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Epidural analgesia versus Remifentanil intravenous patient-controlled analgesia in painless labour

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Abstract
Background: Epidural analgesia is considered the most effective method for maternal pain relief during labor. However, remifentanil patient-controlled analgesia (PCA) serves as an important alternative when epidural analgesia is contraindicated, unavailable, or refused by the patient. Understanding the comparative effectiveness and safety of these two methods is essential for guiding clinical decision-making.
Aim of the Study: The study aimed to compare epidural analgesia with intravenous remifentanil PCA in terms of analgesic effectiveness, maternal safety, labor progression, side effects, and neonatal outcomes.
Materials and Methods: A total of 46 term pregnant women were recruited; two were excluded due to fetal bradycardia requiring cesarean section. The remaining 44 participants were assigned to the epidural group (23 women) or the PCA group (21 women). The epidural group received bupivacaine 0.125%, while the PCA group received intravenous remifentanil with programmed lockout intervals. Pain intensity (NRS score), labor duration, maternal physiological responses, and neonatal outcomes were assessed.
Results: The epidural group showed significantly lower NRS pain scores (1.55±1.52 vs. 4.46±2.16). The PCA group demonstrated shorter active labor duration (130±58 vs. 198±83 minutes). Desaturation and pruritus occurred more frequently in the PCA group, whereas hypotension and increased ephedrine use were more common with epidural analgesia. No significant differences were found in nausea, vomiting, shivering, oxytocin use, neonatal ICU admission, or Apgar scores.
Conclusion: Epidural analgesia provided superior pain control compared to remifentanil PCA. Both methods demonstrated similar neonatal safety, though each had distinct maternal side-effect profiles.

Keywords: Epidural analgesia, PCA Remifentanil, maternal safety, neonatal safety, side effects

Introduction
Labor analgesia receives increased attention from mothers and medical professionals because of the rapid development of medical science and the increasing needs of modern society on pain management and quality of life [1]. During labor, the Dutch Societies of Gynecologists and Anesthetists support epidural analgesia as the initial way of pain management because it is the most successful [2]. Epidural analgesia is frequently the recommended option for analgesia during labor because it is considered the best method to relieve pain [3]. Opioids administered intramuscularly or intravenously may be used as an alternate when regional analgesia is not available or is not recommended, or when the obstetrician or woman chooses le ss invasive techniques [4].
Remifentanil is a strong agonist of opioid receptors. It can be administered under the patient's control to birthing women who need to relieve their pain because of its brief context sensitivity and short elimination [5]. Although epidural analgesia is the recommended approach during labor due to its greater analgesia compared to systemic opioids, several studies show that patient -controlled remifentanil provides comparable mother satisfaction [6]. The vagina, uterus, uterine tubes, and ovaries are the internal genital organs of females as in Figure 1: Internal female genital organs.

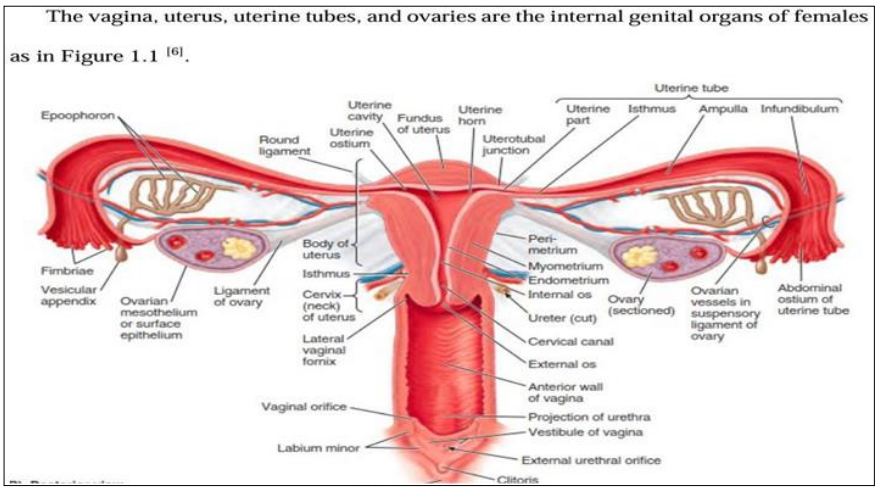

Fig 1: Internal female genital organs [6]

