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Is Epidural Analgesia a Predictor of Low Newborn Apgar? A Hospital-Based Observational Study

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Abstract

A painful labor induces adverse maternal effects and increases fetal stress, yet evidence of lack of adverse effect of epidural anesthesia to the newborn Apgar score has been inconsistent.

The aim of this study was to investigate maternal, newborn and anesthetic factors associated with a low Apgar score, in particular the effect of modality and timing of epidural analgesia, since this may allow for an appropriate neonatal care planning.

We retrospectively analyzed the labor process of 1850 out of 2006 parturients/participants/deliveries at Centro Hospitalar do Porto in 2014.

Our primary outcome was newborn Apgar score at fifth minute post-partum. Statistical significance was set as a p value inferior to 0.05.

Seventy-one newborns (3.8%) had Apgar score below 7 and 1779 (96.2%) above or equal to 7 at fifth minute. None of the variables identified as maternal age, BMI, previous labor, gestational age, cervix dilation and newborn weight have proved to be different between groups of Apgar below and above 7 (t-test). There was also no significant difference between newborns with Apgar above or below 7 in what concerned initiation of labor, mode of epidural analgesia, previous cesarean, type of delivery and newborn sex (Chi-squared). Median hour of birth and median labor length since beginning of epidural analgesia were not different between the two groups of outcome (Kruskall Wallis). The multivariable model showed that the risk for low Apgar was not independently associated with any of the variables analyzed (Chi-squared Omnibus).

In our study, modality and timing of epidural analgesia was not a predictor of low neonate Apgar score at fifth minute postpartum. Nonetheless, we demonstrated that epidural analgesia of low concentration local anesthetics with opioids was non-inferior to the opioid-free variety.

Keywords: Low APGAR predictive factors; Epidural anesthesia and APGAR

Introduction

The Apgar score is a quick and standardized assessment tool for clinical evaluation of the newborn at birth. Developed in the 1950s by the anesthesiologist Dr. Virginia Apgar, it remains useful until present days as a survival prediction score at 28 days of life [1-3].

The score is calculated by assigning a value of zero to two points for each of the five indices of well-being: heart rate, respiratory effort, reflex irritability, muscle tone and color [3]. In practice, Apgar score should be assessed at 1st and 5th minute. A score more than or equal to 7 is considered normal, while if less than 4 is considered severely low, at the 5th minute [4]. Fifth minute Apgar seems a better predictor compared with 1st minute Apgar, as it already signifies newborn answer to resuscitation maneuvers. Fifth minute Apgar score has been shown to be a better predictor of neonatal outcome than umbilical-artery blood pH [2]. The predictive strength of the Apgar score seems to stand beyond the neonatal period as a low value at fifth minute has been associated with cognitive impairment measured by academic achievement in adolescence [5,6].

Previous studies reported several predictors of low apgar score including maternal age [7,8], parity [9,10] smoking [11-15], obesity [16-19] and delivery by C-section [20]. Newborn factors included gestational age [10,21-23], low birth weight [10,22] and breech presentation [20].

The influence of anesthetic factors on neonatal well-being has also been questioned. Epidural analgesia is nowadays considered the standard for labor analgesia, unless contraindicated. It should be offered to all pregnant women, and despite conflicting results on its impact on instrumental delivery incidence, a 2011 Cochrane review concluded it has no significant impact on the rates of cesarean section neither on the newborn outcome assessed by the Apgar score [24,25].

The moment of initiation of epidural analgesia has also been questioned as a potential factor to modify labor progression and

clinical maternal and neonatal outcomes. However, recent studies and a 2014 Cochrane review advocate that epidural analgesia should be initiated as soon as requested by the mother, without impact on Apgar score or cord pH [26-29].

Although Apgar score has been used worldwide for many years to evaluate early neonatal condition, it has been questioned if it is still relevant with all the advances in health-care service provision, neonatal resuscitation and infant care. Few data support its use as isolated criteria to predict mortality and morbidity, especially in preterm neonates [30].

Furthermore, Apgar score presents several limitations. The variables included depend on the newborn physiologic maturity, and no consistent data proved its applicability in preterm infants, so a false low Apgar score could be erroneously attributed to a healthy preterm infant; it could be affected by external factors as drugs, infections, trauma, and other non-controlled factors; and finally the evaluation of some of its components could be significantly subjective [30].

