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The effect of Epidural Analgesia on Maternal and Early Neonatal Outcomes, in Qatar State

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Abstract

Introduction: One of the most effective methods to reduce labor pain at the present time is Epidural analgesia. We aim to describe the maternal and neonatal morbidities associated with labour epidural analgesia.

Methods: This was a retrospective cohort data analysis of PEARL-Peristat Study data, Hamad Medical Corporation- QATAR STATE. The sample for this study comprised of births for the year 2017 in Women's Hospital. Women who had EA compared to women with no EA during labour. We analyzed 7721 singleton vaginal births at 24 weeks and above conducted in Woman's hospital [WH] between January 2017 and April 2018. We then excluded babies with major congenital abnormalities, stillbirths, immediate neonatal death in labour room or operating theatre, birth weights <2500g or >4000g, gestational age at birth <37 weeks or >41+6 weeks, women with diabetes and hypertension, precipitate labour where total labour duration was less than 180 minutes and other missing data. Statistical analysis was performed using IBM SPSS 26 statistical software with statistical significance set at $p<0.05$.

Results: The tables showed a comparison between the group which received EA and the other group which did not receive it. There was a significant association between EA and many risks of mother pregnancy and neonatal outcomes. On the other side, no significant correlation was found between EA and other variables.

Conclusion: The use of EA was associated with many maternal and neonatal-perinatal risks. It may prolong all stages of labour, precipitate instrumental delivery need, increase NICU admission for different risk factors including respiratory distress and rule out sepsis. We recommend including these risk factors in counseling, before choosing EA.

Keywords: Epidural analgesia, Labour, Nulliparous, Qatari, outcome, neonate, pregnancy.

Introduction

One of the most effective methods to reduce labor pain at the present time is Epidural analgesia [EA] [1]. We aim to study the effect of AE on mother and neonate perinatally. Its use in recent years has increased, being used by between 20–70% of all deliveries [2–6]. Compared to parenteral opioids, Epidural analgesia provides significantly more analgesia, as measured by a visual analog scale in both the first and second stages of labour [7]. There is continuing controversy over whether epidural analgesia impedes the progress of labour by causing dystocia and increasing the operative delivery

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rate, although regional anaesthesia has been associated with a reduction in anaesthesia-related maternal mortality [8-10]. Several studies have described various adverse effects among pregnant women users of EA, such as a rise in body temperature, difficulty in the onset of lactation, hypotension, the prolonged second stage of labor, and an increase in instrumental vaginal delivery, among others [1,6,11-15]. In terms of its effect on the newborn, usually expressed using low Apgar scores and pH values of the umbilical artery, the main systematic reviews have found no relationship between the use of EA and an increase in neonatal morbidity [NM] [1,6,7,16-18]. Absolute contraindications to neuraxial labor analgesia are rare. Some relative contraindications include coagulopathy, infection of the lower back, and increased intracranial pressure due to an intracranial lesion. Studies of the effects of neuraxial analgesia on the risk of cesarean delivery, the length of labor, breastfeeding success, and pre-existing or new-onset low back pain have been largely reassuring [19]. We aim to describe the maternal and neonatal morbidities associated with epidural labour analgesia.

Methods

Study design: This was a retrospective cohort data analysis of PEARL-Peristat Study data [Perinatal Neonatal Outcomes Research Study in the Arabian Gulf] Qatar. The PEARL-Peristat Study was a registry-based study designed to study immediate and long-term pregnancy outcomes of births using routinely collected hospital data. The study was funded by Qatar National Research Fund [Grant no. NPRP 6-238-3-059] and sponsored by the Medical Research Centre, Hamad Medical Corporation. The study was approved by the Hamad Medical Corporation Institutional Review Board [IRB], with a waiver of consent [HMC-IRB 13064/13].

Setting and Participants: The sample for this study comprised of births for the year 2017 in Women's Hospital [WH] [now WWRC Women's Wellness and Research Center]; the largest public hospital where delivery is conducted in Qatar. This sample was therefore generally representative of most births in the country. For this study, we retrieved 20625 singleton vaginal births at 24 weeks gestation and above conducted in WH between January 2017 and April 2018. We then excluded babies with major congenital abnormalities, stillbirths, immediate neonatal death in labour room or operating theatre, birth weights <2500g or >4000g, gestational age at birth <37 weeks or >41+6 weeks, women with diabetes and hypertension, precipitate labour where total labour duration was less than 180 minutes and other missing data [20]. We, therefore, analyzed 7721 births after exclusion as described above.

Comparison groups: Women who had epidural analgesia compared to women with no epidural analgesia in labour.

