

Epidural analgesia during labour: a retrospective cohort study on its effects on labour, delivery and neonatal outcome

Wpływ znieczulenia zewnątrzoponowego na przebieg i rodzaj porodu oraz stan urodzeniowy noworodków – badanie retrospektywne

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Abstract

Objectives: to evaluate the impact of epidural analgesia (EA) on labor, delivery and neonatal status.

Material and methods: retrospective, observational, cohort study comprising 5593 pregnant women who met the inclusion criteria (singleton pregnancy, cephalic presentation, 37-42 weeks of gestation). Out of them, 2496 had EA and 3097 constituted the control group.

Main outcome measures: incidence of labor complications and operative deliveries in women who received EA, neonatal status assessed by Apgar score in 1- and 5-minute, and cord pH values.

Results: Labor complications were more frequently observed in the epidural group, with an almost 1.5-fold higher incidence in nulliparous (16.32% vs. 11.29%) and 1.4-fold in multiparous women (9.86% vs. 7.08%). Stepwise logistic regression confirmed that EA is a significant risk factor for labor complications in nulliparous women (OR 1.27, 95% CI 1.03-1.58) and for forceps delivery in multiparous women (5.20, 95% CI 3.31-8.17). Also, EA is an important risk factor for both, low cord arterial pH <7.10 (OR 1.98, 95% CI 1.28-3.09, p=0.0023) and low Apgar score at 1 minute (OR=4.55, 95% CI 2.35-8.80, p<0.0001). Crucially, there was no difference in the incidence of a low Apgar score at 5 minutes.

Conclusions: EA constitutes an independent risk factor for operative vaginal delivery in multiparous women, but has no effect on the incidence of cesarean sections, either in nulliparous or multiparous women. EA also increases the risk of labor complications, low 1-minute Apgar score and low umbilical cord pH, but is not associated with low 5-minute Apgar score.

Key words: **epidural analgesia / labor / delivery / cesarean section /
/ instrumental delivery /**

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Otrzymano: 26.05.2014

Zaakceptowano do druku: 14.07.2014

Streszczenie

Cel: Ocena wpływu znieczulenia zewnątrzoponowego (ZO) na przebieg porodu oraz stan urodzeniowy noworodków.

Materiał i metody: Retrospektywnej analizie poddano 5593 pacjentek spełniających kryteria włączenia do grupy badanej: ciąża pojedyncza, położenie płodu podłużne główkowe, wiek ciążowy ≥ 37 tyg oraz brak stwierdzonych prenatalnie i postnatalnie anomalii rozwojowych. W tej grupie u 2496 ciężarnych zastosowano znieczulenie zewnątrzoponowe porodu, natomiast 3097 stanowiło grupę kontrolną.

Oceniane parametry: Częstość występowania powikłań porodowych oraz porodów operacyjnych w grupie pacjentek rodzących w ZO, stan urodzeniowy noworodków oceniony na podstawie skali Apgar (w 1 i 5 minucie) oraz pH krwi pępowinowej.

Wyniki: W analizie regresji wieloczynnikowej wykazano, że znieczulenie zewnątrzoponowe jest niezależnym czynnikiem ryzyka powikłań porodowych tylko w grupie pierworódek (IS 1,27, 95% CI 1,03-1,58), natomiast w grupie wieloródek wpływa na zwiększenie odsetka porodów kleszczowych (5,20, 95% CI 3,31-8,17). ZO jest również istotnym czynnikiem ryzyka wystąpienia niskiego pH (< 7.10) krwi z tętnicy pępowinowej (IS 1,98, 95% CI 1,28-3,09, $p=0,0023$) oraz niskich wartości w skali Apgar w 1 minucie (IS=4,55, 95% CI 2,35-8,80, $p<0,0001$), nie wpływa jednak na częstsze występowanie niskich wartości w skali Apgar w 5 minucie.