Regarding innervation, only the inferior one -fifth to one -quarter of the vagina is somatic. The deep perineal nerve, a branch of the pudendal nerve that transmits visceral and sympathetic afferent fibers but no parasympathetic fibers, innervates this area of the vagina. Although the cell bodies of the somatic and visceral afferent fibers are found in the same spinal ganglia (S2 –S4), only this somatically innervated region is sensitive to touch and temperature. There is visceral innervation in the upper three-quarters to four -fifths of the vagina. This area of the uterus and vagina receives nerves from the uterovaginal nerve plexus. The uterovaginal nerve plexus is one of the pelvic plexuses that connects the inferior hypogastric plexus to the pelvic viscera. Parasympathetic, sympathetic, and visceral afferent fibers traverse this plexus. The inferior thoracic spinal cord segment is the starting point for sympathetic innervation, which travels via the intermesenteric hypogastric pelvic series of plexuses and lumbar splanchnic nerves. Parasympathetic transmission starts in the S2 –S4 spinal cord segments and travels to the inferior hypogastric -uterovaginal plexus via the pelvic splanchnic nerves. The upper (intraperitoneal) and lower (sub peritoneal) portions of the uterus and vagina have different visceral afferent innervations with various courses and destinations. The sympathetic innervation is followed retrograde by visceral afferent fibers carrying pain signals from the intraperitoneal uterine fundus and body to cell bodies in the inferior thoracic superior lumbar spine ganglia. Following the parasympathetic fibers retrogradely through the uterovaginal and inferior hypogastric plexuses as well as the pelvic splanchnic nerves, afferent fibers carrying pain signals from the sub peritoneal uterine cervix and vagina arrive at cell bodies in the spine sensory ganglia of S2 –S4. Clinically interesting are the two different paths that visceral pain fibers take, which provide women with a range of anesthesia options during labor [6].