Covariates and outcomes

Maternal: Explanatory factors included maternal age, parity grouped into nulliparous or greater than or equal to one parous experience and nationality was grouped into Qatari and no-Qatari. In addition, we examined the use of opioid analgesia [morphine] in labour and calculated the body mass index [BMI] at delivery. Maternal outcomes studied included suspected chorioamnionitis, meconium-stained amniotic fluid [MSAF], labour duration [first stage, second stage and third stage], instrumental delivery using vacuum or forceps, postpartum haemorrhage and admission to intensive care unit.

Newborn: These included gestational age at birth, birth weight and gender. Immediate outcomes included arterial and venous cord PH, Apgar score less than 7 in 1 minute and in 5 minutes, admission to neonatal intensive care [NICU]. In addition, there was admission to NICU for respiratory distress and admission to NICU for suspected sepsis. Other variables were birth trauma and in-hospital mortality. Birth trauma included caput succedaneum, subgaleal hematoma, cephalohematoma, brachial plexus injury, clavicular fracture, facial nerve injuries, and subconjunctival haemorrhage.

Statistical analysis: We summarized the distribution of variables using numbers and percentages, mean and standard deviation or median and interquartile ranges as appropriate. Based on the data type, we compared the proportions and the incidence of the study covariates and outcomes between the epidural and the non-epidural groups using either chi-square tests, Fishers' test, analysis of variance [ANOVA] or Mann-Whitney U test. Statistical analysis was performed using IBM SPSS 26[SPSS Inc., Chicago, IL, USA] statistical software with statistical significance set at $p<0.05$.

Results

Table 1. showed the two groups were comparable in terms of socio-demographic data. Age was lower in females who received epidural, also use of Opioid analgesia was significantly less in the epidural group [$P < 0.001$]. BMI was higher in group B, Nullipara and Qatari females were more prevalent to receive epidural [$P<0.001$], while ≥ para 1 was less to receive [$P<0.001$]. No statistical difference was observed between both groups in gender [P 0.565] and Birth weight [P 0.067].

The study group comprised 7721 nulliparous and Parity ≥1. Both groups were similar in obstetric and maternal demographic characteristics like age, height, weight, BMI, and gestation age.

In Table 2 mother outcome was compared in the two groups, a table showing that many variables [Maternal age, BMI at delivery, Parity, Nationality, Opioid analgesia] were more common in the EA group, with significant difference $P < 0.001$; like intrapartum fever, VBAC [vaginal birth after

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Table 1: Maternal demographic variables of both groups.

	Total [n=7721]		Epidural No [n=4752]		Analgesia Yes [n=2969]		p-value
	n	%	n	%	n	%	
Maternal age*	28.12 ± 5.22		28.44 ± 5.25		27.61 ± 5.14		<0.001
BMI at delivery*	30.26 ± 5.14		30 ± 5.09		30.68 ± 5.2		<0.001
Parity							
Nullipara	2450	31.7%	1074	22.6%	1376	46.3%	
Parity ≥1	5271	68.3%	3678	77.4%	1593	53.7%	<0.001
Nationality							
Non-Qatari	5317	68.9%	3471	73.0%	1846	62.2%	
Qatari	2404	31.1%	1281	27.0%	1123	37.8%	<0.001
Opioid analgesia							
No	6100	79.0%	3414	71.8%	2686	90.5%	
Yes	1621	21.0%	1338	28.2%	283	9.5%	<0.001

* Values are expressed as “Mean ±SD”

Table 2: Maternal Pregnancy Outcomes in both groups.

	Total [n=7721]		Epidural analgesia				p-value
			No [n=4752]		Yes [n=2969]		
	n	%	n	%	n	%	
Intrapartum fever							
No	7602	98.5%	4725	99.4%	2877	96.9%	
Yes	119	1.5%	27	0.6%	92	3.1%	<0.001
VBAC							
No	7160	92.7%	4443	93.5%	2717	91.5%	
Yes	561	7.3%	309	6.5%	252	8.5%	0.001
Clinical chorioamnionitis							
No	7620	98.7%	4726	99.5%	2894	97.5%	
Yes	101	1.3%	26	0.5%	75	2.5%	<0.001
Membrane rupture[a]							
<18hrs	7071	91.8%	4479	94.4%	2592	87.6%	
≥18hrs	631	8.2%	265	5.6%	366	12.4%	<0.001
MSAF							
No	6504	84.3%	4040	85.1%	2464	83.0%	
Yes	1209	15.7%	706	14.9%	503	17.0%	0.015
Instrumental Delivery							
No	6999	90.6%	4539	95.5%	2460	82.9%	
Yes	722	9.4%	213	4.5%	509	17.1%	<0.001
PPH							
No	7323	94.8%	4593	96.7%	2730	92.0%	
Yes	398	5.2%	159	3.3%	239	8.0%	<0.001
1st stage of labour [mins] [a]	300 [230-386]		270 [220-345]		345 [270-448]		<0.001
2nd stage of labour [mins] [a]	15 [6-48]		10 [5-22]		43 [15-112]		<0.001
3rd stage of labour [mins] [a]	5 [5-7]		6 [5-8]		5 [5-7]		<0.001
Total Labour duration [mins] [a]	330 [255-445]		295 [237 - 375]		415 [320-540]		<0.001

