic data and primary and secondary outcomes of both groups were compared using *t*-test (for quantitative measures). The Statistical Package for the Social Sciences (SPSS) version 17 was used for statistical analysis.

Results: There was comparable efficacy of labor pain reduction in paracetamol and pethidine after 1 h of drug administration and up till 3 h after ($P < 0.001$), however, pain reduction was more in pethidine group as expected. The maternal and fetal side effect profile of paracetamol was found to be better than that of pethidine.

Conclusion: This study has shown that paracetamol can be used for labor pain with the added advantage of better side effect profile as compared with pethidine.

Key words: Analgesic; intramuscular; labor; paracetamol; pethidine.

Introduction

Childbirth is a painful process right from the first delivery on the earth, and it has been with pains in accordance with Gods commands in Genesis 3:16 of the Holy Bible.[1]

Several groups of people think that God has made this process painful, and no interference should be done in it.[2] However, as the world has evolved, technological innovations and advancement have changed or affected almost all aspects of life in one way or the other. In the present civilization, there is no circumstance where it is considered acceptable for a person to experience severe pain, amenable to safe intervention while under a physician's care.[3] While most people are aware of the association of labor with pain, the majority of parturients are not aware of the appropriateness of labor pain relief and the modalities of doing so. The level of acceptance of labor

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analgesia after full information was found to be significantly correlated with the level of education and socioeconomic status, fear of delivery complications, fear of labor pains, and their eagerness to deliver without suffering from labor pains.[4]

In Nigeria, it is generally assumed that labor is well tolerated, and pain relief is not usually considered an important part of intrapartum care. In a study at Wesley Guild Hospital, Ilesa, the majority 68.3% of women described labor pain as severe. Only 5.3% described it as mild.[5]

In a questionnaire survey done at the Antenatal Clinic of the Federal Medical Centre, Owo, purposely for this study, of the 60 pregnant women interviewed, 43 (71.67%) indicated that they were unaware of availability of drugs that can be used to relieve labor pains while 17 (28.33%) said that they were aware. However, 52 (86.67%) said that they were willing to utilize any available means of relieving labor pains when they come in labor. Of the 32 of them that have delivered before, only 4 (12.50%) had analgesia in their previous deliveries.

In the modern era, various nonpharmacological and pharmacological methods are being practiced for labor analgesia. The various nonpharmacological techniques of labor analgesia include psychoprophylaxis such as breathing exercise, music therapy, doula, hypnosis, hydrotherapy, acupuncture, and acupressure. Others are yoga and transcutaneous electrical nerve stimulation.[6]

The various pharmacological methods available include parenteral opioids such as pethidine, pentazocine, fentanyl, remifentanil, and sufentanil and nonopioids such as tramadol.

Pethidine is a controlled drug that is prone to be abused by health caregivers or patients making it not to be readily available despite being inexpensive. It has also been found to be associated with maternal sleepiness and reduced neonatal Apgar score among other side effects. Considering the various challenges limiting the use of above-mentioned analgesia, many mothers have been undergoing labor without analgesia because of the fear of the fetomaternal side effects and other associated challenges. The search for safer and effective alternatives has continued over the years.

Then, in 1950, pethidine was made available to midwives, in the belief that it had the analgesic effect of morphine but without its side effects. It was also widely believed to be a more powerful analgesic than nitrous oxide. These assertions were found to be wrong as quite quickly, the ineffectiveness of pethidine,[7] and its adverse effects on the newborn[8] began to emerge, but these findings were often ignored. In the fetus, breathing movements, muscular activity, oxygen saturation, and short-term heart rate variability are all reduced following maternal pethidine.[9]

The impact of these changes on the outcome is unclear, but there is no doubt that numerous adverse effects are observed also in the newborn. Neonatal sequelae of pethidine are prolonged. Neonatal respiratory depression has been extensively documented and is worst if pethidine is given repeatedly and 3 h or more before delivery and least if given only within the last hour of labor.[10,11] Large doses of pethidine depress the Apgar scores,[9] but though smaller doses may not, it must be remembered that Apgar scores are only applicable to the first few minutes of life, a stimulating time for the newborn, who may later become severely depressed. Indeed reduced oxygen saturation, increased carbon dioxide levels and metabolic acidosis have been observed in the first few hours of life, even after small doses of pethidine.[12,13]