Moreover, neonatal resuscitation guidelines applied today are beyond the scope of the Apgar score and its prediction power. During neonatal resuscitation maneuvers, Apgar score should not be applied, as it was assigned for infants breathing spontaneously and not for neonates under resuscitation. In these newborns, score should be mentioned as "assisted", however no predictive power has been tested for this new concept [30,31].

Despite all this recent discussion around Apgar score, understanding its multiple limitations, it continues to present to date as a worldwide easy, standardized and immediate tool for neonatal assessment [30].

The aim of this study was to investigate if mode and timing of epidural labor analgesia is associated with a low Apgar score, since this may allow for an appropriate neonatal care planning.

Methods

Study design and sample

We performed a retrospective analysis of all labors occurred in our Obstetric Department in Centro Hospitalar do Porto, between 1st January and 31st December 2014. Centro Hospitalar do Porto is a grade-1 public hospital, offering all medical and surgical specialties, with the exception of cardiothoracic surgery.

Elective cesarean sections were excluded. To avoid possible bias, twins were excluded from the analysis. All labors that were converted into urgent cesareans due to fetal stress or other maternal related factors, as well as breech deliveries were included in the analysis. Women submitted to intravenous analgesia for labor were also excluded, as this regimen is only an option in parturient with specific pathologies that prevent the use of regional analgesia techniques. Maternal associated pathology and obstetric conditions (e.g. placenta previa, placental abruption, premature membrane rupture, cord prolapse) were not registered in the analyzed charts and these variables were not taken into account in this analysis. Importantly, all women with previous cesareans that were included in the analysis had only one previous cesarean, as the trial of scar is not performed in out maternity in women who had had 2 or more cesarean deliveries.

Data were collected in charts designed to register all steps of labor analgesia in our Department, fulfilled by an anesthesiologist attending or resident. All data were posteriorly transcripted and analyzed in Excel - Microsoft Windows®.

Variables

The following variables were registered: maternal age (years), maternal body mass index (BMI) (kg/m^2), parity(n), previous labor (n), gestational age (weeks), previous cesarean (yes or no), birth weight (g), beginning of labor (spontaneous or induced), cervix dilatation at beginning of analgesia (inferior or equal to 4 cm and superior to 4 cm), mode of epidural analgesia (Ropi+S: patient-controlled epidural analgesia (PCEA) with ropivacaine 0.1% and sufentanil 0.25 ug/mL (10 ml/h), with 5 mL bolus (lockout time: 30 min) Or the same mixture but in continuous infusion; Ropi 0.2%: continuous epidural infusion with high local anesthetic concentration, ropivacaine 0.2% (6-8 ml/h) and bolus given by the anesthesiologist as needed; others: including other choices of combination of local anesthetics and opioid or mixed options with more than one mode of analgesia), type of delivery (eutocic, dystocic, cesarean) delivery hour (hh:mm:ss) and labor length since beginning of analgesia (hh:mm:ss).

Outcome

Our primary outcome was to analyze predictive factors of newborn Apgar score below 7 at fifth minute post-partum.

Statistical analysis

Statistical analysis was performed using IBM SPSS statistics version 22.

Categorical variables are presented as frequency and percentage and continuous variables are presented as mean ± standard deviation (SD). For comparison between groups, the t-student´s test was used for continuous variables; chi-squared test was used for categorical variables. Levene's test was used to check the homogeneity of variances. Non parametric Kruskal-Wallis test was used to compare the delivery time of day, and duration of delivery. Logistic Regression was used to identify independent risk factors for low Apgar score (below 7). A p-value<0.05 was considered to be statistically significant.

Results

Two thousand and six labors were performed in our Department in 2014 (excluding elective cesareans). Twins, newborns from mothers who received intravenous analgesia and registers with missing outcome data were excluded (n=156).

One thousand eight hundred and fifty newborns were included in the analysis. Among those, 3.8% (n=71) had Apgar score below 7 and 1779 (96.2%) above or equal to 7 at fifth minute. 906 (48.4%) were female. Demographic data of study population is presented in Table 1.

Initiation of labor was spontaneous in 1282 (79.8%) patients and medically induced in 325 (20.2%).

