ORIGINAL ARTICLE

Effect of Epidural versus Parenteral Opioid Analgesia on Labor Pain and Maternal and Neonatal Outcomes among Jordanian Women: A Retrospective Study

Heba Khalil[1,2], Abedalmajeed Shajrawi[1], Aaliyah Momani[1], Dalia Khalil[3], Raghad Abdelkader[1]

[1] Applied Science Private University, Faculty of Nursing, 21 Al Arab St., Amman, Jordan 11931
[2] Faculty of Health Sciences, Ras Al Khaimah Women's College, Higher Colleges of Technology, United Arab Emirates
[3] Wayne State University, College of Nursing, 42 W. Warren Ave. Detroit, MI, USA 48202

ABSTRACT

Introduction: Pain is a major concern during labor. Opioids commonly used to reduce pain during childbirth. However, the most effective route for opioid administration remains controversial. Thus, this study aimed to compare the effect of epidural and parenteral opioid analgesia on pain relief, opioid consumption, opioid-related side effects, and maternal and neonatal outcomes during labor. **Methods:** This was a retrospective chart review of Jordanian Arab pregnant women admitted for an uncomplicated normal vaginal birth. Data extracted from patients' medical records and analyzed with t-test for parametric variables and chi-square and fisher's exact tests for non-parametric variables. **Results:** Women with epidural analgesia had less pain ($t = -32.96$, $p \leq .001$), consumed less opioids ($t = -5.23$, $p \leq .001$) and complained of fewer opioid side effects ($t = -10.35$, $p \leq .001$) compared to those with parenteral analgesia. However, they had a longer duration of labor ($t = 2.05$, $p \leq .05$) and hospital stay ($t = 6.13$, $p \leq .001$). Induced labor ($\chi^2 = 10.93$, $p \leq .001$) and cesarean section ($\chi^2 = 19.09$, $p \leq .001$) were higher in women with epidural analgesia and their neonates had lower Apgar scores at 1 minute ($t = -2.75$, $p \leq .05$) and 5 minutes ($t = -2.47$, $p \leq .05$) after birth and higher incidence of fetal heart rate abnormalities ($\chi^2 = 5.95$, $\leq .05$). **Conclusion:** The use of epidural analgesia is more effective in relieving labor pain compared with parenteral analgesia. However, it is associated with negative maternal and neonatal outcomes.

Keywords: Epidural analgesia, Labor, Opioids, Pain, Parenteral analgesia

Corresponding Author:
Heba Khalil, PhD
Email: h_khalil@asu.edu.jo; heba.khalil@yahoo.com
Tel: +962-65609999

INTRODUCTION

The United Nations International Children's Emergency Fund (UNICEF) estimates an average of 140 million births occur every year around the world (1). Although labor is a normal physiologic process, it can produce severe pain. Pain during labor is a major concern for women, their spouses, and the health care team worldwide (2). Severe pain during labor may result in many negative consequences for the mother and the fetus (3). Evidence suggests that pain is associated with catecholamines release which increases the minute volume and oxygen consumption during contractions, reduces the uterine contractile activities, and contract uterine blood vessels causing a reduction of the uterine-placental blood flow (4). These pain-related physiological changes may lead to fetal hypoxia and acidosis (4).

Adequate pain relief could enhance the mother's comfort and fetal outcomes, decrease unnecessary medical interventions, and thus decrease cost during labor (5). While some women manage their pain well with no or minimal assistance, others request pharmacological analgesia throughout labor (6). Findings from previous studies investigating the opioid administration route for pain relief during labor are not consistent. For instance, it has been shown that epidural opioids provide better analgesia quality compared to parenteral administered opioids (7). Pregnant women who received epidural opioid analgesia during labor were more active, had a lower incidence of opioid side effects, and lower the length of stay after birth compared with those who received parenteral analgesia (8, 9). When compared with non-epidural or no pain relief during labor, epidural anesthesia found to decrease the stress response associated with surgical trauma, however, had no impact on the risk of having a cesarean section (CS), long-term backache, and did not appear to have an immediate effect on neonatal status as determined by Apgar scores (10, 11). Studies found that epidural analgesia was associated with an increased risk of instrumental vaginal birth (10, 11), an increased likelihood of hypotension episodes, and pruritus compared to parenteral opioids

(12).