Various substitutes for pethidine have been introduced, with the intent of producing superior labor analgesia without neonatal depression hitherto seeming to be a forlorn hope. Unfortunately, fetal and neonatal outcomes for these alternative drugs have been even less thoroughly studied than those of pethidine, surely an omission, given its many known adverse neonatal effects.[14]

In a study that reviewed the perception and practice of epidural analgesia among women attending the antenatal clinic in Federal Teaching Hospital, Abakaliki, about 43.3% of respondents are aware of the use of epidural analgesia in labor, but only 7.5% had used it. About 95% of these were satisfied and desire to use it again. The desire to experience natural labor, cost, and fear of side effects were part of reasons for not using.[15] Other challenges of obstetric analgesia in Nigeria include lack of resources, competing priorities, and death of anesthesiologists.[16]

Nonopioid medications for analgesia are drugs that have principally analgesic, antipyretic, anti-inflammatory actions with or without sedative effect. These include acetaminophen (paracetamol), the nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin and antispasmodic drugs such as hyoscine.[17]

Paracetamol is the active metabolite of phenacetin, once popular as an analgesic and antipyretic in its own right. However, unlike phenacetin and its combinations, paracetamol is not carcinogenic at therapeutic doses.[18] The words acetaminophen (used in the United States,[19] Canada, Japan, South Korea, Hong Kong, and Iran) and paracetamol (used elsewhere) both come from a chemical name for the compound: para-acetylaminophenol and

para-acetylaminophenol by taking the underlined alphabets together to form acetaminophen and paracetamol, respectively. In some contexts, it is simply abbreviated as APAP for acetyl-para-aminophenol.

Paracetamol is used for the relief of pains associated with many parts of the body. It has analgesic properties comparable to those of aspirin, whereas its anti-inflammatory effects are weak. Its better tolerated than aspirin in patients in whom excessive gastric acid secretion or prolongation of bleeding time may be a concern. Available without prescription, it is on the World Health Organization (WHO) list of essential medicines, the most effective and safe medicines needed in a health system.[20] Regarding comparative efficacy, studies show conflicting results when compared to NSAIDs. A randomized controlled trial of chronic pain from osteoarthritis in adults found similar benefits from paracetamol and ibuprofen.[21] In recommended doses and for a limited course of treatment, the side effects of paracetamol are mild to nonexistent.[22] Paracetamol is part of the class of drugs known as "aniline analgesics," and it is the only such drug still in use today.[23] It was discovered in the 1890s and marketed as painkiller since 1950s. To date, the mechanism of action of paracetamol is not completely understood. The main mechanism proposed is the inhibition of cyclooxygenase (COX), and recent findings suggest that it is highly selective for COX-2.[24]

The COX family of enzymes is responsible for the metabolism of arachidonic acid to prostaglandin H_2, an unstable molecule that is in turn, converted to numerous other pro-inflammatory compounds. Classically, anti-inflammatories such as the NSAIDs block this step. Only when appropriately oxidized is the COX enzyme highly active,[25,26] paracetamol reduces the oxidized form of the COX enzyme, preventing it from forming pro-inflammatory chemicals.[27,28] This leads to a reduced amount of prostaglandin E_2 in the central nervous system, thus lowering the hypothalamic set point in the thermoregulatory center.

An Egyptian University double-blind, randomized trial that evaluated the efficacy of intravenous infusion of paracetamol as intrapartum analgesia in the first stage of labor, the efficacy of intravenous infusion of paracetamol in comparison with placebo[28] in laboring women starting from the time of medication till the end of the first stage of labor. Participants were followed for the duration of labor, an expected average of 8 h, and the degree of pain and the need for an additional analgesia were noted and assessed with the visual analog scale (VAS).

This local pilot single-arm trial in Ain Shams University Hospital, Cairo, Egypt, provided reassuring data regarding this new use of the drug, but it did not have a comparison arm.[29]

Another study in Egypt evaluated the efficacy and adverse effects of an intravenous infusion of 1000 mg of paracetamol during the active phase of labor as compared with an intravenous injection of 50 mg of pethidine hydrochloride as a method for intrapartum analgesia.[30] One hundred and two participants were enrolled in the study. All of the participants in the two groups were primigravidae in the active phase of labor with comparable age, gestational age, body mass index (BMI) (at the end of pregnancy), and cervical dilatation. Compared with the pretreatment score, the mean VAS score was lower at 15 min, 1, and 2 h after treatment in both groups. There was, however, no reduction in score after 3 h in either group; conversely, there was an increase in VAS score after 4 h in comparison to the initial score. Adverse maternal and fetal effects were recorded only in the pethidine group, in which 32 women (64%) had one or more of the following symptoms: dizziness, blurred vision, dryness of the mouth, vomiting, dyspnea, tachycardia, and a significant change in blood pressure; in addition, fetal bradycardia was recorded in two women in the pethidine group.