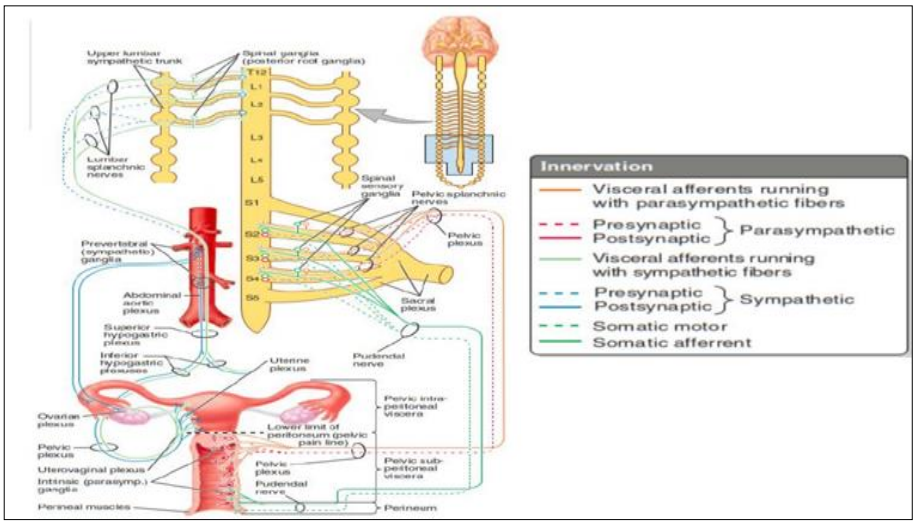

Fig 2: Internal genital organ innervation in females

Labor Pain and Stages of Labor

Almost all women who give birth suffer labor pain, which for many is the most intense pain they will experience in their lives [7]. The International Society for the Study of Pain defines pain as "an undesirable emotional and sensory experience that is linked to or described in terms of actual or potential tissue damage" [8]. The body is filled with nociceptive afferents, which include small -diameter, slow -conducting, unmyelinated C fibers, and medium -diameter, slightly myelinated A -delta fibers. Most labor pain is caused by Polymodal C -fiber nociceptors, which react to various chemical and physical stimuli. During labor, pain occurs in multiple places [9]. There are three stages to this process: the first is from the beginning of the cervical change to 10 cm or full dilatation; the second is from complete cervical dilatation to the baby's birth; and the third is from the baby's delivery to the placenta and membranes are released [10].

Pain in the initial stage of labor starts as visceral cramping sensations that are widespread and poorly localized. The pressure produced du ring uterine contractions and cervix stretching stimulates higher -threshold mechanoreceptors [11]. Furthermore, uterine chemoreceptors are triggered to facilitate cervical dilation and ripening [12]. The A -delta and C primary sensory nerve fibers carry the pain signal from the uterus to the spinal cord when these mechanoreceptors and chemoreceptors are stimulated. These fibers terminate by communicating with the dorsal rami of T10 –L1 [13]. Mostly somatic pain is caused by distension and traction on the pelvic structures, pelvic floor, and perineum throughout the first and second stages of labor. The parasympathetic branch of the pudendal nerve carries these signals mostly via A -delta fibers to the dorsal rami of S2 –4, where t hey cause acute, localized pain [14].

The pain of labor has historically been reduced by the use of non -pharmacologic approaches such as massage therapy, hypnosis, and acupuncturist [15]. Western medicine didn't use drugs for relieving labor pain until the middle of the 1800s [16]. While nitrous oxide is widely utilized for labor analgesia, volatile anesthetics are no longer used. For self -administration by the patient, it is usually mixed with O2 in a 50:50 ratio and inhaled both before and during contractions [17].

The most typical type of analgesia during labor is systemic drugs. The many ways in which these drugs act is different, Figure 3. As a result, their efficacy and adverse effect profiles are different for both the mother and the infant [10].