The use of opioids to relieve pain during labor is considered part of standard care worldwide. Though there is still considerable controversy surrounding the best route for opioid administration. In the Middle East countries, intramuscular and intravenous are the most common routes for controlling labor pain followed by epidural analgesia (13). Parenteral opioid analgesia is still widely used in Jordan as the epidural is not being covered by insurance plans and not easily affordable for many women during childbirth. Jordanian health care providers would benefit from data relevant to pain management during labor to enhance their counseling regarding treatment preferences. Moreover, investigating ethnic differences in pain and the response to pharmacologic pain treatment may enhance the cultural sensitivity and increase cultural awareness to improve pain assessment and management for ethnic minorities (14). Thus, this study aimed to compare the effect of epidural versus parenteral opioid analgesia on pain outcomes, opioid dose consumption and related side effects, and maternal and neonatal outcomes during labor among Arab pregnant women in Jordan.

MATERIALS AND METHODS

Sample

This study was a retrospective chart review of Jordanian pregnant women admitted for normal vaginal birth. Pregnant women were included in this study if they had an uncomplicated pregnancies at 37 to 42 weeks' gestation, were 18 years of age or older, and were admitted for a vaginal birth. Women with planned cesarean section, complicated pregnancies, or induced for stillbirths or fetal congenital anomalies were excluded.

Data Collection

Data collected from medical records include demographic and obstetric data; age, weight, gravidity, parity, length of gestation (in weeks), induction of labor (yes, no), duration of labor (in minutes), and postpartum hospital stay (in hours).

Mean labor pain scores were calculated from medical records where the pain was assessed and documented hourly throughout labor. Pain scores were measured using the Numeric Rating Scale (NRS), an 11-point verbal pain response scale that ranges from 0 (no pain) to 10 (pain as bad as I can imagine). Total opioid consumption during labor (converted to morphine equivalents), routes of opioid administration (epidural, parenteral), and opioid-related side effects were collected from medical records. The dose of opioids administered (100 µg fentanyl, 1.5 mg hydromorphone, and 75 mg of meperidine) were all converted to 10 mg of morphine (15). The administration of epidural opioid analgesia during labor was continuous through an infusion pump with a concentration of 0.1% levobupivacaine and 2 micrograms/mL fentanyl, with a rate between 12–14 mL/hr depending on women's need.

Maternal and neonatal outcomes were obtained from medical records. Maternal adverse outcomes such as assisted vaginal birth, unplanned cesarean section, and postpartum hemorrhage. Neonatal outcomes were measured by Apgar scores at one and five minutes after birth, Fetal Heart Rate (FHR) abnormalities, neonatal resuscitation, and admission to neonatal intensive care unit (NICU).

Ethical Consideration

This study was conducted under the principles of the Declaration of Helsinki and approved by the Institutional Review Board committee. Medical records from January 2017 to and December 2018 were reviewed by study personnel. No identifying information was obtained, all collected data were kept confidential and anonymous and saved in a locked file cabinet. Institutional Review Approval (IRB) was obtained from the Institutional Ethical Committee of the Applied Science Private University, and the participated hospital (IRB no.: 2018-2019-1-4).

Statistical Analysis

All statistical analyses were preceded by descriptive analysis using mean and standard deviation for continuous variables and frequency and percentages for categorical variables. For the comparison between epidural and parenteral opioid groups, independent t-test was conducted for parametric data including mean labor pain score; total opioid consumption during labor (in mg); the number of opioid-related side effects, duration of labor (in minutes); postpartum hospital stay (in hours) and Apgar scores at one and five minutes after birth. Chi-square test was conducted for non-parametric data including induction of labor (yes, no); assisted vaginal birth (yes, no); cesarean section (yes, no); and persistent FHR abnormalities (yes, no). Finally, Fisher's exact test was used for non-parametric data variables with a small sample size including postpartum hemorrhage (yes, no); neonatal resuscitation (yes, no), and admission to NICU (yes, no). All analyses were conducted using SPSS statistics version 24 (IBM Corp., Armonk, NY). A p-value of less than .05 was considered to be statistically significant.

RESULTS

A total of 314 pregnant women charts were included in this study. The average age of women was 29.46± 4.13 years and gestational age of 38.51±1.12 weeks. The average number of pregnancies (gravidity) was 2.6±1.7, whereas the mean number of live births (parity) was 1.5±1.2. Approximately, 91% (n= 285) of the women had normal vaginal birth, 11% (n= 33) of them had instrumental vaginal birth, 24% (n=74) underwent induction of labor, and 9% (n= 29) had unplanned cesarean section. The average duration of labor was

292±184 minutes with an average of postpartum hospital stay of 24.6±8.5 hours.