Wnioski: Znieczulenie zewnątrzoponowe porodu jest niezależnym istotnym czynnikiem ryzyka zabiegowego ukończenia porodu wśród wieloródek, natomiast nie wpływa na zwiększenie odsetka cięć cesarskich (niezależnie od rodności). ZZO zwiększa także ryzyko wystąpienia powikłań porodu (deceleracje zmienne/późne) oraz niskich wartości w skali Apgar w 1 minucie i pH krwi z tętnicy pępowinowej, nie ma natomiast związku z niską punktacją w skali Apgar w 5 minucie.

Słowa kluczowe: **znieczulenie zewnątrzoponowe / poród / cięcie cesarskie / poród zabiegowy /**

Abbreviations:

BMI – body mass index

EA – epidural analgesia

PROM – premature rupture of membranes

VBAC – vaginal birth after cesarean section

Introduction

Epidural analgesia (EA) has been used for many years as one of the most effective methods for pain relief. The first documented use of EA was reported in 1946 and a rapid increase of its usage has been observed ever since. Currently, 20-50% of parturient women in the developed countries choose EA, without even considering other methods of pain relief.

Despite its common use in modern obstetric practice, there is still great concern about possible side effects associated with EA, especially related with the progress of labor, mode of delivery, and neonatal outcome. Some investigators reported that EA has been associated with a significant prolongation of labor, as well as an increased rate of labor augmentation, likelihood of instrumental deliveries and cesarean sections [1, 2, 3], while others did not observe such effects [4, 5, 6]. The influence of EA on neonates varies and while some authors emphasize the positive effect on the neonatal cord pH [7], there have also been reports about higher rates of neonatal resuscitation [8]. Moreover, the literature offers multi-analyses, based on retrospective and/or prospective studies [9, 10, 11, 12], which are consistent that EA is associated with an increased risk of labor augmentation and instrumental delivery, but has no effect on the neonatal outcome. However, the multi-analyses are questionable, primarily due to their study design [13].

Taking into consideration the widespread use of EA during labor and its efficacy in pain relief, nowadays it is almost impossible to perform a prospective, randomized trial on EA during labor [14]. After decades of EA use in the delivery rooms, the clinical management in such situations has evolved significantly [15]. Thus, we think that a retrospective analysis can deem valuable, clinically significant data. The primary purpose of the study was to evaluate the effect of EA on labor and delivery mode and, additionally, on neonatal outcomes.

Material and methods

According to the hospital database, 11 046 women delivered in the Research Institute of the 'Polish Mother's Memorial Hospital' between 21 January 2005 and 31 December 2012. Out of them, we selected women who delivered vaginally and met the following inclusion criteria: singleton pregnancy, cephalic presentation, 37-42 weeks of gestation. Exclusion criteria were based on obstetrical pathology or pre-existing chronic medical conditions that could possibly affect maternal and/or neonatal outcome. Additionally, patients with general anesthesia required for the cesarean section and patients with opioid analgesia (pethidine) were withdrawn from the final analysis to avoid a potential effect on the newborns. In the end, the study group consisted of 5593 patients who met the criteria. In that group, 2496 received EA, and the remaining 3097 patients were used as controls for the statistical analysis.

The patients usually receive intermittent EA. The initial dose typically was 10 mL 0.1-0.25% of bupivacaine, this was adjusted using the visual analogue pain scale, in combination with 0.025-0.1 mg of fentanyl. Boluses of the same doses or in doses increased proportionally to pain intensity were repeated every 90 min.

All patients were managed with the above described regimen. The dilatation of the cervix at the time of EA administration was at least 3cm.

Data were extracted from patient medical charts and hospital database. The following data were recorded for each patient: age, pre-pregnancy BMI, marital status, place of residence, parity, gestational age at delivery, onset of labor, oxytocin augmentation, length of the first stage of delivery, labor complications and the mode of delivery. Labor complications were classified according to the International Classification of Diseases, Tenth Revision (ICD-10). For statistical analysis, complications were categorized as variable/late decelerations (O68.0), meconium stained amniotic fluid (O68.1), and decelerations with meconium in the amniotic fluid (O68.2). When operative delivery occurred, indications were analyzed separately. Additionally, newborn weight, Apgar score at 1 and 5 minutes, and cord arterial pH were recorded.