The conclusion from the study was that the effectiveness of intravenous paracetamol was comparable to that of intravenous pethidine, but paracetamol had fewer maternal adverse effects. However, pain reduction in the first 15 min of administration was more in the pethidine group because of its more rapid onset of action. The study also suggests that paracetamol causes shortening of the active phase of labor as compared with pethidine. From available information, the only drug that has been shown to shorten the duration of labor is hyoscine N-butyl bromide (hyoscine).[31,32] It is thought that hyoscine acts as a cervical spasmolytic.[33]

This presumed effect of paracetamol is intriguing and warrants further and future study. If shown to be true, paracetamol would be advantageous as a single medicament for intrapartum analgesia as compared with pethidine with shortening of labor duration as added benefit.

Aim of the study

This study explored the possibility of the use of intramuscular paracetamol, a readily available and cheap analgesic without the various side effects associated with pethidine for labor analgesia.

Objectives of the study

General objective

The study was aimed at comparing the use of intramuscular paracetamol and intramuscular pethidine as analgesics in labor.

Specific objectives

1. To compare the efficacy of intramuscular paracetamol and intramuscular pethidine as analgesics in the first stage of labor

2. To compare the fetomaternal side effect profile of paracetamol and that of pethidine when used as analgesic in the first stage of labor.

The hypotheses

Null hypothesis

1. The efficacy of intramuscular paracetamol is not similar to that of intramuscular pethidine when used as analgesics in the first stage of labor
2. Fetomaternal side effect profile of paracetamol is not better than that of pethidine when used as analgesic in the first stage of labor.

Alternate hypothesis

1. The efficacy of intramuscular paracetamol is similar to that of intramuscular pethidine when used as analgesics in the first stage of labor
2. Fetomaternal side effect profile of paracetamol is better than that of pethidine when used as analgesics in the first stage of labor.

Materials and Methods

Study site

The study was carried out at the Department of Obstetrics and Gynaecology of the Federal Medical Centre, Owo, Ondo State, Nigeria. The hospital has an average of 1600 total deliveries every year and serves as referral center for hospitals in Ondo State, parts of Ekiti, Edo, Kogi, and Osun States.

Study design

This study is a randomized comparative clinical study in which a double-blinded interventional approach was adopted. This single-centered, randomized clinical trial recruited women in labor presenting for delivery at the labor ward of the Federal Medical Centre, Owo. Following approval of the study protocol by the hospital research and ethics committee, all women fulfilling the recruitment criteria received informative discussion about the nature of the study. Those that agreed to enter the study signed written informed consent.

Study population

The study population consisted of parturients that are primigravida who are in active phase of labor from 4 cm to 7 cm cervical dilatation and that are having pains requiring analgesia. The pregnancies were at term, with normal singleton fetus in cephalic presentation, longitudinal lie. They qualified for classification into the American Society of Anesthesiologists physical status I and II (ASA I-II).

Exclusion and inclusion criteria

Exclusion criteria

The exclusion criteria include previous cesarean section, hypertension, preeclampsia, eclampsia, intrauterine growth retardation, intrauterine fetal death, morbid obesity, and allergy to any of the study drugs. Others are extremes of ages (<18 years and > 35 years), multiparity, multiple gestations, malpresentation, cephalopelvic disproportion, induction of labor, scarred uterus, fetal distress, antepartum hemorrhage, and use of any other kind of analgesia before recruitment to the study.

Inclusion criteria

The inclusion criteria are primigravida low-risk parturients aged 18–35 years, spontaneous onset of labor at term (37–42 weeks gestation), cervical dilatation of 4–7 cm with adequate uterine contractions, and a single live fetus in cephalic presentation. Cervical dilatation and demographic data, including age, gestational age, and BMI (BMI; calculated as weight in kilograms divided by the square of height in meters), were recorded.

Patient information and consent taking

All eligible women were informed about the study using the patient information sheet and were appropriately counseled. Patients who cannot read or write English had their questionnaires interpreted to them. Informed written consent was obtained. All eligible women who gave written consent were recruited for this study.