The mean NRS scores for pain assessment was 6.19±2.22 at admission and 4.07±3.23 during labor. During labor, 66% (n=207) of women had parenteral opioid analgesia and 34% (n=107) had epidural opioid analgesia. The mean opioid consumption during labor was 33.0±13.29 morphine milligram equivalents. Forty-three percent (n=134) did not experience any side effects of the opioid. Forty percent (n= 127) of the total sample experienced one adverse event, whereas 14% (n= 45) and 3% (n= 8) experienced "at least two "and "at least three "adverse events, respectively. The most common side effects of opioid usage were drowsiness (n= 132 (42%)) followed by nausea (n= 62 (20%)), vomiting (n= 22 (7%)), and hypotension (n= 16 (5%)). In terms of neonatal outcomes, the average of Apgar scores were 7.89±0.67 and 9.05±0.52 at one and five minutes after birth, respectively. Seven percent (n=23) of newborns developed complications at birth. Of these, 5% (n= 14) had persistent late decelerations, 1% (n= 3) had neonatal resuscitation and 2% (n= 6) were admitted to NICU. The total sample characteristic is summarized in Table I.

Table I: Descriptive statistics for the study participants (n=314)

Variables	Descriptive statistics
Age (years)	29.46± 4.13
Weight (cm)	75.45± 9.81
Height (kg)	161.75±12.74
Gestational age (week)	38.51±1.12
Gravidity	2.6±1.7
Parity	1.5±1.2
Types of birth	
Normal vaginal birth	285 (91%)
Unplanned cesarean section	29 (9%)
Induction (yes)	74 (24%)
Duration of labor (minutes)	292±184
Postpartum hospital stay (hours)	24.6±8.5
Pain score	
At admission	6.19±2.22
During labor	4.07±3.23
Labor analgesia	
Parenteral	207 (66%)
Epidural	107 (34%)
Total opioid consumption during labor (in mg)	33.0±13.29
Opioid side effects	
No side effect	134 (43)
One side effect	127 (40)
Two side effects	45 (14)
At least three side effects	8 (3)
Apgar scores	
At 1 minutes	7.89±0.67
At 5 minutes	9.05±0.52
Neonatal complications	
Persistent late decelerations	14 (5%)
Neonatal resuscitation	3 (1%)
Admission to NICU	6 (2%)

Descriptive statistics reported in cell are expressed as M ± SD for continuous variables and n (%) for categorical variables. NICU: Neonatal Intensive Care Unit

Results of the independent samples *t*-test showed that women who received epidural analgesia experienced less labor pain (t = -32.96, p =.000), consumed less opioids (t = -5.23, p = .000) and complained of less opioid side effects (t = -10.35, p = .000) compared with women who received parenteral analgesia (Table II). Approximately, 82% (n=88) of women with epidural analgesia had no opioids side effects compared with only 22 % (n= 46) of women with parenteral analgesia. The most common side effect of epidural opioid analgesia was hypotension (n=13(12%)) followed by drowsiness (n= 2 (1.9%)), whereas the most side effect of parenteral opioid analgesia was drowsiness (n=84 (41%)) followed by nausea and vomiting (n=26 (13%)).

Despite the benefits of epidural analgesia, women who received epidural analgesia had significantly longer duration of labor (t = 2.05, p =.041) and postpartum hospital stay (t = 6.13, p=.000) (Table II). Moreover, they had significant higher rate of induced labor (χ^2 = 10.93, p=.001) and CS section (χ^2 = 19.09, p = .000). However, there was no statistically significant differences in the rates of instrumental birth or postpartum hemorrhage between the two groups (χ^2 = 3.41, p = .065) and (0.9%

Table II: Paired sample *t*-test comparing epidural and parenteral opioid analgesia

Variables	Epidural analgesia		parenteral analgesia		*t*-test
	M	SD	M	SD	
Maternal data					
Labor pain score	0.11	0.48	6.11	1.85	-32.96 [b]
Total opioid consumption during labor (in mg)	11.66	4.68	14.13	3.54	-5.23 [b]
Number of opioid-related side effects	0.21	0.51	1.05	0.75	-10.35 [b]
Duration of labor (in mins)	321.29	214.95	276.48	164.76	2.05 [a]
Postpartum hospital stay (in hrs)	28.39	10.23	22.55	6.58	6.13 [b]
Neonatal data					
Apgar scores at 1minutes after birth	7.75	0.87	7.97	0.53	-2.75 [a]
Apgar scores at 5 minutes after birth	8.95	0.56	9.11	0.50	-2.39 [a]

