



A Comparison of Tramadol and Pethidine Analgesia on the Duration of Labour

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Abstract

Background: The ideal obstetric analgesia should provide good analgesic efficacy without reducing intensity of uterine contractions. The aim of this study was to compare the efficacy of pethidine and tramadol as labour analgesia on duration of labour.

Materials and Methods: A total of 170 multigravida women in active labour were randomly assigned to two equal groups. Then, 85 pregnant women received pethidine (50mg) and 85 pregnant women received tramadol (100mg) intramuscularly. Primary outcome measures were: the duration of labour, the analgesic efficacy, maternal side-effects, mode of delivery. The secondary outcomes were also assessed.

Results: The duration of labour was shorter in tramadol group in stage one (64.7%) delivered between 120 +/- 30 minutes, while it was longer in pethidine group (67.1%) delivered between 180 +/- 30 minutes. In stage two, 44.7% of tramadol group delivered within 15 +/- 5 minutes while 51.8% in pethidine group delivered between 25 +/- 5 minutes. Visual analog score (VAS) for pain was used just before administration of drugs, 1 hour and 3 hours after drug administration. The women in pethidine group had lower VAS pain score than those in tramadol group after 1 hour (4 vs 6; $P = <0.001$). There was a significantly higher incidence of vomiting and dizziness in pethidine group (29.4% vs 1.2%; $P = <0.001$).

Conclusion: Tramadol seems to result in a shorter duration of labour and lower incidence of maternal side effects. However, its analgesic efficacy was not as effective as pethidine.

Keywords: Labour duration, Pethidine, Randomized trial, Tramadol, VAS score

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Introduction

Labour can be defined as regular contractions bringing about progressive cervical change. Therefore, a diagnosis of labour is usually made retrospectively (1). There are three stages of labour.

First stage is the time from the diagnosis of labour till full dilatation of the cervix (10 cm), which can be divided into two phases: A. The latent phase: is generally defined as beginning at the point at which the woman perceives regular uterine contractions and cervical effacement, which is the thinning and stretching of the cervix which is usually complete for most women once dilatation of 3 to 4 cm is achieved (2). B. The active phase is the time between the end of the latent phase (3–4 cm cervical dilatation) to full dilatation (10 cm) (1).

Second stage is the time from full dilatation of the cervix to delivery of the fetus or fetuses. It may also be subdivided into two phases: A. The passive phase is the time between full dilatation and the onset of involuntary expulsive contractions. There is no maternal urge to push (1). B. The active second stage is a maternal urge to push

(3).

Third stage is the period from just after the fetus is expelled until just after the placenta and membranes are expelled (4).

Pain is an important part of the physiology of normal labour. Given optimal support, a woman can cope with levels of pain in normal labour using her own natural endorphins, which are opioids produced by the body in response to pain and other stressors (5). Pain accompanying uterine contractions causes marked physiological changes in oxygen consumption, academia and cardio-pulmonary functions. In addition, it's associated with generalized neuroendocrine stress response (6). The pain experienced in labour is complex and is affected by many physiological and psychological factors; the pain experienced by pregnant women during labour is intermittent, and accompanies uterine contractions (7).

In the first stage of labour, the pain occurs during contractions, is visceral or cramp-like in nature, originates in the uterus and cervix, and is produced by

distension of uterine tissues and dilation of the cervix. The pain is transmitted via spinal nerves T10-L1; thus, it can be transferred to the abdominal wall, lumbosacral region, iliac crests, gluteal areas, and thighs (8).

In the second stage of labour, the pain occurs from distension of the vagina, perineum, and pelvic floor. In the second stage, pain is transmitted via the pudendal nerves, entering the spinal cord via nerve roots S2-S4. Stretching of the pelvic ligaments is the hallmark of the second stage of labour. Second stage pain is characterized by a combination of visceral pain from uterine contractions and cervical stretching and somatic pain from distension of vaginal and perineal tissues⁹. In addition, the woman experiences rectal pressure and an urge to 'push' and gives birth to her baby as the presenting part descends into the pelvic outlet (9).

