Journal of Anesthesia & Clinical Research

Costa et al., J Anesth Clin Res 2016, 7:10
DOI: 10.4172/2155-6148.1000672

Research Article OMICS International

Predictive Factors of Apgar Scores below 7 in Newborns: Can We Change the Route of Current Events?

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Received date: July 16, 2016; **Accepted date:** September 28, 2016; **Published date:** October 05, 2016

Abstract

Introduction: The Apgar score is a useful and immediate tool used in the assessment of newborns. The factors that influence its final score may be related with labor, mother or infant itself. The impact of epidural analgesia in the Apgar score is still controversial and not fully understood. One of the limitations while attributing this score is inter-observer variability.

Objectives: The objective of this study was to determine possible predictive risk factors of low Apgar scores at 5 minutes, namely the influence of maternal factors, labor and newborn characteristics, as well as the effect of different analgesic concentrations used in epidural analgesia.

Methods: This was a cross-sectional, institutional study conducted during two consecutive years-2014 and 2015, in Centro Materno Infantil do Norte, Portugal. Anesthesiology Department database was used to collect all the relevant information.

Results: 3085 deliveries were included in the study. A significant higher number of deliveries with lower Apgar scores in 2015 compared to 2014 were noticed; furthermore a similar result was found when a certain hospital team of obstetricians was on duty (Team 4), when compared with other similar teams.

Conclusion: Statistically significant differences on the Apgar indexes were found between delivery teams. Inter-observer variability on Apgar classification might explain these results. Low concentrations of local anesthetic combined with opioid in an initial moment of labor do not seem to influence Apgar scores at birth. No other factor was considered predictive of low Apgar scores.

Keywords: Apgar; Neonatal; Outcome; Variability; Analgesics; Opioids; Labor epidural analgesia

Background and Objectives

The first minutes after birth are crucial for newborn's adaptation to extra-uterine life. During this period, reliable and objective tools are required to assess its clinical state. Ever since it was described in the late fifties by Virginia Apgar, this score has been attributed virtually to every infant in western countries. It is an easy, immediate, standardized method of classification and a predictor of neonatal morbidity and mortality [1-4]. A total of seven points or more is considered normal while an Apgar score (AS) below three, combined with a low umbilical cord pH, is associated with perinatal asphyxia in children without malformations and increases the risk of cerebral paralysis 20-100 times compared to 5th minute AS scores equal or above seven (AS5th ≥ 7) [5-9]. Nevertheless, the vast majority of children with AS5th<7 will be healthy at birth and later in life [5,8].

However, despite its undeniable usefulness in infant's clinical primary appraisement, attributing an Apgar score is not free of limitations. Given the main parameters accounted for, the AS can be objective in some of them (heart rate, respiration), and subjective in others (muscle tone, irritability); thus, variability among observers needs to be noted. Recent studies tried to evaluate subjectivity between neonatologists using questionnaires and videos, and inconsistencies were evident regardless of newborns' clinical states [9-11].

Previously described factors associated with AS5th<7 include extremes in gestational age and birth weight, male sex and maternal obesity [1,3,4,12-14]. Additionally, maternal age, smoking habits, both low socioeconomic status and educational level, mode of delivery and previous caesarean appear linked to lower AS in some studies [1,3,15-17]. Prolongation of second stage of labor may justify the reason why nuliparity and epidural analgesia (EA) emerge as potential causes of AS5th<7 in several researches [1,3,13,16,18,19].

The influence epidural analgesia on sustaining the progression of labor and the possibility of increasing instrumental delivery are still controversial topics. Besides, the role played by EA in ambulation and maintenance of physiological bear down reflex is yet to be understood [20-24]. Some studies suggest that administering lower doses of local anesthetics along with an adjuvant opioid may bring benefits on neonatal outcome when compared with higher doses where such combination was not used [25], nonetheless, other studies advocate otherwise [26,27].