[a] =Missing data: Membrane rupture [n=19], 1st stage of labour [n= 9], 2nd stage of labour [n=55], 3rd stage of labour [n=100], Total duration of labour [n=2], Labour data reported in median and interquartile range [IQR], VBAC= vaginal birth after caesarean, MSAF= meconium stained amniotic fluid.

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Table 3: Neonatal Outcomes in both groups.

			Epidural analgesia				P- value
	Total [n=7721]		No [n=4752]		Yes[n=2969]		
	n	%	n	%	n	%	
Birth weight*	3252.3 ± 343.9		3246.6 ± 341.5		3261.4 ± 347.8		0.067
Gestational age*	39.20 ± 1.08		39.16 ± 1.07		39.25 ± 1.10		<0.001
Cord Arterial pH[a] *	7.29	0.10	7.29	0.10	7.28	0.09	0.002
Cord Venous pH[a] *	7.32	0.09	7.33	0.09	7.31	0.08	<0.001
NICU admission							
No	7357	95.3%	4581	96.4%	2776	93.5%	
Yes	364	4.7%	171	3.6%	193	6.5%	<0.001
NICU admission for suspected sepsis							
No	7506	97.2%	4662	98.1%	2844	95.8%	
Yes	215	2.8%	90	1.9%	125	4.2%	<0.001
NICU admission for respiratory distress							
No	7623	98.7%	4706	99.0%	2917	98.2%	
Yes	98	1.3%	46	1.0%	52	1.8%	0.003
Gender							
Male	3887	50.3%	2380	50.1%	1507	50.8%	
Female	3834	49.7%	2372	49.9%	1462	49.2%	0.565
Apgar <7 at 1min							
No	7665	99.3%	4719	99.3%	2946	99.2%	
Yes	56	0.7%	33	0.7%	23	0.8%	0.686
Apgar <7 at 5mins							
No	7716	99.9%	4749	99.9%	2967	99.9%	
Yes	5	0.1%	3	0.1%	2	0.1%	0.636
Birth Trauma							
No	7658	99.2%	4724	99.4%	2934	98.8%	
Yes	63	0.8%	28	0.6%	35	1.2%	0.005
Newborn Outcome							
Discharged alive	7717	99.9%	4748	99.9%	2969	100.0%	
In-hospital mortality	4	0.1%	4	0.1%	0	0.0%	NA

[a] = Missing data: Cord arterial PH [n=6551], cord venous PH [n= 6605]
* Data reported as mean and SD NA= not applicable

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cesarean], suspected Chorioamnionitis, Amniotic membrane rupture ≥ 18 hr. before birth, Instrumental Delivery, PPH [post-partum hemorrhage], 1st stage, 2nd stage, 3rd stage of labour [mins] more prolonged, Total Labour duration [mins] more prolonged, also MSAF [meconium-stained amniotic fluid] is more in epidural limb [P-value 0.015].

Regarding neonate's outcome in Table 3, many variables were higher in the epidural group [P <0.001, <0.005] like Gestational age, total NICU admission, Birth trauma, NICU admission for suspected sepsis, and respiratory distress is higher in the epidural group [P = 0.003]. Cord venous and arterial pH is lower in the epidural group [P<0.001and P< 0.002]. There was no statistical difference between both groups in Apgar < 7 at 1 min and at 5 min [P= 0.686 and P= 0.636].