Childbirth can be extremely painful and the provision of pain relief during labour is a humanitarian duty and a vital component of a positive maternal experience (10). Decisions regarding analgesia should be coordinated closely among the obstetrician-gynecologist or other obstetric care provider, the anesthesiologist, the patient, and skilled support personnel (11).

Pain management and the prevention of suffering during labour are complex processes that may not be effectively addressed by administering the best available analgesics (12).

Opioids are the most commonly used systemic medications for labour analgesia. Although opioids do not typically provide complete analgesia, they do allow the parturient to better tolerate labor pain. In addition, they are easily accessible worldwide, and easy to administer in most facilities as they do not usually need any specialized equipment or personnel (13).

Opioid drugs work by binding to opioid receptors, which are found principally in the central and peripheral nervous system and the gastrointestinal tract (14). The efficacy of systemic opioid analgesia and the incidence of side effects appear to be largely dose-dependent rather than drug-dependent (15).

Pethidine is a synthetic opioid and the most commonly used opioid in the obstetric setting. Its popularity and widespread use are perpetuated by familiarity, ease of administration, low cost, and a lack of extensive evidence that alternative opioids would show any significant superiority (10).

It acts mainly through the μ_1 and μ_2 opioid receptors. It is metabolized in the liver to produce normeperidine, a pharmacologically active metabolite which is a potent respiratory depressant. The norpethidine crosses the placenta and is excreted into breast milk by passive diffusion and equilibrating between materno-fetal compartments in 6 minutes. Decreased FHR variability occurs 25-40 minutes after administration and resolves within an hour (16). It reaches its maximum effect after 30-40 minutes and can be re administered after 3-6 hours.

Its elimination half-life in neonates is around 23 hours because of the neonate's immature elimination pathways, while in adults the elimination half-life of pethidine is only 3 hours (17). Maternal side effects are similar to those of other opioids, namely respiratory depression, delayed gastric emptying, nausea, vomiting, sedation, and hypotension (18). Fetal effects reduced muscular activity, oxygen saturation, and short-term heart rate variability. While neonatal effects depressed Apgar scores, respiration, neurobehavioral scores, muscle tone and suckling detrimental effect on breast feeding (19).

Tramadol is a synthetic analog of codeine and a weak opioid agonist, and has been found to have analogous analgesic efficacy to pethidine but with a less sedative effect on the mother and less neonatal respiratory depression (20). Tramadol hydrochloride is a centrally acting analgesic opioid. Intramuscular tramadol hydrochloride is commonly used in labor analgesia in developing countries as it is inexpensive; no special monitoring is required and has been widely studied and proved for its safety and efficacy in labor analgesia (21). The analgesic effect of 100 mg IM tramadol occurs within 10 minutes and has a duration of 2 hours (22). Accordingly, the aim of this study was to compare the efficacy of intramuscular administration of pethidine and tramadol on the duration of labour as labour analgesia.

Material and Methods

Statistical Analysis

Data were entered into Microsoft Excel and coded, then transferred into SPSS software (v.22), in which two approaches were used for data analysis: the descriptive approach to find mean age, frequencies, percentages, and constructive tables and diagram; and the white analytical approach to find associations, in which t-test and Chi-square test were used. ANOVA test was also used and P -value $<0,05$ was considered as statistically significant.

Patients and Methods:

The present study is a single-blinded prospective-randomized study conducted on 170 multigravida women in Sulaimani maternity teaching hospital from 1 June 2019 to 1 December 2019.

After obtaining an informed consent, the subjects were randomly distributed into two equal groups of pethidine group ($n=85$) and tramadol group ($n=85$).

The subjects in the pethidine group received 50 mg pethidine, and those in the tramadol group received 100 mg tramadol. Both groups received pethidine and tramadol via intramuscular route as a single dose in upper outer quadrant of gluteal region with a 2-mL syringe.