Epidural analgesia was initiated early in labor with cervix dilation inferior to 4 cm in 239 (13.3%) women. Ropi+S were the analgesic option in 953 (49.1%) women, Ropi 0.2 in 587 (30.3%). Four hundred (20.6%) parturients received other treatments.

Delivery was eutocic in 1080 (58.4%) cases, dystocic in 568 (30.7%) from which 294 (26,7%) were vaginal instrumented and 274 (14.8%)

ended in cesarean section. Among the parturients, 152 (8.6%) had a previous cesarean.

	Media	APGAR<7	APGAR>7	P
Maternal age	30.06 ± 6.333	29.63 ± 7.539	30.06 ± 6.293	>0.05
BMI	29.2180 ± 4.44777	28.8294±4.301883	29.2058±4.42733	>0.05
Para	0.65 ± 1.265	0.57 ± 1.258	0.65 ± 1.260	>0.05
Idade gestacional	38.371 ± 2.4893	38.460 ± 2.1984	38.369 ± 2.4923	>0.05
Cervix dilation	4.63 ± 1.245	4.63 ± 1.112	4.63 ± 1.248	>0.05
Newborn weight	3166.67 ± 487.203	3111.96 ± 552.966	3173.31 ± 473.600	>0.05
APGAR - 5º minute	9.326 ± 1.4534			

Table 1: Demographic data.

The median hour of birth was 13h46m00s and the median labor length since beginning of epidural analgesia was 3h09m00s.

None of the variables identified as maternal age, BMI, previous labor, gestational age, cervix dilation and newborn weight have proved to be different between groups of Apgar below and above 7 (t-test p>0.05).

There was also no significant difference between newborns with Apgar above or below 7 in what concerned initiation of labor, mode of epidural analgesia, previous cesarean, type of delivery and newborn sex (Chi-squared p>0.05).

Median hour of birth and median labor length since beginning of epidural analgesia were not different between the two groups of outcome (Kruskall wallis p>0.05).

The multivariable model showed that the risk for low Apgar was not independently associated with any of the variables analyzed (Chi-squared Omnibus p>0.05) (Table 2).

Discussion

Identifying independent and modifiable predictors of low Apgar is warranted to improve medical care. With this observational study, we were not able to identify any factor independently associated with newborn Apgar score below 7.

In a recent study, low Apgar score at fifth minute has been shown to be strongly associated with the risk of neonatal and infant death [32], remaining an important indicator of neonatal well-being.

In our study the global prevalence of Apgar score below 7 at fifth minute postpartum of 3.8% was substantially higher than described in other European developed countries [29]. For this high value may have contributed the high heterogeneity of our sample. We did not exclude high-risk pregnancies, such as babies from diabetic mother, advanced maternal age and previous cesarean delivery, nor have we excluded premature neonates or with severe malformations, or babies born from emergent cesarean sections. Most studies do exclude these confounding variables and some only included nulliparous mother to achieve a more homogenous low-risk sample.

Variables		Co-efficient (β-values)	Standard Error (SE)	P-value	Odds Ratio (OR)	95% CI of odds ratios	
						Lower limit	Upper limit
IMC		0.008	0.042	0.850	1,008	0.928	1.095
Parity		-0.108	0.178	0.544	0.897	0.633	1.272
Gestational Age		0.009	0.073	0.905	1.009	0.874	1.165
Baby's weight		0.000	0.000	0.578	1.000	0.999	1.001
Baby's Gender	Female	0.092	0.351	0.792	1.097	0.551	2.183
	Male (RC)						
Beginning of Labor	Spontaneous	-0.817	0.548	0.136	0.442	0.151	1.294
	Induced (RC)						
Cervix dilation		0.231	0.557	0.679	1.260	0.422	3.756
Type of Labor	Eutocic	0.455	0.464	0.327	1.576	0.635	3.914
	Cesarean	-0.020	0.422	0.963	0.980	0.429	2.242
	Dystocic (RC)						
Type of epidural analgesia	PCEA	0.364	0.522	0.485	1.439	0.517	4.005
	Ropi 0.2	0.164	0.564	0.771	1.179	0.390	3.563
	Others (RC)						
Time of Labor		0.000	0.000	0.319	1.000	1.000	1.000
Duration of Anesthesia		0.000	0.000	0.521	1.000	1.000	1.000

Table 2: Results of logistic regression of risk factors for APGAR<7. *P<0.05; RC: Reference Category.