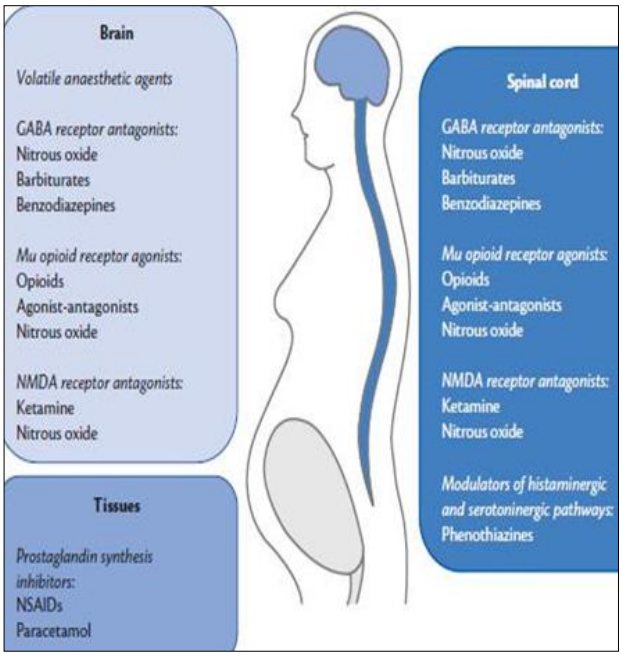

Fig 3: Sites of systemic analgesia act

Systemic opioids

The association between systemic opioids and obstetric anesthesia is controversial. Although these medications are the most often used systemic analgesia during labor, their usage has been limited because of their variable effectiveness, a wide range of maternal adverse effects, and concern about newborn depression. The way that opioid drugs act is by connecting themselves to opioid receptors, which are primarily found in the gastrointestinal tract, central, and peripheral nervous systems. Opioids can cause vomiting, nausea, delayed stomach emptying, sedation, disorientation, pruritus, and respiratory depression in mothers. These side effects, which are mostly dependent on dose rather than drug -dependent, may affect parturient in different ways. Opioids can have an indirect effect on the fetus through changes in the mother's MV or uterine tone, or they can have a direct effect through placental transfer. Because of their low molecular weight and high lipid solubility, opioid drugs often diffuse easily across the placenta. The degree of placental absorption, fetal metabolism, and clearance limit the number of drugs available to the fetus, whereas placental blood low and maternal protein binding limit how much free drug travels to the placenta. Drugs and administration methods affect the rate and amount of placental transfer and the resulting concentration ratios between the maternal artery and the umbilical vein [10].

Modes of administration of systemic opioid

1. Intermittent bolus

Opioid analgesia may be administered by buccal, transdermal, oral, intramuscular, subcutaneous, intravenous, epidural, or intrathecal methods. The intravenous, intramuscular, and neuraxial routes are the most often used for labor analgesia. The main advantage of intermittent intramuscular injections is that they are easily accessible and administered by a midwife; however, they may cause pain. Intramuscular analgesia varies in quality and duration. Opioids administered intravenously provide the advantages of faster onset, titration to effect, and more constant analgesia quality and duration. However, in many facilities, administering opioids by IV needs a doctor's presence [10].

2. Patient -controlled analgesia

The use of constant intravenous (IV) infusion or intermittent bolus of opioids for postoperative pain has mostly been replaced by patient -controlled (IV) analgesia (PCA). Lower doses of the drug can produce good analgesia, which reduces side effects and improves patient satisfaction. Patient satisfaction during birth is crucial, and while PCA cannot eliminate pain, several studies have shown that it can help patients feel more in control of their labor process. Increased utilization of PCA systems for analgesia in labor is a result of this advantage as well as the increasing need for a successful replacement for neuraxial analgesia for those who do not want, or cannot have an epidural. In contrast with intermittent bolus IV delivery, frequent smaller amounts of opioids provide analgesia that is more consistent and may result in reduced placental transfer due to a more stable plasma drug concentration. Many opioids have been considered for PCA use during labor; however, rapid -onset and quick -acting drugs, such as remifentanil, are most appropriate because of the variable nature, frequency, and degree of labor pain. To provide the parturient with significant analgesia, the optimal intravenous opioid should have a start and offset that match the duration of uterine contractions. Maintaining uterine contractility and fetal heart rate variability, as well as avoiding respiratory depression side effects in both mothers and newborns, are essential for maintaining the course of treatment until and throughout delivery [10].

3. Epidural analgesia in labor

In labor and delivery, epidural and spinal (intrathecal) analgesia more frequently use local anesthetics, either by itself or in combination with opioids. Neural blockade at the T10–L1 sensory level is necessary for analgesia during the first stage of labor, while neural blockade at the T10–S4 sensory level is necessary for pain reduction during the second stage. The most flexible and widely used method is continuous lumbar epidural analgesia, which can be used to relieve pain during the early stage of labor and, if required, to provide analgesia or anesthesia for a subsequent vaginal delivery or cesarean cut. When medication for pain is started before vaginal delivery (the second stage), "singles hot" epidural, spinal, or combined spinal -epidural analgesia may be suitable. Following her obstetrician's evaluation, epidural analgesia for labor may be given in the early stages of labor [3].

Epidural analgesia has little to no impact on the duration of labor when diluted combinations of an opioid and a local anesthetic are used. It is incorrect for concerned that restricted analgesia will raise the risk of oxytocin augmentation, functioning delivery (such as using forceps), or cesarean section. Early placement of an epidural catheter, when the patient is l ess discomfort and simpler to position, is frequently helpful. Furthermore, having an effective epidural catheter allows for the avoidance of general anesthesia if an urgent or emergent cesarean section is required. Regional anesthesia is absolutely contraindicated in cases of patient refusal, infection at the site of injection, coagulopathy, severe hypovolemia, and local anesthetic allergies. If the patient is unable to cooperate, regional anesthesia may not be successful [3].