The main aim of this study was to investigate if there were any variables regarding the mother, the delivery, or the newborn that negatively influence AS, comparing analgesic technics that use high local anesthetic (LA) concentrations with those where low LA concentrations and an opioid where applied.

Methods

Study population, design and criteria

This was a cross-sectional, institutional study conducted in Centro Materno Infantil do Norte (CMIN), part of Centro Hospitalar do Porto (CHP), after approval by institutional ethics committee. CHP is a central, university and tertiary level hospital.

Data regarding deliveries that occurred between January 2014 and December 2015 was collected from the anesthesia records in patients' clinical files.

Information concerning maternal age, height, weight and parity was listed. Data included in clinical records on the birth comprised year, the obstetrician team that performed the delivery, type of delivery, time of delivery, beginning of labor, and duration of labor under EA was also collect.

Additionally, newborn's gestational age, sex, weight and 1st and 5th minute Apgar scores, were registered. Anesthesia administration features like technique (subarachnoid, intravenous or epidural), mode of administration (bolus, continuous perfusion or PCEA), used drugs, time of administration, and ambulation after EA and cervix dilatation when EA was instituted, were also listed into the database and subsequently collected for the study.

Given the similar statistical distribution, missing values on ambulation were considered as those where women did not ambulate.

To diminish the possibility of potential bias, all cesarean sections, twins deliveries, stillbirths and women submitted to intravenous or subarachnoid analgesia were not included in the analysis.

Concerning the classification of categorical variables previously mentioned, the obstetrician team of delivery was named from 1 to 8; the parity in primiparous or multiparous; the mode of delivery in eutocic or instrumental; the beginning of labor in spontaneous or induced; the duration of labor in <5 h, 5-10 h, 10-15 h and >15 h and the cervix dilatation in <3 cm or ≥ 3 cm.

The different types of anesthetics used were grouped according with concentration and combination with opioid. Regimens using 0.2% ropivacaine in either bolus or continuous perfusion (or combination of both) were considered as high concentrations. At the same time, both bolus administrations of 0.15% ropivacaine+5 μg sufentanil and either continuous perfusion or PCEA with 0.1% ropivacaine+0.25 μg/ml sufentanil (or a combination of the three) were considered as low concentrations. Other modes of administration when a combination of high and low doses was used were not the analyzed.

Continuous variables were represented using mean and standard deviation and analyzed with the Student's t-Test for independent samples. Categorical variables were presented in percentage and analyzed using Chi-Square test. After the individual analysis, a binary logistic regression was performed and both Odds Ratio and 95% Confidence Intervals were displayed. A $p<0.005$ was considered statistically relevant.

Statistical analysis was performed with SPSS Statistics, 22® (IBM®, EUA) for Windows software.

Results

3914 cases were analyzed. Apgar score data was present in 3737 deliveries. After exclusion criteria, stillbirths (n=17) and twins (n=76) were eliminated from the analysis. Simultaneously, cesarean sections (n=547) and women submitted to intravenous or subarachnoid analgesia were excluded (n=32 and n=28). Once these exclusions were made, the final sample included 3085 births, corresponding to 78.8% of the sample. Out of these, 104 newborns were classified AS5th<7, representing 3.4% of infants.

Mean women age included in the study was 30 years old, and their average BMI was 29.1 kg/m^2. The remaining anthropometric data (weight and height) are represented on Table 1, which also includes the newborns' mean gestational age (38.3 weeks) and their approximate mean weight (3158 g).

Parameters	AS5th<7		AS5th ≥ 7		Total		p
	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	
Women							
Age(years)	97	29.9 (7.6)	2817	29.9 (6.2)	2914	29.9 (6.3)	0.928
Weight (kg)	100	78.5 (13.3)	2845	77.4 (12.8)	2945	77.4 (12.8)	0.402
Height (cm)	97	162.8 (7.5)	2815	163.2 (6.2)	2912	163.2 (6.2)	0.562
BMI (kg/m^2)	95	29.7 (4.9)	2742	29.1 (4.5)	2837	29.1 (4.5)	0.204
Infants							
Gestational Age	92	38.2 (2.7)	2679	38.3 (2.5)	2771	38.3 (2.5)	0.676
Weight (g)	98	3131 (453.4)	2887	3159 (480.9)	2985	3158 (479.9)	0.574

Table 1: Descriptive data-Continuous Variables. Differences between groups analyzed with Student's t-Test.