Advanced maternal age has been associated with poor neonatal outcomes [33], including low Apgar score. However, this has not been confirmed in other studies [5]. In our study, no relation was evident between maternal age and low Apgar score. This opposite result may have turned from the fact that the impact of this variable is significantly influenced by socioeconomic factors, namely level of education. It has been shown that a high level of education for women over 41 years-old mitigates the higher risk that these mother would present when compared to younger individuals, showing that the risk increment is probably multifactorial [33].

Obesity is one of the most concerning public health issues, and maternal overweight has been associated with adverse perinatal events and, neonatal death. In our study, we did not find a significant association between maternal obesity and low Apgar score. Nonetheless, most studies document an increased risk of low Apgar score in babies born from these parturients [34,35]. The precise mechanisms by which obesity negatively influences newborn outcome are not completely understood. As we have a high percentage of overweighed mothers in our sample, we would expect a significant

result as described in literature. This showed that probably other important non-controlled factors might have dissuaded the impact of maternal obesity in outcome.

The association of multiparty and poor neonatal outcome has not been consistent for decades. In some studies, the odds of a low Apgar score were higher for women with no previous live births compared to those without previous live births [2,28], but others did not share similar results. According to the literature, having more than 6 childbirths is associated with an increased prevalence of maternal and neonatal complications such as malpresentation, meconium-stained liquor, placenta previa and a low Apgar score, comparing with other multiparous women [36]. In our sample 1066 (58.5%) of women are nulliparous. We were not able to show any effect of parity on Apgar score and further studies seem necessary to better clarify this subject.

Nowadays, it is consensual that women who have had a previous cesarean section can safely go through a vaginal labor, as it is assumed that the risk for the mother and newborn are low [37]. Furthermore, there is no difference in neonatal outcome among those delivered by trial of scar (VBACS) compared to those who underwent emergency CS due to failed trial of scar. Despite this agreement, the risks are still higher than those associated with repeated elective cesareans [38]. In fact, babies born from women with one previous cesarean seem to be at increased risk of low Apgar score and perinatal death, when compared with neonates from mothers with history of one previous vaginal delivery [39]. In our study, history of previous cesarean was not an independent risk factor for low Apgar score. Further studies are needed for professionals to provide their patients with better counseling regarding the choice of the most appropriate route of delivery.

As it was previously stated, the Apgar score suffers the influence of many factors, one of the most important being the gestational age [30]. In our study, this variable was not a predictor of Apgar score inferior to 7 at fifth minute. This might reflect the high efficacy of the current neonatal resuscitation maneuvers immediately instituted after birth, and the generalized availability of invasive mechanical support in our hospital.

The Apgar score has been traditionally inversely related to neonate birth weight [40]. Nowadays, with the increase of maternal metabolic risk factors and neonatal overweight, it has been shown that the heaviest infants are also at risk for low apgar score, that can be six-fold higher than for infants with normal birth weight. Furthermore, this has been proved even after exclusion of mothers with pre-existing and gestational diabetes mellitus [28]. Also, newborn sex has been investigated as a risk factor for low Apgar score. In one study, girls had a reduced risk for low 5-minute Apgar score than boys, and the difference remained significant even after stratification for birth weight [28]. The predisposition for preterm delivery in male gestations has been implied it the low Apgar score that neonatal boys present. However, this phenomenon has been shown even when preterm boys are compared with preterm girls [41]. In our study neither birth weight nor newborn gender was associated with low Apgar score. In what concerns the sex issue in particular, the relevance of this matter may be more of the statistical and academic field than of the clinical setting interest.

Controversy has been following the indication for elective induction of labor before 41 weeks of gestation. It was previously stated that elective induction of labor at 37 weeks of pregnancy, without medical indication was associated with increased cesarean rates [42]. In fact, a recent systematic review concludes that only induction of labor at 41 weeks of gestation and beyond is associated with low risk of cesareans. In that review, thirteen studies contributed to show no difference if Apgar score at fifth minute between elective induction of labor and expectant management [43]. However, in another study, induction of labor at 37 to 40 weeks of gestation was associated with low incidence of cesarean section. The authors further demonstrated that this practice was not related with increased perinatal mortality or neonatal admission to intensive care unit, when compared with expectant management [44]. In our center, induction of labor is currently performed after 41 weeks of gestation, being anticipated only if there is a valid medical indication. In the present study, we found no difference in Apgar scores between inducted and spontaneous labors.