For statistical analysis, software for biomedical research, MedCalc for Windows, ver. 11.6.1.0 (MedCalc Software, Mariakerke, Belgium) was used. The categorical data were analyzed with the Chi-square test or the Fisher's exact test (when the groups were limited in number). For numerical variables with normal distribution a t-test was used, and Mann-Whitney test for other numerical variables. Multiple logistic regression analysis was also performed to assess the independent contribution of various parameters on labor complications, instrumental delivery, low Apgar score at 1 and 5 minutes, and low arterial cord pH. A value of $p < 0.05$ was considered as statistically significant.

Results

There were no significant differences in marital status, place of residence and pre-pregnancy BMI between the groups, although patients with EA were slightly younger (27.94 vs. 28.37, < 0.0001). The statistical difference in parity was more significant, with more than a 3-fold greater prevalence of nulliparous women in the EA group, while the incidence of nulliparous and multiparous women in the control group was comparable. Taking into consideration the significant difference in parity between women in the epidural and the control groups, further analyses were performed separately for nulliparous and multiparous women.

Among the nulliparous women, patients with EA had a significantly increased incidence of cesarean sections (24.61% vs. 18.82%). Labor complications were also more frequently observed in the EA group, with a significant increase of variable/late decelerations. When all categories of labor complications (fetal heart rate pattern) were analyzed, the incidence in the EA group increased almost 1.5-fold (16.32% vs. 11.29%). Administration of oxytocin for labor augmentation was also more frequent in the EA group. Among the multiparous women, the analysis of the delivery mode revealed a significant increase in the rate of forceps delivery (3-fold) in the EA group. On the contrary, the percentage of cesarean section was similar in both groups. Labor complications also significantly differed between those groups. In the EA group, variable/late decelerations were observed more frequently. Administration of oxytocin for labor augmentation was also more frequent in the EA group. Detailed data on labor and delivery are presented in Table I.

In order to perform a thorough analysis of the indications for cesarean section, we classified them into six categories: fetal

distress, cervical dystocia, fetopelvic disproportion, imminent rupture of the uterus (only cases of VBAC), failed induction of labor, and others. The category of fetopelvic disproportion included fetal malposition, contracted pelvis and protracted descent. In the EA group, there was an increased rate of cesarean sections due to fetal distress and fetopelvic disproportion, in both, nulliparous (11.84% vs. 6.38%, $p < 0.0001$) and multiparous (4.84% vs. 2.78%, $p < 0.0001$) women. What is noteworthy, the incidence of cervical dystocia was significantly lower, again in both, nulliparous and multiparous women. There were no differences in indications to forceps delivery, but we observed a tendency for a higher incidence of fetal distress.

Further analyses of the possible effect of EA on labor and delivery required a stepwise logistic regression to be performed. For the assessment of the EA effect on labor complications, the following parameters were included in the model – BMI, patient age, gestational age (weeks), onset of labor, oxytocin administration and EA. VBAC was also included in the model for multiparous women. EA appeared to be a significant risk factor for labor complications only in the nulliparous group (OR 1.27, 95% CI 1.03-1.58). Additional risk factors in the group of nulliparous women were: labor induction (OR=1.82, 95% CI 1.21-2.17), prolonged pregnancy (OR=1.34, 95% CI 1.21-1.49), and PROM without contractions (OR=1.31, 95% CI 1.02-1.68). In the multiparous group, the risk factors of labor complications were as follows: labor induction (OR=2.44, 95% CI 1.17-5.07), PROM without contractions (OR=1.81, 95% CI 1.19-2.73) and prolonged pregnancy (OR=1.37, 95% CI 1.16-1.61).

A similar analysis was performed for operative delivery (cesarean section or forceps delivery). The logistic regression revealed that EA was a significant risk factor for forceps delivery only in the multiparous group (Table II).

The second aim of the study was to assess the effect of EA on newborn outcome. The analysis of the neonatal outcome was based on cord arterial pH and 1- and 5-minute Apgar score. In both, nulliparous and multiparous women, the neonatal outcome was slightly worse in the EA group. Mean 1- and 5-minute Apgar score was significantly lower, the difference was also observed in the distribution of the Apgar score groups (more frequently observed, medium interval, i.e. Apgar score of 4-7). Mean arterial cord pH was also significantly lower and there was a higher percentage of neonates born with pH < 7.10 (in the nulliparous group) and < 7.15 . All data were represented separately for nulliparous and multiparous women (Table III).