Discussion

For reducing pain during labour, Epidural analgesia [EA] appears to be effective in this aspect. We aim to describe the maternal and neonatal morbidities associated with epidural labour analgesia. Regarding socio-demographic data in our study, age was lower, and the use of Opioid analgesia was significantly less in the epidural group [*P* < 0.001]. BMI and gestational age were higher in the epidural group. Nullipara and Qatari females were more prevalent to receive epidural [*P*<0.001], while ≥ para-1 was less to receive [P<0.001]. Between the two groups, there was a significant difference [*P* < 0.001] in many variables like intrapartum fever, VBAC [vaginal birth after cesarean], suspected Chorioamnionitis, Amniotic membrane rupture ≥ 18 hr. before birth, Instrumental Delivery, PPH[post-partum hemorrhage], 1st stage, 2nd stage, 3rd stage of labour [mins] and total labour duration [mins] were more prolonged, Also MSAF [meconium-stained amniotic fluid] was observed more in epidural limb [*P*-value 0.015]. In concordance with our study, one study compared the two groups in terms of socio-demographic data, the duration of the second stage of labour was prolonged in the epidural group [33.13 ± 12.78 min], as compared to the control [27.53 ± 11.73 min]. On the contrary, the same study showed that the first stage of labour was shorter in the epidural group [4.83 ± 1.59 h] compared with the control group [5.48 ±1.56 h], Instrumental vaginal or caesarean delivery rate did not increase in the epidural group [21]. Another study found The EA and the second stage of labor duration are not related to the NM and the second stage of labor does not need to be terminated for duration alone, while the instrumental delivery doubles the risk of NM compared to the normal vaginal delivery [22,23]. Recent studies suggested that, although the duration of the second stage of labour is associated with increased risks of certain adverse maternal outcomes, there is no relationship between the duration of the second stage and adverse neonatal outcomes. However, most studies on this issue are from single centers [24,25,26]. For another aspect, one study showed that EA increases NICU admission, antibiotic exposure, neonatal birth injuries, need for positive pressure ventilation at birth, and respiratory distress in the first 24 hours of life. Mothers on epidural analgesia have a prolonged second stage of labour, a higher rate of instrumental delivery, meconium-stained amniotic fluid, fetal distress, and temperature elevation [6,27]. Mothers who received EA, had a long second stage [*P*<0.001], temperature elevation >37.5°C [P<0.001], and instrumental delivery [*P*<0.001] [6,27]. In our study, many variables were higher in the epidural group. [*P* <0.001, <0.005] like total NICU admission, Birth trauma, NICU admission for suspected sepsis, and for respiratory distress are higher in the epidural group. Previous single-center studies have found conflicting results regarding the contribution of maternal epidural analgesia to neonatal receipt of antibiotics [28,29]. One of the major criteria for sepsis evaluation is maternal intrapartum fever. However, epidural analgesia can also lead to maternal fever and is not associated with an increased risk of infection in the neonate, thus leading to unnecessary neonatal exposure to antibiotics [30]. Among a large cohort of mother-neonate pairs across the state of Colorado over 6 years, EA was associated with a 26% increased odds of neonate exposure to antibiotics. Although mothers who received EA were 5 times more likely to have a fever, the proportion of neonates treated with antibiotics did not differ by epidural status. This result supports the hypothesis that EA is a risk factor for noninfectious maternal fevers, but neonates born to mothers with fever were treated without respect to whether the mother had an epidural [31]. In other studies, it was documented that Epidural analgesia is associated with increased rates of maternal intrapartum fever [29, 32-34]. However, the relationship between EA, maternal fever, and neonatal antibiotic treatment has been limited to conflicting single-center studies at academic, and tertiary care institutions. Goetzl et al. [28]. conducted a follow-up study of a cohort of 1934 births which demonstrated that in mothers with low grade [<37.5°C] or no fever, EA was associated with a three-fold increased risk of sepsis evaluation in neonates as well as increased rates of neonatal antibiotic treatment. In contrast, Kaul et al. [29] found no association [*p* =0.23] between EA and neonate sepsis evaluation in 1177 primiparous births at Magee-Women's Hospital [Pittsburg, Pennsylvania, USA]. In our study, Cord venous and arterial pH is lower in the epidural group [*P*<0.001and *P*< 0.002]. No statistical difference was observed between both groups in Apgar < 7 at 1 min and at 5 min [*P* = 0.686 and *P* = 0.636], and that was in concordance with some studies that demonstrated no significant difference in neonatal outcome [APGAR score=AS] between epidural and control groups as in many other studies [7,21, 27,35-37]. In one Cochrane review by Anim-Somuah et al., EA did not appear to have an immediate effect on neonatal status as determined by AS, where an odds ratio of 0.70 [0.44–1.10, 95% CI] was found for an AS of < 75 after EA [28]. On the contrary, the incidence of low AS

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was higher in the EA group and higher needs for neonatal resuscitation among users of EA [29,37,38].

Conclusion

Our study suggests that labour epidural analgesia adversely affects the short-term neonatal outcome. Neonatal birth injuries, the NICU admission rate, antibiotic exposure, respiratory distress, and need for oxygen in the first 24 hours of life increase. Mothers on EA had a prolonged second stage of labour, a higher percentage of instrumental delivery, meconium-stained amniotic fluid, and fever. The need for Caesarian delivery remains unaffected. Although there was some dysconcordance with some studies, healthcare staff needs to provide information on this topic to all pregnant women who request EA. The main limitation of this study is the retrospective design. Addressing the safety of EA perinatally and later, well-designed prospective studies are needed.

Conflict of Interest

Each author declares that he or she has no commercial associations [e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc], that might pose a conflict of interest in connection with the submitted article.

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