Inclusion Criteria:

1. Vertex presentation and expectancy for a non-complicated vaginal delivery.
2. Uncomplicated singleton and term pregnancy in

active labour (that was defined as the presence of at least three regular, painful uterine contractions over 10 minutes with cervical dilatation 3 cm).

3. Patients who preferred labour analgesia.

Exclusion Criteria:

1. Primigravida and grand multiparity.
2. Cervical dilatation of ≥ 5 cm.
3. Any evidence of cephalopelvic disproportion (CPD).
4. Uteroplacental insufficiency or presence of any medical/surgical complications.
5. Patients using monoamine-oxidase inhibitors, opioids, and psychotropic drugs.

A detailed medical history, general physical examination, vital signs (pulse rate, blood pressure, oxygen saturation) were taken before administration of drugs and 1 and 3 hours after administration.

Obstetric examination including vaginal examination were done and basic investigations (complete blood count, blood group and Rh factor, and viral markers (HBV, HCV)) were carried out.

Labor was monitored using a partogram. Fetal monitoring by intermittent fetal heart rate auscultation using sonicaid. The pain intensity before administering the drug was recorded by visual analogue scale, then at 1 and 3 hours after drug administration (Figure 1).

All the women were followed up throughout labour till the end of 3rd stage and the following parameters were recorded:

- Maternal side effects, up to the end of 3rd stage of labour, including: oxygen saturation (pulse oximetry), whilst breathing room air, nausea and vomiting requiring antiemetic administration, dizziness, requirement and indication for supplemental oxygen, respiratory depression (respiratory rate below eight breaths/min).
- The incidence of fetal distress requiring delivery, meconium stain liquor.
- Mode of delivery
- Neonatal status at delivery: 1-minute Apgar score & 1-minute Apgar score.
- Requirement for neonatal resuscitation, and admission to neonatal care unit.
- Postpartum hemorrhage.

Results

From total number of both groups, the mean age for tramadol group was 24.1 \pm 4.2 and for pethidine group was 23.9 \pm 4.4. For the gestational age (GA) in weeks (wk), the mean GA for the tramadol group was 38.9 \pm 1.01 wk, and for pethidine group was 38.9 \pm 1.02 wk. Regarding the cervical dilatation in centimeter (cm), the mean for tramadol group was 3.8 cm and for the pethidine group was 3.7 cm.

Regarding the duration of labour, in 1st stage: (64.7%) of tramadol group delivered between (120 \pm 30) minutes

while (67.1%) of pethidine group delivered between (180 \pm 30) minutes (Table 1).

In the 2nd stage: (44.7%) of tramadol group delivered between (15 \pm 5) minutes while in pethidine group (51.8%) delivered between (25 \pm 5) minutes (Table 1).

The pain intensity was observed by using visual analogue scale.

Just before drugs: tramadol group (61.2 %) had score 8 (moderate to worst pain) and (27.1%) had score 10 (worst pain). In pethidine group, (51.8%) had score 8 and (40%) had score 10. Thus, the pain intensity between the two groups before drug administration was not statistically significant ($P=0.190$).

After 1 hour of drug administration: in tramadol group, (55.3%) had score 6 and (28.2%) had score 4. While in pethidine group, (58.8%) had score 4 and (29.4%) had score 2. The difference in the two groups was statistically significant ($P=0.001$).

After 3 hours of drug administration: in tramadol group, only (2.4%) had score 0, (36.5%) had score 2, and (45.9%) had score 4. In pethidine group, (20%) had score 0, (50.6%) had score 2, and (29.4%) had score 4. The difference in the two groups was statistically significant ($P=0.001$, Table 2).

Maternal side effects

In tramadol group, (57.6%) complained of nausea compared to (7.1%) in pethidine group; in addition, (29.4%) in pethidine group complained of vomiting and dizziness compared to (1.2%) in tramadol group (Table 3).