Considering the categorical variables analyzed, 58.8% of women were primiparous; 51.1% of infants were males; 69% of deliveries were eutocic and 82.2% occurred spontaneously. Regarding analgesia, 95% of epidurals were administered when cervix dilation was ≥ 3 cm, 66% performed with low concentrations combined with opioid. 96.9% of women did not ambulate after EA and 53.3% of deliveries lasted between 1 and 5 hours under epidural analgesia (Table 2).

Parameters	AS5th<7		AS5th ≥ 7		Total		p
	n	%	n	%	n	%	
Parity							
Primiparous	59	58.4	1716	58.4	1775	58.8	0.937
Multiparous	42	41.6	1202	41.6	1244	41.2	
Infant's sex							
Male	52	50.5	1512	51.1	1564	51.1	0.897
Female	51	49.5	1445	48.9	1496	48.9	
Year							
2014	39	37.5	1535	51.5	1574	51	0.005***
2015	65	62.5	1446	48.5	1511	49	
Team							
Team 1	14	15.4	420	16.4	434	16.4	0.016***
Team 2	8	8.8	297	11.6	305	11.5	
Team 3	6	6.6	287	11.2	293	11.1	
Team 4	24	26.4	320	12.5	344	13	
Team 5	8	8.8	310	12.1	318	12	
Team 6	10	11	271	10.6	281	10.6	
Team 7	8	8.8	317	12.4	325	12.3	
Team 8	13	14.3	338	13.2	351	13.2	
Beginning of Labour							
Spontaneous	74	83.1	2059	82.3	2133	82.3	0.836
Induced	15	16.9	443	17.7	458	17.7	
Type of delivery							
Eutocic	73	73	2006	68.9	2079	69	0.382
Instrumented	27	27	906	31.1	933	31	
Dilatation							
<3 cm	6	7.2	104	4.1	110	4.2	0.165
≥ 3 cm	77	92.8	2423	95.9	2500	95.8	
Type of EA							
Low+opioid	64	71.1	1700	66.7	1764	66.6	0.387
High concentrations	26	28.9	847	33.3	873	33.4	
Ambulation							
No	99	95.2	2889	96.9	2988	96.9	0.323

Yes	5	4.8	92	3.1	97	3.1	
Time under EA							
<1 h	3	3.8	144	6.2	147	6.2	0.505
1-5 h	50	63.3	1237	53.5	1287	53.3	
5-10 h	18	22.8	669	28.9	687	28.7	
10-15 h	5	6.3	180	7.8	185	7.7	
≥ 15 h	3	3.8	81	3.5	84	3.5	
***Statistically significant difference							

Table 2: Descriptive data-Categorical Variables. Differences between groups analysed with Chi-square test.

The remaining categorical variables and their association with AS5th<7 are also displayed on Table 2. Both the obstetrician team that performs the delivery and year of delivery were found to be statistically significant (p=0.016 and p=0.005, respectively). Obstetrician team #4 showed a higher percentage of infants with AS5th<7 (26.4%), when compared with other teams (7-15%). Moreover, an overall higher percentage of deliveries with low Apgar scores were obtained in 2015 (62.6%) when compared with 2014 (37.5%).

No differences were found between groups in regarding maternal age, weight, height or BMI, nor in infant's gestational age or birth weight (Table 1).

Likewise, no statistically significant differences were found regarding parity, gender, beginning of labor, type of labor, cervix dilatation, type of analgesia, ambulation after neither EA nor time under EA (Table 2).