Materials and methods

This prospective randomized clinical trial -single blind technique was conducted between August 2023 and Novembe r 2024, at Al_Zahra Teaching Hospital -Najaf - Iraq. The study was approved by the Iraqi scientific council of Board of Medical Specialization/ Anesthesia and Intensive Care.

46 patients were included in this study; 2 patients were dropped due to fetal bradycardia and terminated by cesarean section. The final number of our patient's study was 44, divided into two groups; the epidural group (N=23), and the PCA group (N=21).

Inclusion criteria:

1. patients for painless lobar
2. Age older than 18 years.
3. ASA II.
4. Gestational age ≥ 38 weeks.

Exclusion criteria:

1. Contra -indication to epidural analgesia.
2. BMI ≥ 35kg/m2.
3. 150cm ≥ Height ≥ 185cm
4. Patients refusal

All women taken written informed consent before starting either technique, women were randomized into 2 groups: the patients control analgesia group (PCA group) and the epidural group, in both groups, intravenous access was secured with attached standard monitoring. We s tarted either technique when cervical dilatation was above 4 cm, cooperating with the examining gynecologist. The PCA group received intravenous remifentanil for 4 minutes locked time intervals, the dose of remifentanil was 20 mcg/ml. A 20mcg/ml solution w as prepared, and all patients were instructed on how to handle the pump and when to administer the bolus dose. We encouraged all patients to put on the bolus as they recognized the pain rising.

The patients in the epidural group received epidural analgesia with injections of bolus dosing of 10 ml of 0.125 bupivacaine and repeated doses (5 ml) as patients requested through the epidural catheter were placed in the L3 -L4 level.

Both groups were continuously monitored for hemodynamic parameters, systolic and diastolic blood pressure, blood oxygen saturation, heart rate, and respiratory rate, and recorded before (baseline) and during labor analgesia until the end of birth with 15 -30-minute intervals.

Ephedrine (2.5 –10 mg) or IV fluid as needed was used to treat hypotension, which is defined as a drop in systolic blood pressure of more than 2 0% from baseline or a drop. below 90 mmHg. IV atropine (0.6 –1 mg) was used to treat bradycardia, which is defined as a heart rate < 6 0 bpm.

Ondansetron was given if patients developed nausea or vomiting or both. A simple oxygen mask with 5 -6 L/min was used to treat hypoxia, which is defined as SPO2 < 92 %. During labor analgesia, the average degree of sedation was assessed using the Ramsey score, where (1) Anxious, (2) Oriented, (3) Responds to commands, (4) Brisk response to light glabellar tap, (5) Sluggish response to light glabellar tap, and (6) No response to painful stimulation. Pain intensity was evaluated using a numerical pain rating scale, where (0) is no pain, (1 -3) is mild pain, (4 -6) is moderate pain, and (7 -10) is severe pain.

Active labor was also recorded which is defined as the time interval between cervical dilatation of (4 -5 cm) and childbirth. The incidence of associated side effects was also recorded such as nausea, vomiting, pruritus, shivering, hypoxia, hypotension, and bradycardia.

Fetal heart rate (FHR) was monitored during labor analgesia using a sonic aid. If the FHR became pathological bradycardia, we stopped remifentanil. At the first and fifth minutes after delivery, the pediatrician established Apgar scores. Neonatal care unit (NCU) admission and drug consumption were noted after the end of birth. Obstructed labor. Epidural failure, fatal bradycardia was dropped.

Statistical methods

All data were collected and analyzed using SPSS version 26. The quantitative data were expressed as mean and standard deviation. Independent tests (t -test, Mann - Whitney U test, Chi-square Pearson test, Fisher exact test) were used to compare variables between the two groups. A p -value of less than 0.05 was considered significant.