Regarding mode of delivery, meconium stained liquor, and postpartum hemorrhage

All cases in both groups delivered vaginally. Meconium was seen in 3 and 1 cases in tramadol and pethidine

Table 1. Relationship Between Delivery Time and Treatment

| Variable | Treatment N (%) | | P-value |
|---------------------------------|--------------------|-----------|---------|
| | Tramadol | Pethidine | |
| First stage delivery time (min) | 0(0) | 0(0) | |
| 0-30 | 7(8.2) | 0(0) | |
| 30-60 | 12(14.1) | 0(0) | |
| 60-90 | 27(31.8) | 3(3.5) | <0.001 |
| 90-120 | 28(32.9) | 7(8.2) | |
| 120-150 | 7(8.2) | 22(25.9) | |
| 150-180 | 1(1.2) | 35(41.2) | |
| 180-210 | 3(3.5) | 18(21.2) | |
| 210-240 | | | |
| Second stage delivery (min) | 34(40) | 14(16.5) | |
| 0-10 | 38(44.7) | 13(15.3) | |
| 10-20 | 13(15.3) | 44(51.8) | <0.001 |
| 20-30 | 0(0) | 13(15.3) | |
| 30-40 | 0(0) | 1(1.2) | |
| 40-50 | | | |

Table 2. Relationship Between Pain Score and Treatment

| Pain score | Treatment N (%) | | P-value |
|----------------------------------|--------------------|-----------|---------|
| | Tramadol | Pethidine | |
| Pain score (Before treatment) | | | |
| 0 | 0(0) | 0(0) | 0.190 |
| 1 | 0(0) | 0(0) | |
| 2 | 0(0) | 0(0) | |
| 3 | 0(0) | 0(0) | |
| 4 | 0(0) | 0(0) | |
| 5 | 10(11.8) | 7(8.2) | |
| 6 | 0(0) | 0(0) | |
| 7 | 52(61.2) | 44(51.8) | |
| 8 | 0(0) | 0(0) | |
| 9 | 23(27.1) | 34(40) | |
| 10 | | | |
| Pain score (After 1hr treatment) | | | |
| 0 | 0(0) | 0(0) | <0.001 |
| 1 | 2(2.4) | 0(0) | |
| 2 | 0(0) | 25(29.4) | |
| 3 | 24(28.2) | 0(0) | |
| 4 | 0(0) | 50(58.8) | |
| 5 | 47(55.3) | 0(0) | |
| 6 | 0(0) | 10(11.8) | |
| 7 | 12(14.1) | 0(0) | |
| 8 | 0(0) | 0(0) | |
| 9 | 0(0) | 0(0) | |
| 10 | | | |
| Pain score (After 3hr treatment) | | | |
| 0 | 2(2.4) | 17(20) | <0.001 |
| 1 | 0(0) | 0(0) | |
| 2 | 31(36.5) | 43(50.6) | |
| 3 | 0(0) | 0(0) | |
| 4 | 39(45.9) | 25(29.4) | |
| 5 | 0(0) | 0(0) | |
| 6 | 12(14.1) | 0(0) | |
| 7 | 1(1.2) | 0(0) | |
| 8 | 0(0) | 0(0) | |
| 9 | 0(0) | 0(0) | |
| 10 | 0(0) | 0(0) | |

groups, respectively. In addition, 4 cases of tramadol group developed postpartum hemorrhage, which was minor, while only 1 case in pethidine group developed it.

Discussion

In the present study, tramadol was more effective than pethidine in reducing the duration of labour. This is consistent with the results of Khooshideh et al (23) who found the duration of labour was shorter in tramadol group than pethidine one (first stage (190 vs 140 min; $P < 0.0001$) and second stage (33 vs 25 min; $P = 0.001$) statistically significant in both groups)²³. However, our results were different from those reported by Keskin et al ²⁴, who found no significant difference between the groups (24).