Ethical considerations

Ethical clearance was obtained from the institutional ethical committee. Verbal and written consent were obtained from the participants as well. Patients refusal to participate in the study were respected with no attempt at coercion or inducement to gain consent. Moreover, the decline in participation by any patient did not adversely affect their management in any way.

Confidentiality of information was ensured by the use of initials to identify patients.

Sample size determination

The minimum sample size for the study was calculated using the following formula:[34] $N = 2\,(z_{\alpha} + z_{\beta})^2/(\delta/\sigma)^2$. This gave the minimum total sample size to 108.

Methodology

One hundred and twenty patients were recruited to include 10% attrition. One hundred and eight were analyzed. After enrollment, each participant was allocated the next available number in a concealed sequence of a computer-generated randomization plan, which determined the drug that was used. The participants were randomly allocated to 1 of 2

groups, paracetamol = 1 and pethidine = 2 groups. In the paracetamol group ($n = 54$), women received a 600 mg (4 ml) of intramuscular paracetamol with the same brand used for all participants in the group; in the pethidine group ($n = 54$), women received an intramuscular injection of 50 mg (1 ml) pethidine hydrochloride, same brand for all participants in this group.

Pain was assessed with the VAS. Participants reported pain intensity on a 100-mm VAS, bounded by "no pain" and "the worst pain," immediately before receiving the study drug and at 30 min, 1, 2, 3, and 4 h after drug administration. The primary outcome measure was the efficacy of the drug to supply adequate analgesia as was measured by a change in the VAS pain intensity score after drug administration. A mean reduction in VAS score of 30 mm represents a clinically important difference in pain severity that corresponds to patients perception of adequate pain control.[35]

Management of labor was done according to the hospital's protocols with artificial rupture of membranes done as required.

Justification

There is a need to continue to explore more options of obstetric analgesia. Intramuscular route of administration was favored in consideration of the intended applicability of the study because of challenges in instituting intravenous therapy, especially in low-resource or developing parts of the world. The skills and personnel to establish and monitor intravenous access may not be available in primary health centers and maternity homes where most of the deliveries take place. It is also safer to avoid oral intake during established labor because of problems of possible aspiration in case vomiting occurs, or there is a need for emergency operative intervention.

Data collection: Instrument

Pain assessment was performed by only one person, the researcher, who had no role in patient enrollment and was blind to the drug administration. A VAS was used to assess pain before drug, 30 min, 1, 2, 3, and 4 h after drug. Pain was not assessed after 4 h because, despite the possibility of repeated drug intake, it was estimated that by then, more than 50% of participants would have delivered either vaginally or by cesarean section.

The baseline maternal and fetal vital sign parameters were recorded, and this was repeated at each time pain assessment was done.

Spontaneously observed and reported adverse events both maternal (dizziness, tachycardia, dyspnea, vomiting, blurred vision, dryness of the mouth, and significant changes in blood pressure [≥30 mmHg systolic or ≥15 mmHg diastolic]) and fetal or neonatal (nonreassuring cardiotocography including fetal tachycardia, low Apgar scores at 1 and 5 min, and need for admission to the intensive care unit [ICU]) were looked out for and noted. The interval between drug administration and delivery was also recorded.

The primary outcome measure was the efficacy of the drug to supply adequate analgesia, as measured by a change in the VAS pain intensity score at 30 min, 1, 2, 3, and 4 h after drug administration. When responding to the visual analog item, respondents specified their level of agreement to a statement by indicating a position along a continuous line between two endpoints of a straight line on a plane white paper. Participants reported pain intensity on a 100-mm VAS, bounded by "no pain" and "the worst pain," immediately before receiving the study drug and at 30 min, 1, 2, 3, and 4 h after drug administration.

Secondary outcome measures included the need for additional analgesia and the presence of maternal or fetal adverse events during the study.

Data presentation

Data were presented as descriptive statistics (range, mean, and standard deviation [SD] for metric data; and range, median, and interquartile range for discrete data).

Data analysis

The Statistical Package for the Social Sciences (SPSS) version 17.0 (SPSS Inc., Chicago) was used for data statistical analysis. Demographic data and primary and secondary outcomes of both groups were compared with *t*-test (for quantitative measures). Categorical variables were compared by cross tabulation with Chi-square and significance determined. Charts were produced using the chart builder soft wear on SPSS.