In this study we also investigated whether the hour of birth was associated with differences in Apgar scores. It has been reported an increased risk of being born with a low Apgar score during "non-office hours" and during the periods of general holiday [28]. Also, a Welsh study found that infant death was higher for babies delivered at night and during July and August [45]. Although we have not found any difference in neonatal Apgar score at any hour of the day, these results should alert the medical community to the importance and significance of maintaining an elevated and irreprehensible high standard of care, especially in such a sensitive field of clinical practice.

Impact of labor analgesia techniques on neonatal apgar score

A painful labor induces adverse maternal effects and increases fetal stress. For the mother, there will be an increase of circulating catecholamines, hyperventilation during contractions and hypoventilation during rest. Those mechanisms can induce deterioration in pH and base excess both in babies and mother, which can easily be attenuated by adequate analgesia [29].

Neuraxial analgesia is the actual gold standard for maternal pain relief during labor. However, controversy still follows the exact moment in labor when it should be performed, and its influence of maternal and neonatal outcomes.

Meta-analysis of the literature determined that the timing of neuraxial analgesia does not affect Apgar scores at first and fifth minutes [26]. Nonetheless, the definition of early epidural varies among studies, being typically defined as initiation of epidural analgesia when cervix dilation is inferior to 4 to 5 cm. According to the American Society of Anesthesiologists' guidelines for obstetric anesthesia; the insertion of a spinal or epidural catheter may precede the onset of labor or a patient's request for labor analgesia [46]. In our study, we considered an early epidural as that performed with cervix dilation inferior to 4 cm. As according to the literature, we found no influence on Apgar scores at fifth minute.

In the past few years, many studies have searched for evidence of the best epidural analgesic regimens for labor. Meta-analysis of the literature concluded that low concentrations of local anesthetics with opioids presents as one of the best options for labor analgesia, improving its quality and duration. It also allows for sparing of higher local anesthetics concentration, reducing adverse effects, such as motor block. Furthermore, the use of opioids in neuraxial infusions until the moment of birth does not increase fetal or neonatal side effects [46]. In our study, no difference was found between epidural infusion of high concentration of local anesthetics and lower concentrations with opioids.

Limitations

As a retrospective study there are inherent limitations in data collection that cannot be controlled. The ideal study design to better investigate predictive factors of low Apgar score in what concerns the impact of epidural analgesia would be a randomized controlled trial. However, these are very difficult, if not unethical, to perform, as epidural is a gold standard for labor analgesia nowadays. For most of the factors that can possibly affect neonatal Apgar score, such as maternal and biological factors, no randomization is ever possible.

We chose to work on a more comprehensive and heterogeneous sample, so we did not exclude from out study preterm infants, high-risk pregnancies or multiparous mothers. With this approach, we intended to have more generalizable results; however we cannot avoid a bias effect induced by this miscellaneous sample.

Also, the size or our sample, although high in absolute and reflecting only one year of clinical practice in our institution, may not be sufficient to adequately investigate such a rare event, as an Apgar score inferior to 7 at fifth minute. We chose not to include data from previous years, as obstetric and anesthetic practice has been changing, and misleading conclusion could arise from such analysis.

The impact of the socioeconomic factors may be of great importance on this issue and the study was not controlled for these variables.

Furthermore, maternal satisfaction is an important endpoint of quality and it is assessed in our institution in a subjective way. As we do not routinely use international validated instruments for this assessment, we did not use these data in our study. In a near future, we intend to establish an objective method of evaluation of this important outcome.

Conclusions

In our study we did not find any maternal, newborn, obstetric and anesthetic-related predictive factors for low neonate Apgar score at fifth minute postpartum. In particular, modality and timing of epidural analgesia was not a predictor of worse neonatal outcome.

Importantly, we were able to demonstrate the non-inferiority on neonatal Apgar score of epidural analgesia with infusion of low concentration local anesthetics with opioids until the moment of delivery, when compared to an opioid-free approach.

Controversy still surrounds which factors may be implicated in a worse fetal outcome, as assessed by Apgar score, as important methodological barriers hinder flawless investigations. Baring this challenges in mind, future studies are required to achieve conclusions to support changes in clinical practice towards improved neonatal well-being.

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