Stepwise logistic regression was performed to assess the effect of different risk factors on the neonatal outcome. The model included EA, onset of labor, oxytocin administration, complications of pregnancy, gestational age and sex of the baby. The analysis was done separately for low (below 7) 1- and 5-minute Apgar score, as well as cord arterial pH below 7.10 and 7.15 (Table IV). EA was an important risk factor for both, low cord arterial pH and low Apgar score at 1 minute (OR=4.55, 95% CI 2.35-8.80). More importantly, there was no difference in the incidence of low Apgar score at 5 minutes. However, the number of babies with a low 5-minute Apgar score was limited (13 cases, 0.23%), what in turn limited the statistical analysis.

Table I. Labor and delivery parameters.

	nulliparous women					multiparous women				
	EA-0		EA-1		p	EA-0		EA-1		p
Gestational age (weeks), mean, SD	39.16	1.09	39.31	1.07	<0.0001	39.03	1.08	39.06	1.10	NS
Gestational age ≥41 weeks (N, %)	111	7.33	190	9.91	0.009	82	5.18	36	6.23	NS
Onset of labor (N, %)										
– spontaneous	921	73.09	1328	72.85	NS	1107	80.33	451	81.41	NS
– rupture of membranes	266	21.12	414	22.71		235	17.05	85	15.34	
– labor induction	73	5.79	81	4.44		36	2.62	18	3.25	
Mode of delivery (N, %)										
– spontaneous vaginal delivery	1109	73.25	1263	65.85	<0.0001	1401	88.51	497	85.99	0.0001
– emergent cesarean section	285	18.82	472	24.61		165	10.42	58	10.03	
– forceps delivery	119	7.93	183	9.54		17	1.07	23	3.98	
Labor complications (N, %)										
– no labor complications	1342	88.64	1605	83.68	<0.0001	1471	92.92	521	90.15	0.0134
– meconium stained amniotic fluid (O68.1)	76	5.02	109	5.68		65	4.11	23	3.98	
– variable/late decelerations (O68.0)	69	4.56	152	7.92		34	2.15	30	5.19	
– decelerations with meconium in amniotic fluid (O68.2)	27	1.78	52	2.71		13	0.82	4	0.68	
Labor complications together (N, %)	172	11.29	313	16.32	<0.0001	112	7.08	57	9.86	0.04
Oxytocin (N, %)	621	41.02	1450	75.60	<0.0001	494	31.21	392	67.82	<0.0001
Duration of 1 st stage of labor (min), mean, SD	334	148	414	157	<0.0001	260	122	361	150	<0.0001

Discussion

Women in labor often consider EA due to it being the most effective form of pain relief. However, the safety of EA, both for the mother or the baby, continues to raise concern. Various controversies still exist on the matter, especially a possible association of EA use with the increased incidence of cesarean delivery. There have been many studies, both retrospective and prospective, which found an increase in the rate of cesarean section in patients with EA [2,3,16]. Thorp et al., performed one of the first randomized studies on EA in labor [3]. The incidence of cesarean section reached 25% in the EA group, compared with 2.2% in the control group on opiates. The study was terminated preterm due to a negative impact of EA on labor. Ramin et al., also found a 2-fold increase in the rate of cesarean sections in patients with EA [2]. However, the effect of EA observed in those studies was not confirmed in subsequent publications and the earlier studies were widely criticized [5,6,17,18,19]. The association between EA and the cesarean section rate is still a much debated issue [10,13].

In our study, the initial analysis revealed an increased rate of cesarean sections in the nulliparous women with EA as compared to controls (24.61% vs. 18.82%, $p < 0.0001$). Among the multiparous women, the rate of cesarean section was approximately 10% and was similar in the EA and the control group. However, when all possible factors were included in the stepwise logistic regression analysis, we ruled out the negative impact of EA on the incidence of cesarean sections. The most important risk factors were induction of labor and complications of labor. Thus, we can confirm that EA has no association with

Table II. Risk factors of operative delivery.