Limitation(s) of the study

The initial limitation experienced was that of getting pethidine because it is a controlled drug that could not be purchased by an individual or over the counter. However, this was surmounted by liaison with the Hospital's Director of Pharmaceutical Services that facilitated the use of the hospitals platform to stuck the Hospital's pharmacy with the drug from the Nigeria Central Drug Store.

Results

The sample size for this study was 108 which excludes the 10% number of nonresponse (attrition). The total number of patients interviewed was 120 of which 108 were recruited for

the study. Of the 108 pregnant women recruited, 67 (62.0%) were booked while 41 (38.0%) were unbooked patients of the Federal Medical Centre, Owo, Ondo State [Table 1]. Most of the women were self-employed, 53 (49.1%). Yoruba ethnic group accounted for 86.1% of recruited patients [Table 1]. Majority of the recruited patients were in the age range of 25–34 years [Table 1]. Other sociodemographic data analyzed revealed that 99 (91.7%) of 108 patients were married, while 9 (8.3%) were not married but had partners. The Olusanya *et al*. system of social class classification was used to allocate recruited patients into social classes. This revealed that 38 (35.18%) were in social Class 1, 41 (37.96%) were in social Class 2, while 29 (26.85%) were in Class 3. All the patients recruited were at term with the lowest and highest gestational ages of 37 and 42 weeks, respectively. It was observed that 89 (82.45%) parturients had their labor in lateral position making it to be the most adopted labor position in this study. Eighteen (16.67%) adopted dorsal position while 1 (0.93%) preferred to sit. Adopted labor positions were almost equally distributed among the two groups. The BMI of all patients recruited ranged from 20.90 kg/m^2 to 29.10 m^2 [Table 2]. The mean BMI was 24.63 kgm^2 and 25.00 kgm^2 for paracetamol and pethidine groups, respectively.

All the patients recruited were at cervical dilatation of 4 cm or 5 cm at the time of administration of the drug. The mean cervical dilatation before drug administration was 4.43 ± 0.57 cm and 4.6 ± 0.72 cm for paracetamol and pethidine, respectively.

This study revealed that labor pains are highly rated by parturients with 107 (99.1%) paturients having VAS score of at least 9 over a maximum score of 10 before administration of analgesic. Only 1 (0.9%) parturient had a VAS score of 8 which is still a considerably high pain score. The mean baseline VAS score for the two groups was 9.7 and 9.8, respectively. Both paracetamol and pethidine reduced labor pains significantly as revealed in this study though pain reduction was less in the paracetamol group than the pethidine group. However, VAS score started to increase after 2 h in both groups [Table 3].

The mean pain reductions 30 min after administration of analgesic were 1.96 ± 0.82 cm and 3.00 ± 1.12 cm for paracetamol and pethidine, respectively, $t = -5.495$ and $P < 0.005$ [Table 4]. At 1 h after drug administration, mean pain reductions were 3.07 ± 0.08 and 4.09 ± 1.12 cm, for paracetamol and pethidine, respectively, $t = -5.949$ and $P < 0.005$. At 2 h after drug, mean pain reductions were 3.39 ± 0.92 and 4.61 ± 1.04 cm for paracetamol and pethidine, respectively, $t = -6.489$ and $P < 0.005$. At 3 h after drug administration, the mean pain reductions were 3.11 ± 1.00 cm and 4.30 ± 1.14 cm, $t = -5.726$ and $P < 0.005$. At 4 h after drug administration, the mean pain reductions were 2.50 ± 0.947 cm and 3.61 ± 1.172 cm for paracetamol and pethidine, respectively, $t = -1.106$ and $P < 0.005$. Pain reduction was more in pethidine group as expected.

The interval between drug administration and delivery was 5.24 ± 1.12 h and 5.50 ± 1.31 h for paracetamol and pethidine, respectively, $t = -1.106$ and $P = 0.271$.