Result

44 patients were randomized to receive either PCA with remifentanil (21 patients) or intermittent epidural analgesia (23 patients) for painless delivery. The patient's demographic profile s is presented in Table 3.1, with no statistically significant differences concerning age, parity, gestational age, and height with a p -value > 0.05, except weight, the women in the epidural group have body weight (77.826 kg) lower than PCA group (83.238 kg), p -value < 0.05.

Table 3.1: Demographics profile

-----	Epidural group	PCA group	p-value
Age (years)	23.652±3.797	797 24.190±3.880	0.644 ns
Parity (Mean±Sd)	2.0±1.128	2.428±1.325	0.253 ns
Gestational age (Mean±Sd)	38.808±0.638	638 38.923±0.743	0.584 ns
Wight (Mean±Sd)	77.826±8.574	83.238±4.182	0.012*
Height (Mean±Sd)	161.260±4.276	161.666±4.139	0.751 ns

ns: non-significant, *: significant

In Table 3.2, there were statistically significant differences regarding time for active labor time, the PCA group associated with early delivery at 130±58 minutes while longer with the epidural group at 198±83 minutes, with a p -value less than 0.05.

Table 3.2: Comparison of study groups according to active labour time

------	Epidural Group	PCA Group	p-value
active labour time in min (Mean±Sd)	198±83.168	130±58.094	0.003*

*: significant

Table 3.3 shows the baseline NRS scores were comparable in the epidural and PCA groups with a p -value more than 0.05. During labor analgesia, until the end of delivery, the average NRS score significantly decreased in both groups, the epidural group was associated with a statistically significant lower NRS score (1.55±1.521) compared with the PCA group (4.466±2.16), with a p -value < 0.001.

The difference in average sedation scores in patients from both groups was analyzed at different time points before (baseline) and after the onset of analgesia. The average sedation scores were statistically insignificant differences at two times, with a p -value > 0.05.

Table 3.3: Comparison of study groups according to NRS and sedation scores before and after analgesia

NRS score	Epidural group	PCA group	p-value
Baseline (Mean±Sd)	5.869±2.201	5.952±1.465	0.885 ns
Average pain (Mean±Sd)	1.55±1.521	4.466±2.16	0.0001*
Sedation score	-------	----------	-------
Baseline (Mean±Sd)	1.956±0.366	1.904±0.300	0.613 ns
Average sedation (Mean±Sd)	1.977±0.047	1.965±0.109	0.649 ns

*: significant

Some side effects were presented more often in women who received analgesia, pruritus was significantly higher and hypoxia was more common in women who received remifentanil with PCA with a p -value < 0.05. Hypotension was markedly higher in the epidural group. However, nausea and vomiting, shivering, and neonatal care unit admission were statistically comparable in both groups with p -values of more than 0.05 Table 3 .4.

Table 3.4: Comparison of study groups according to side effects during labor analgesia until the end of delivery

Side effect	Epidural group	PCA group	p-value
Nausea & Vomiting Positive N (%) Negative	11 (47.8) 12 (52.2)	7 (33.3) 14 (66.7)	0.329 ns
Pruritus Positive N (%) Negative	0 23 (100)	4 (19.0) 17 (81.0)	0.028 *
NCU admission Positive N (%) Negative	5 (21.7) 18 (78.3)	4 (19.0) 17 (81.0)	0.825 ns
Shivering Positive N (%) Negative	6 (26.1) 17 (73.9)	2 (9.5) 19 (90.5)	0.155 ns
Hypoxia Positive N (%) Negative	0 23 (100)	11 (52.4) 10 (47.6)	<0.001*
Hypotension Positive N (%) Negative	12 (52.2) 11 (47.8)	0 21 (100)	<0.001*

There were no differences between the two groups regarding the Apgar score in the first and fifth minutes after delivery with a p-value > 0.05 Table 3.5.

Table 3.5: Comparison of study groups according to APGAR score

Time interval	Epidural group	PCA group	group p-value
1 min	8.739±1.483	8.9048±1.261	0.693 ns
5 min	9.6957±0.764	9.7143±0.643	0.931 ns

Nine patients in the epidural group received oxytocin while ten patients in the PCA group with a p -value > 0.05. 12 patients in the epidural group consumed ephedrine compared with the PCA group zero, with a p -value < 0.001 Table 3.6.