	OR	95% CI	p
Cesarean section:			
nulliparous women	5.82	4.00-8.46	<0.0001
-onset of labor: induction	3.42	2.72-4.29	<0.0001
-labor complications	1.95	1.57-2.43	<0.0001
-oxytocin administration	1.38	1.11-1.73	0.0045
-onset of labor: PROM	1.15	1.05-1.26	0.0034
-gestational age	1.07	1.04-1.10	<0.0001
-BMI	1.05	1.02-1.07	0.0001
-patient age			
Cesarean section:			
multiparous women	13.61	9.37-19.78	<0.0001
-VBAC	5.20	3.31-8.17	<0.0001
-labor complications	3.88	1.88-7.98	0.0002
-onset of labor: induction	1.95	1.27-2.98	0.0022
-onset of labor: PROM	1.08	1.04-1.13	0.0001
-patient age			
Forceps delivery:			
nulliparous women	3.06	2.28-4.09	<0.0001
-labor complications	1.57	1.16-2.13	0.0032
-oxytocin administration			
Forceps delivery:			
multiparous women	11.49	5.59-23.61	<0.0001
-labor complications	5.25	2.47-11.20	<0.0001
-epidural analgesia of labor	4.15	1.89-9.13	0.0004
-VBAC			

Only significant factors are presented

Table III. Neonatal outcome.

	nulliparous women					multiparous women				
	EA-0	EA-1	EA-0	EA-1	p	EA-0	EA-1	EA-0	EA-1	p
Birth weight (grams), mean, SD	3338	423	3391	412	0.0002	3425	442	3449	422	NS
1-minute Apgar, mean, SD	9.13	0.76	8.93	0.92	<0.0001	9.41	0.67	9.21	0.87	<0.0001
1-minute Apgar (groups), N, %										
- 8-10	1460	96.43	1794	93.53	0.0001	1566	98.93	550	95.16	<0.0001
- 4-7	54	3.57	122	6.36		16	1.01	27	4.67	
- 0-3	0	-	2	0.10		1	0.06	1	0.17	
5-minute Apgar, mean, SD	9.24	0.64	9.11	0.72	<0.0001	9.46	0.63	9.33	0.73	0.0008
5-minute Apgar (groups), N, %										
- 8-10	1500	99.07	1877	97.86	0.046	1574	99.43	567	98.10	0.0065
- 4-7	14	0.93	41	2.14		8	0.51	10	1.73	
- 0-3	0	-	0	-		1	0.06	1	0.17	
Cord arterial pH, mean, SD	7.29	0.08	7.26	0.09	<0.0001	7.32	0.08	7.30	0.08	<0.0001
pH <7.10 (N, %)	26	2.73	67	5.28	0.0043	13	1.37	10	2.55	NS
pH <7.15 (N, %)	56	5.89	149	11.74	<0.0001	29	3.06	24	6.12	0.0139

the increased incidence of cesarean sections, and the observed difference in the group of nulliparous women can be attributed either to additional risk factors or the well-known observation that EA is more frequently administered in patients with higher risk of obstetrical interventions, which has been a bias of all retrospective studies [10, 15, 20].

Another possible effect of EA on the mode of delivery is an increased rate of operative vaginal deliveries. In our hospital, only low or outlet forceps are applied (vacuum extractor is not used), therefore, the analysis was limited to forceps only. In the nulliparous group, rates of forceps deliveries were similar in the EA and the control groups, but in the multiparous group forceps deliveries were found to be significantly more common in the EA group as compared to controls (3.98% vs. 1.07%). That finding was confirmed by logistic regression, in which a significant, independent effect of EA on forceps delivery in multiparous women was still evident (OR=5.25). Interestingly and contrary to other studies [12], the difference was observed only among the multiparous women. In our opinion, the decision about the delivery mode (cesarean section or forceps delivery) depends strongly on the management protocol in the hospital and individual experience of the attending obstetrician. Also, randomized studies on EA were performed in the nineties and since that time, legal issues and a growing number of lawsuits have often prompted doctors to choose a cesarean section instead of the 'difficult' forceps delivery, especially in nulliparous women.