The mean Apgar score of the babies at 1 min after the administration of analgesics was 8.67 ± 0.614 and 7.85 ± 0.656 in the paracetamol and pethidine groups, respectively, $t = 6.662$ and $P < 0.005$. At 5 min, the

Table 1: Sociodemographic data of parturients

Variable	Paracetamol ($n=54$), *n* (%)	Pethidine ($n=54$), *n* (%)	Total, *n* (%)
Age group			
15-19	1 (1.9)	1 (1.9)	2 (1.9)
20-24	17 (31.5)	13 (24.1)	30 (27.8)
25-29	22 (40.7)	29 (53.7)	51 (47.2)
30-34	13 (24.1)	9 (16.7)	22 (20.4)
35-39	1 (1.9)	2 (3.7)	3 (2.8)
Booking status			
Booked	30 (55.6)	37 (68.5)	67 (62.1)
Unbooked	24 (44.4)	17 (31.5)	41 (37.9)
Employment status			
Self employed	29 (53.7)	24 (44.4)	53 (49.1)
Salary earner	13 (24.1)	20 (37.0)	33 (30.6)
Not employed	1 (1.9)	4 (7.4)	5 (4.6)
Farming	3 (5.6)	4 (7.4)	7 (6.5)
Student	8 (14.8)	2 (3.7)	10 (9.3)
Ethnicity			
Yoruba	47 (87.0)	46 (85.2)	93 (82.3)
Hausa	1 (1.9)	2 (3.7)	3 (2.7)
Edo	1 (1.9)	2 (3.7)	3 (2.7)
Ebira	5 (9.3)	3 (5.6)	8 (7.1)
Igbo	0	1 (1.9)	1 (0.9)
Marital status			
Married	47 (87.0)	52 (96.3)	99 (91.7)
Single	7 (13.0)	2 (3.7)	9 (8.3)

Values are given as number and percentages from cross tabulation of the two groups. Age group: Pearson's $\chi^2=2.555$, P=0.635; Booking Status: Pearson's $\chi^2=1.926$, $P=0.165$; Employment: Pearson's $\chi^2=7.499$, $P=0.112$; Ethnicity: Pearson's $\chi^2=2.177$, $P=0.703$; Marital status: Pearson's $\chi^2=3.030$, $P=0.080$

Table 2: Comparison of demographic and clinical data between the two groups

	Paracetamol ($n=54$)	Pethidine ($n=54$)	*t*	*P*
Age (years)	26.52±4.01	26.81±3.50	−0.405	0.686
Gestational age (weeks)	38.69±1.21	39.04±1.34	−1.421	0.158
BMI (kg/m^2)	24.62±1.81	25.00±1.57	−1.14	0.257
Cervical dilation before drug (cm)	4.43±0.57	4.46±0.719	−0.297	0.767
Baseline VAS (cm)	9.72±0.49	9.78±0.420	−0.631	0.529

Values are given as mean with 95% CI. VAS, Visual analog scale; BMI, Body mass index; CI, Confidence interval

mean Apgar scores of the neonates were 9.93 ± 0.264 and 9.97 ± 0.536 for paracetamol and pethidine groups, respectively, $t = 4.329$ and $P < 0.005$ [Table 5].

All side effects noticed in this study occurred in the pethidine group as ten (10) parturients experienced dizziness after administration of analgesic in pethidine group while no parturient in the paracetamol group experienced dizziness after drug administration ($t = 2.011$, $P < 0.047$). Seven parturients had vomiting ($t = 2.810$ and $P < 006$) while three other parturients also had dry mouth after drug administration all in the pethidine group ($t = 2.059$, and $P = 0.042$) [Table 6].

No parturient had tachycardia, blurring of vision, or dyspnea after drug administration in this study. The most common side effect of pethidine in this study was dizziness which was experienced by ten parturients accounting for 18.52% of parturients in the pethidine group. Four parturients in the paracetamol group and five in the pethidine group eventually had cesarean section due to other obstetric indications and not fetal distress or prolonged labor.

Three (5.5% of parturients in pethidine group) neonates had temporary inability to suck well within the first few hours after delivery while none had similar experience in the paracetamol group ($t = 1.766$ and $P = 0.080$) [Table 6].

The maternal vital signs were essentially not affected by either of the drugs given [Table 5], and there was no significant effect of any of the two analgesics on the fetal heart rate of the neonates delivered [Table 7].

There were no any other neonatal abnormalities detected in any of the groups [Table 6].