Table 3.6: Comparison of study groups according to drugs used during labor analgesia until the end of delivery

Drugs used	Epidural group	PCA group	p-value
Oxytocin	9 (39%)	10 (48%)	0.200 ns
Ephedrine	12 (52.05 %)	0	<0.001*

Discussion

The outcome of this single -center trial shows that PCA with remifentanil is not parallel with epidural labor analgesia. This research proves the results reported by Douma *et al*, Liu ZQ *et al*, and Verwey *et al* [3, 5, 2 1-22] that epidural analgesia pro vides superior pain when measured using the NRS score. Several previous studies by Thorbiörnson *et al* [18] reported that the women in the epidural group had prolonged active labors compared with the PCA group, which aligns with our reported finding. The reason behind the shorter active labor in the women with PCA may have been due to their ability to administer analgesics independently and easily as required. Acute stress hormones decrease uterine function and delay labor advancement, therefore reducing stress can promote it. As a result, the anti -stress hormone, oxytocin, promotes labor progress which is presented in the study of Lieberman *et al* [19].

Additionally, Research suggests that women with epidural analgesia are more likely to experience longer labor than those without, Barber *et al*, and Rahm *et al* [25-26]. Women with epidural analgesia had decreased endogenous oxytocin

concentrations in their plasma and were more likely to need intravenous oxytocin during delivery, Barber *et al*, and Stocki *et al* [22, 25], In current research oxytocin intake, was statistically comparable in both groups.

In 25 -75% of cases, a percentage of maternal desaturation below 95% in remifentanil analgesia was reported by Douma e t al, and Volikas *et al* [27-28], which is similar to our reported result. The incidence of nausea and vomiting did not differ between the groups, which is consistent with findings from earlier research, by Barber *et al*, and Freeman *et al* [25, 29].

Unlike previous trials, Volmanen *et al*, and Thorbiörnson *et al* [30, 23] have demonstrated greater sedation with remifentanil PCA, there was no difference in sedation scores between the groups in the current research. Because the present research could not identify sedation differences, the sample size might have been insufficient to identify this impact. Comparing the observer scale to subjective ratings, the latter may be more sensitive in assessing sedation. Hypotension and ephedrine use were significantly higher in the epidural group compared with the PCA group, Liv M Freeman *et al* [29] provided an outcome similar to our results. Additionally, in the current research, there were no statistically significant differences in the outcomes for neonates, Douma *et al* [31] presented the same results. The mean Apgar scores were almost 9.7 in both groups five minutes after delivery, although five neonates in the epidural group and four in the remifentanil group had been admitted to the neonatal care unit.

Conclusion

In conclusion, both epidural analgesia and remifentanil PCA provide effective pain relief during labor, but they differ significantly in their safety profiles and clinical outcomes. Epidural analgesia offers more stable and continuous pain control, while remifentanil provides shorter but rapid relief. Maternal side effects vary between the two methods, yet neonatal outcomes remain largely comparable. These findings highlight the importance of individualized decision-making when selecting analgesia for labor.

Findings

The study found that epidural analgesia with bupivacaine produced stronger and more consistent analgesia but was associated with maternal hypotension. Remifentanil PCA resulted in effective but shorter-lasting pain relief and was linked to episodes of oxygen desaturation. Side effects such as nausea, vomiting, and shivering occurred with both techniques, without major differences between them. No significant differences were observed in neonatal safety outcomes.

Recommendations

1. Epidural analgesia should remain the preferred method for painless labor unless clear contraindications exist.
2. Additional research is recommended to compare epidural analgesia with Entonox to further evaluate maternal and neonatal outcomes.
3. When using remifentanil PCA, continuous monitoring of maternal SpO_2, heart rate, and blood pressure is essential to ensure safe administration.

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