The second aim of our study was to evaluate the neonatal outcome after EA. In most of the published studies the neonatal outcome was assessed by the 5-minute Apgar score, another parameter taken into consideration was the percentage of neonates with acidosis defined as cord arterial pH below 7.20 or 7.15 [9]. Randomized studies did not find the association between EA and the 5-minute Apgar score [5,7,9]. Our study confirmed that there is no significant effect of EA on neonatal outcome assessed by the 5-minute Apgar score.

However, we found that 1-minute Apgar score was significantly lower in the EA group and there were also a higher percentage of neonates with 1-minute scores <7. Logistic

Table IV. Risk factors of poor neonatal outcome.

	OR	95% CI	P
Cord arterial pH <7.10			
- epidural analgesia	1.98	1.28-3.09	0.0023
- complications of labor	1.91	1.20-3.04	0.0065
- oxytocin administration	1.78	1.11-2.86	0.016
- onset of labor: PROM	1.66	1.08-2.55	0.022
Cord arterial pH <7.15			
- epidural analgesia	2.54	1.90-3.41	<0.0001
- complications of labor	2.32	1.68-3.19	<0.0001
- onset of labor: PROM	1.39	1.01-1.90	0.042
1-minute Apgar score <7			
- complications of labor	4.61	2.74-7.33	<0.0001
- epidural analgesia	4.55	2.35-8.80	<0.0001
- sex of the baby (male)	2.36	1.34-4.16	0.003
5-minute Apgar score <7			
- complications of labor	4.21	1.37-12.90	0.012

Only significant factors are presented

regression confirmed that EA is a significant risk factor for low 1-minute Apgar score (OR=4.55). In most of the studies, an improvement of the 1-minute Apgar score was observed in labors with EA [9, 7, 19]. In our opinion, the short-term effect of EA (i.e. lower 1-minute Apgar) observed in our study can be attributed to fentanyl used together with bupivacaine and different anesthetic modalities [21, 22].

There were also lower cord arterial pH values in the EA group. It was quite surprising, as EA is believed to have a positive effect on the umbilical cord pH [9]. Nonetheless, it has to be remembered that retrospective studies compared EA with systemic analgesia, usually administered in boluses or as continuous infusion [7,9]. In these studies, the observed negative effect of systemic analgesia was confirmed and described as dose dependent [12]. It is a well-known fact that umbilical artery pH is influenced by maternal hyperventilation, and in painful labor, without any form of analgesia, arterial pH usually increases

both, in maternal and fetal circulation, and therefore may mask fetal acidosis [22]. Thus, it is possible that direct comparison of women with EA with patients without any other pharmacological form of pain relief could bring the same results as observed in our study [23].

Conclusion

In summary, our study revealed that EA is an independent risk factor for operative vaginal delivery (forceps) in multiparous parturient women, but has no influence on the incidence of cesarean sections. EA also increases the risk of labor complications (variable/late decelerations), low 1-minute Apgar score, and low umbilical cord pH, but is not associated with low 5-minute Apgar score. Thus, this retrospective study confirms that EA is safe for both, mothers and babies. Our data and presented conclusions are of clinical importance and can be used in everyday clinical routine when counselling women who wish to use EA during labor.

Oświadczenie autorów:

1. Piotr Hincz - autor koncepcji i założeń pracy, przygotowanie manuskryptu i piśmiennictwa – autor zgłaszający i odpowiedzialny za manuskrypt.
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3. Mariusz Grzesiak – współautor tekstu pracy, współautor protokołu, zbieranie materiału.
4. Wojciech Horzelski – współautor protokołu, obliczenia statystyczne, analiza i interpretacja wyników.
5. Jan Wilczyński – ostateczna weryfikacja i akceptacja manuskryptu.

Źródło finansowania:

Praca nie była finansowana przez żadną instytucję naukowo-badawczą, stowarzyszenie ani inny podmiot, autorzy nie otrzymali żadnego grantu.

Konflikt interesów:

Autorzy nie zgłaszają konfliktu interesów oraz nie otrzymali żadnego wynagrodzenia związanego z powstawaniem pracy.

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