Discussion

This study which compared the use of intramuscular paracetamol and pethidine as labor analgesic in the first stage of labor has shown that the use of intramuscular paracetamol injection for intrapartum analgesia in the first stage of labor is effective. A mean reduction in VAS score of 3 cm represents a clinically important difference in pain severity that corresponds to patients perception of adequate pain control[35] and makes patients feel relative comfort since pain may not be totally eliminated in labor. This was achieved with the use of paracetamol 1 h after administration and sustained up to 3 h after paracetamol was administered. Therefore, analgesic effect of paracetamol lasted for at least 2 h, as determined by the significant reduction in pain at 1, 2, and 3 h in comparison to the pretreatment pain score. It was, however, noticed that the significant pain reduction was achieved earlier in the pethidine group at 30 min after administration due to its rapid onset of action, moreover, pethidine produced more sustained relief of pain as depicted by the VAS scores. This is similar to the results

Table 3: Visual analog scale score in the two groups after drug administration

	Paracetamol ($n=54$)	Pethidine ($n=54$)	t	P
At 30 min	7.76±0.775	6.78±1.040	5.559	<0.001
At 1 h	6.65±0.756	5.59±1.019	6.112	<0.001
At 2 h	6.33±0.869	5.17±0.927	6.750	<0.001
At 3 h	6.61±0.979	5.48±1.059	5.754	<0.001
At 4 h	7.28±0.979	6.17±1.077	5.608	<0.001

Values are given as mean VAS score at different times of assessment after drug administration (95% CI). VAS, Visual analog scale; CI, Confidence interval

Table 4: Reduction in pain scale score (visual analog scale) after drug administration

	Paracetamol ($n=54$)	Pethidine ($n=54$)	t	P
30 min	1.96±0.82	3.00±1.17	−5.49	<0.001
1 h	3.07±0.79	4.19±1.12	−5.95	<0.001
2 h	3.39±0.92	4.61±1.04	−6.49	<0.001
3 h	3.11±1.00	4.30±1.14	−5.73	<0.001
4 h	2.50±0.95	3.61±1.17	−5.35	<0.001

Values are given as mean reduction±SD of VAS score after drug administration (95% CI). SD, Standard deviation; VAS, Visual analog scale; CI, Confidence interval

Table 5: Maternal vital signs during labor before and after drug administration

	Systolic blood pressure	Diastolic blood pressure	Pulse rate
Before drug			
Paracetamol	76±5	120.4±9.5	76.1±8.9
Pethidine	76±4	121.7±7.9	79.4±7.3
P	0.580	0.827	0.038
30 min			
Paracetamol	77±4	119.8±9.2	78.1±8.0
Pethidine	77±4	119.6±6.9	80.0±6.8
P	0.860	0.907	0.204
1 h			
Paracetamol	77±4	119.3±8.7	79.1±8.3
Pethidine	77±4	118.7±6.2	80.6±6.8
P	0.740	0.608	0.302
2 h			
Paracetamol	76±4	119.3±8.6	79.3±8.4
Pethidine	77±4	118.7±6.2	79.5±6.3
P	0.367	0.664	0.847
3 h			
Paracetamol	76±4	118.3±6.3	77.8±8.3
Pethidine	77±4	119.3±8.4	79.6±7.5
P	0.367	0.343	0.230
4 h			
Paracetamol	76±4	119.3±8.5	78.9±8.6
Pethidine	76±4	118.5±5.6	78.5±7.3
P	0.768	0.577	0.811

Table 6: Comparison of fetal and neonatal parameters between the two groups

	Paracetamol ($n=54$)	Pethidine ($n=54$)	*t*	*P*
Fetal heart rate after drug				
30 min	141±5	142±4	−1.421	0.158
1 h	140±5	143±4	−2.363	0.020
2 h	141±5	142±4	−0.541	0.590
3 h	142±4	141±4	0.472	0.638
4 h	142±5	141±4	0.428	0.669
Apgar score (min)				
1	8 (8-9)	7 (7-8)	6.662	<0.001
5	9 (9)	9 (9)	4.329	<0.001

Values are given as mean±SD for fetal heart rates (95% CI) and mode for Apgar score. SD, Standard deviation; CI, Confidence interval

Table 7: Fetal and maternal side effects of the drugs

	Paracetamol ($n=54$)	Pethidine ($n=54$), *n* (%)	*t*	*P*
Fetal				
Apgar score at 1 min ≤7	0	10 (18.52)	−0.581	0.562
Apgar score at 5 min ≤7	0	0		
Suckling abnormality	0	3 (5.55)	1.766	0.080
Maternal				
Dizziness	0	10 (18.5)	2.011	0.047
Vomiting	0	7 (12.9)	2.810	0.006
Dry mouth	0	4 (7.4)	2.059	0.042

Values given are numbers and percentages of side effects as observed in the group

of the single-arm pilot study by Ahmed EHE in Cairo[28] (unpublished data), which showed a significant reduction in pain perception for up to 3 h after drug (intravenous paracetamol) administration but an insignificant reduction at 15 min. The choice of 15 min as time of first pain assessment in the earlier study as against 30 min in this study was because intravenous drug was used which has more rapid onset than intramuscular drug as in this study. At 4 h, the lowering of the mean difference from the pretreatment pain score in paracetamol group indicated diminished clinical effect.