[a] p <.05,[b] *p* <.001
Note. M=Mean. SD= Standard Deviation

Table III: Chi-square and Fisher's exact tests comparing epidural and parenteral opioid analgesia

Variables	Epidural analgesia n= 107 (34%)	Parenteral analgesia n=207 (66%)	*P* Values
Maternal data			
Induction of labor	37 (34.6%)	37 (17.9%)	≤.001 [a]
Assisted vaginal delivery	16 (15%)	17 (8.2%)	.065 [a]
Cesarean section	21 (19.6%)	8 (3.9%)	≤.001 [a]
Postpartum hemorrhage	1 (0.9%)	3 (1.4 %)	.579 [b]
Neonatal data			
Persistent FHR decelerations	9 (8.4%)	5 (2.4%)	≤.05 [a]
Neonatal resuscitation	2 (1.9%)	1 (0.05%)	.269 [b]
Admission to NICU	1 (0.9%)	5 (2.4 %)	.668 [b]

[a] Chi-square test; [b] Fisher's exact test.

vs 1.4%; $p = .70$), respectively (Table III).

In regard to neonatal outcomes, neonates of women who received epidural analgesia, had significantly lower Apgar scores at one-minute ($t = -2.75$, $p = .006$) and five-minutes after birth ($t = -2.47$, $p=.014$). Further, neonates of women who received epidural analgesia had a higher incidence of FHR abnormalities (persistent late decelerations) ($\chi^2 = 5.95$, $p= .015$) compared to women who received parenteral analgesia. However, there were no differences in the rate of neonatal resuscitation or NICU admission between the two groups (1.9% vs 0.5%; $p = .23$) and (0.9% vs 2.4%; $p = .36$), respectively.

DISCUSSION

Our findings revealed that epidural opioid analgesia provided significantly better pain relief when compared with parenteral opioid analgesia. Moreover, we found that women with epidural analgesia consumed less opioid and complained of fewer opioid side effects during labor. Our findings corroborate findings from the recent Cochrane review published in 2018. This review included 40 trials of 11,000 women and reported women with epidural opioid analgesia had more effective pain relief and more satisfaction with pain management than those with injectable opioids (16). Moreover, the review showed that women who received epidural analgesia reported less pain compared to women who received other interventions such as placebo, no treatment, or acu-stimulation. In addition, a recent review of randomized trials that included 16 studies with 7150 women suggested that epidural analgesia provided significantly better labor pain relief when compared with parenteral opioids (7).

In terms of maternal outcomes, we found that epidural opioid analgesia women had longer duration of labor and postpartum hospital stay than women with parenteral opioid analgesia. Our findings are consistent with previous studies that reported the effect of epidural analgesia on the duration of labor and postpartum hospital stay (17-19). Though, others did not find this association to be significant (20, 21). This inconsistency could be explained by the fact that previous studies did not take into account the various clinical risk factors that may impact the duration of labor and hospital stay. Moreover, the inconsistent findings might be also explained by the differences in research methodologies among prior studies.

Several studies have described the effects of epidural analgesia on the induction of labor and found that women with epidural analgesia had higher induced labor compared with women with parenteral analgesia (16, 22). Our findings also showed that the induction rate was higher among women with epidural analgesia. It has been shown that epidural analgesia is associated with a greater percentage of oxytocin usage and a longer first and second stage of labor (11).

There is conflicting evidence regarding the effect of epidural analgesia on CS rates. We found that women with epidural analgesia had higher CS rates. Consistent with these findings, a population-based cohort of 210708 pregnant women showed that epidural analgesia during labor was associated with an increased risk of CS (23). Others found no evidence of a significant difference in the overall risk of CS between epidural and parenteral opioid analgesia (7, 16, 17). The reasons for these inconsistencies could be related to differences in the methodologies and designs among previous studies, variations in obstetric practice and pain management methods of different hospitals.