The study agreed with Kushtagi et al (25), who studied (A thought for tramadol hydrochloride as labor analgesic)?

Table 3. Relationship Between Side Effects and Treatment

| Side effects | Treatment N (%) | | P-value |
|-------------------------------|--------------------|-----------|---------|
| | Tramadol | Pethidine | |
| Nausea | 49(57.6) | 6(7.1) | <0.001 |
| Vomiting | 6(7.1) | 4(4.7) | |
| Dizziness | 0(0) | 3(3.5) | |
| No symptom | 22(25.9) | 6(7.1) | |
| Nausea + Vomiting | 4(4.7) | 3(3.5) | |
| Vomiting + Dizziness | 1(1.2) | 25(29.4) | |
| Nausea + Vomiting + Dizziness | 0(0) | 19(22.4) | |
| Nausea + Dizziness | 3(3.5) | 19(22.4) | |

Primiparous women were allocated to three groups (Tramadol 50 mg, Tramadol 100 mg and Meperidine 75 mg) Parturient who were willing to participate in the study but not desirous to take analgesics were recruited as the comparative control group. The mean duration of labor was shorter in the tramadol and meperidine groups than in controls (25).

In the present study, both drugs were effective in reducing the severity of pain but pethidine was significantly more effective. This result agreed with Khooshideh et al (23) who found more than 50% of women rating analgesia as either good or excellent after administration of pethidine in the first stage, and the pethidine seemed to be a better alternative than tramadol for analgesia in second stage of labour.

The results of the present study agreed with those of Keskin et al²⁴, who showed analgesic efficacy of pethidine and tramadol., The study did not show a significant difference at 10 minutes after drug administration ($P_s = 0.257$) but a statistically significant better pain relief was provided with pethidine than tramadol ($P_s 0.000$) at 30 and 60 minutes (24).

In comparing the maternal side effects of the two drugs in the present study, findings showed that about 29.4% of subjects in pethidine group had both symptoms of vomiting and dizziness, while in 1.2% of tramadol group, this was significant ($P < 0.001$).

Our results agreed with those of Khooshideh et al (23) in terms of maternal side effects; there was a significantly higher incidence of nausea and vomiting ($P = 0.003$) and dizziness ($P < 0.0001$) in pethidine group compared with tramadol group²³. Further, our results agreed with those of Michelle et al (26) in that the pethidine was associated with maternal sedation, nausea, and vomiting (26).

In the present study, nausea was the most common side effect of tramadol in 57.6% of subjects and vomiting in 7.1% of cases. Our results corroborated those of Lallar et al (27) who found that nausea was the most common side effect seen in the tramadol group (6.4 %) followed by vomiting (4.3 %) (27).

In line with the study of H.L keskin et al (24),

significantly higher incidence of nausea was observed in the tramadol group. On the contrary, there was no significant difference between the two groups in the incidence of drowsiness (24).

Regarding the comparison of the results in terms of mode of delivery, in the present study, both groups delivered vaginally as was observed in the study of Khooshideh et al (23), though the findings were insignificant.

Conclusion

Tramadol seems to cause a shorter duration of labour, but the analgesic efficacy of tramadol was not found to be as good as pethidine. Tramadol may be preferred over pethidine as it is associated with less maternal side effects. However, its duration of efficacy was not found to be as good as pethidine. Analgesic efficacy of each drug could have been better if administered at regular intervals in multiple doses or as alternatives if one of them was not available. Further studies on each drug together with a placebo and with each other in the same cervical dilatation are needed in order to assess labour pain and duration of labour more accurately.

Conflict of Interests

There is no conflict of interests to be declared.

Ethical Approval

Approval has been taken from Scientific and Ethical committee of Kurdistan Board for Medical Specialties (NO 1360).

Informed Consent

All participants signed the informed consent after receiving explanations on the study objectives.

Authors' Contributions

R Kh: project management/ revising and editing/ methodology; GF: data analyze/writing/data gathering,

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