An Egyptian study that compared intravenous paracetamol and intravenous pethidine as labor analgesic[30] had revealed that there was significant pain reduction at 15 min and at 1 and 2 h in both groups ($P < 0.001$). The reduction in pain was significantly greater in the pethidine group only at 15 min ($P = 0.004$). This is similar to what was observed in this study with significant and comparable pain reduction in both groups at 1, 2, and 3 h ($P < 0.001$), but pain reduction in the pethidine group at 1 h was greater than that of paracetamol group ($P < 0.001$). This difference in time of achieving effective pain control between the two studies may be due to the different route of drug administration with intravenous route achieving minimum inhibitory concentration earlier than intramuscular route. However, intramuscular route was chosen for the study because it is more applicable for low-resource settings such as ours, maternity homes, and health centers where most of the deliveries take place, and there may be challenges with intravenous drug administration in terms of expertise to establish and monitor intravenous access.

In this study, there was significant pain reduction up till 3 h after paracetamol administration following which there was marked decrease in pain reduction at 4 h. This is unlike the observation in the Egyptian study where significant pain reduction was only achieved for 2 h after drug administration. This is probably due to the fact that intravenous route used in the Egyptian study had earlier time of onset of action and faster clearance from the system; therefore, giving a shorter duration of action while intramuscular drugs used in this study has slower release into the system and longer duration of action.

All pharmacologic methods for intrapartum analgesia have drawbacks. Pethidine is a simple and cheap drug for the management of labor pain, especially in low-resource countries with limited availability of facilities with effective methods for pain management during labor. However, its maternal adverse effects which include sedation, respiratory depression,[36] delayed gastric emptying, nausea, and vomiting are limiting its use. In addition, pethidine readily crosses the placenta, and neonatal adverse effects which include respiratory depression and decreased Apgar scores[37] are of great concerns. Regarding this, in the present study, 38.9% of women who received pethidine had one or more of the following symptoms: dizziness, dryness of the mouth, and vomiting. This is similar to the study of Elbohoty *et al*.[30] where 64% of the women who received pethidine had one or more of the following symptoms: dizziness, blurred vision, dryness of the mouth, dyspnea, tachycardia, vomiting, and significant change in blood pressure.

The mean 1-min Apgar score in the pethidine group was significantly lower than that of the paracetamol group ($P < 0.001$); however, the comparable 5-min Apgar scores and the absence of neonatal ICU admissions in both groups despite a difference in drug-to-delivery interval show the absence, in both groups, of serious neonatal adverse effects. Ten neonates (18.52%) in the pethidine group had 1-min Apgar score ≤7. No maternal adverse effects were recorded in the women who received paracetamol, confirming the safety and tolerability of paracetamol reported in other studies.[38] Paracetamol is a frequently used over-the-counter painkiller and antipyretic drug that is commonly used by pregnant women. As compared with other analgesics including opioids, it has a better favorable safety profile.[39,40]

The drug-to-delivery interval was compared between the two study groups. The mean drug-to-delivery interval was shorter with paracetamol use (5.2 h) ($P = 0.271$) as compared with pethidine use (5.5 h) although the difference was not statistically significant. Similar observation had been made by previous studies.[30] This might suggest that paracetamol may be associated with shorter duration of active phase of labor as compared with pethidine. The potential benefits that will be derivable from the reduction of the duration of the first stage of labor include a lower incidence of complications associated with prolonged labor. Further large-scale studies are required to fully unravel and establish the effect of paracetamol on the duration of labor which may be beneficial to women.

Conclusion

The findings of this study demonstrate the effectiveness of intramuscular paracetamol as an intrapartum analgesic with a duration of action up till 3 h after administration. Its effect is, however, less pronounced than that of pethidine. Paracetamol is, however, associated with fewer maternal adverse effects and might be associated with shortening of labor duration as compared with pethidine. Neonatal outcome profile also seems better with paracetamol than pethidine.

Recommendation

Further research with increased dose of intramuscular paracetamol which will like give more pain relief is recommended.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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