Evidence demonstrated that epidural analgesia increased the need for instrumental vaginal birth such as forceps/vacuum-assisted birth (7, 17). However, we found no differences between the two groups in terms of instrumental vaginal birth. The reason for this could be due to the research design and methodology of this study including the data collection procedure and the relatively small sample size. These findings are consistent with findings reported by Deshmukh et al. who reported no increase in the rates of operative and instrumental births among women with epidural or parenteral analgesia (20). Moreover, the Cochrane review of 2018 did not report a significant relationship between epidural analgesia and increased the risk of instrumental vaginal births. This finding was explained by the fact that the recent use of patient-controlled epidural analgesia (PCEA) with a lower concentration of local anesthetic may help in reducing the effect of epidural analgesia on the need for an instrumental vaginal birth. The recent changes in the obstetric guidelines and practice may have also contributed to the change in the rate of instrumental vaginal births among women with epidural analgesia.

Regarding neonatal outcomes, we found that neonates of women who received epidural opioid analgesia had significantly lower Apgar scores at one and five minutes after birth compared with women who received parenteral opioid analgesia. Similar findings have been reported in the literature. Apgar index values at one minute and five minutes were reported to be slightly but significantly lower in neonates whose mothers had received epidural analgesia (24, 25). Furthermore, Hincz et al. revealed that epidural analgesia is an important risk factor for the low Apgar score at 7 minutes and low pH values of the umbilical artery (17). We have also found that neonates of women with epidural analgesia had a significantly higher incidence of FHR abnormalities (late decelerations) compared to those with parenteral opioids. The precise mechanism of action for the effect of epidural analgesia on fetal heart rate is still not well understood. However, different mechanisms were proposed to explain this effect mostly by causing

maternal hypotension or uterine hyperstimulation (26). A retrospective study of 6676 pregnant women who had epidural analgesia during labor demonstrated that eleven percent of the participated women presented anomalies of FHR in the hour following the epidural analgesia. The majority of these women, around forty percent, showed prolonged decelerations, others showed a variable degree of variable decelerations, early decelerations, late decelerations and bradycardia (27). Others found that epidural analgesia is associated with transient FHR changes without modification in the FHR baseline (28). Neonatal resuscitation and admission to the intensive care unit were found to be more frequent in neonates of epidural women compared with non-epidural in a recent retrospective study of 2399 newborns (24). However, we did not find this association to be significant. Similarly, the Cochrane review of 2018 showed that epidural analgesia has no effect on neonatal resuscitation or on the number of babies who were admitted to the neonatal intensive care unit (16). Recently, neonatal morbidity (assessed by low Apgar scores (Apgar scores <7 at 5 min), pH values of umbilical artery (artery pH < 7.10), and higher needs of neonatal resuscitation) and composite morbidity were not found to be associated with the use of epidural analgesia (29).

This study had some limitations such as incomplete documentation for some participants charts and the poor quality of documentation, this is common for most retrospective chart review studies. Also, some data could not be obtained due to the nature of the design in this study. This includes data about medical and surgical management during labor, the causes for CS and neonatal admission to NICU, and neonatal outcomes such as cord blood arterial pH and meconium staining of labor.

Despite the limitation of this study, it is the first in Jordan to examine the differences between epidural and parenteral opioid analgesia in terms of pain relief and maternal and neonatal outcomes among pregnant women in labor. Thus, the findings of this study may improve health care providers including nurses and midwives' decisions regarding the choices of pain relief during labor and will enhance their ability to anticipate the risk of any potential complications that could affect the mother, the fetus, or both. Moreover, this study's findings will also improve health care providers' communication strategies to educate women of the potential benefits and risks of opioid therapy which will improve women's autonomy in decision-making. Lastly, our findings will inform future research investigating the effect of pain management strategies on labor pain and outcomes in Jordan.

CONCLUSION

Findings from this retrospective study suggest that epidural opioid analgesia is potentially an effective method for pain relief during labor. Yet, it is likely associated with negative maternal and neonatal outcomes. These include prolong the duration of labor and postpartum hospital stay, increase the risk for induced labor, CS rate, and fetal heart rate abnormalities, and decrease Apgar scores at one minute and five minutes after birth. Health care providers play a vital role in assessing labor pain, opioids related side-effects and short-term outcomes during labor. Thus, continuous maternal and fetal monitoring is essential to identify any potential complications of epidural opioid analgesia during labor. Moreover, health care providers should implement strategies to improve pain relief particularly among women receiving parenteral opioid analgesia. Finally, they should educate women with the different opioid options for labor pain relief and their potential maternal, fetal, and neonatal side-effects. Future research utilizing a stronger design is needed to investigate the effect of opioid administration techniques on pain control during labor in Jordan.

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