Regarding the fact that Obstetrician Team 4 showed lower Apgar scores when compared to other teams (Figure 1), this variable was grouped (Team 4), and compared with the remaining Teams. Table 3 shows the results of univariable and multivariable logistic regression analysis, between Team 4 and all the other Teams, along with other variables. On univariable method both the variable Team 4 and the variable 2015 presented higher association with AS5th<7 (OR=1.77 and 2.71; p=0.006 and p<0.001. respectively).

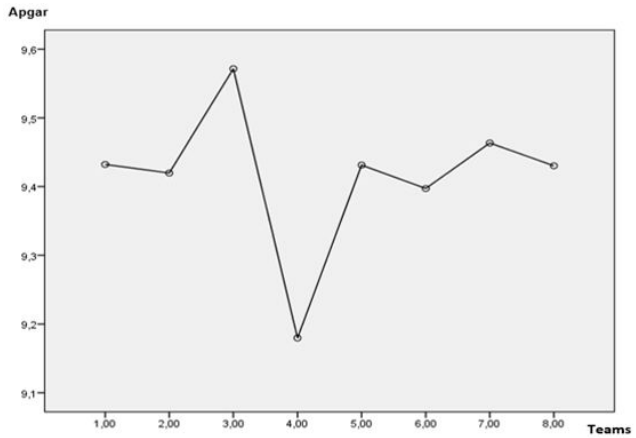

Figure 1: Teams' meandistributions of Apgar scores.

However, on multivariable regression, only Team 4 exhibit lower Apgar scores (OR=2.07 and p=0.043). According to this method, no other factor was considered statistically significant (Table 3).

Parameters	Univariable			Multivariable		
	OR	95 % C.I.	p	OR	95 % C.I.	p
Age (years)	1.01	0.97-1.03	0.928	0.99	0.95-1.05	0.959
Weight (kg)	1.01	0.99-1.02	0.402			
Height (cm)	0.99	0.96-1.02	0.526			
BMI (kg/m^2)	1.03	0.99-1.07	0.204	1.02	0.96-1.08	0.602
Primiparous *vs.* Multiparous	0.98	0.66-1.47	0.937	0.85	0.46-1.57	0.598
Gestational Age	0.98	0.91-1.06	0.676	1.08	0.94-1.24	0.304
Infant's weight (g)	1	0.99-1.00	0.574	1	0.99-1.00	0.071
Males *vs.* Females	0.97	0.66-1.44	0.897			

2015 *vs.* 2014	1.77	1.18-2.65	0.006*	1.52	0.84-2.75	0.164
Team 4 *vs.* Others	2.51	1.55-4.06	<0.001*	2.07	1.02-4.19	0.043**
Induced *vs.* Spontaneous	0.94	0.53-1.66	0.836			
Instrumented *vs.* Eutocic	0.82	0.52-1.28	0.383	0.94	0.49-1.81	0.856
<3cm *vs.* ≥ cm	1.82	0.77-4.26	0.171	1.9	0.65-5.56	0.281
High *vs.* Low+opioid	0.82	0.51-1.30	0.388	1.4	0.76-2.57	0.281
No ambulation *vs.* Yes	0.63	0.25-1.59	0.327	0.58	0.13-2.51	0.463
Time under EA (*vs.*<1h):						
1-5 h	1.94	0.60-6.30	0.27			
5-10 h	1.29	0.38-4.44	0.685			
10-15 h	1.33	0.31-5.67	0.697			
15 h	1.78	0.35-9.01	0.487			
*Statistically significant difference-univariable method, **Statistically significant difference-multivariable method.						

Table 3: Univariable and multivariable logistic regression.

Given that any cases with missing data in any of the variables were automatically excluded on multivariable regression, the sample included on this analysis consisted in 1489 cases, out of these; only 48 infants had low 5th minute Apgar scores.

In order to better elucidate what changed from 2014 to 2015 that could explain the differences found on Apgar scores, some variables were further analyzed between years (type of analgesia, cervix dilation when EA, duration of labor under EA, ambulation, type of labor and beginning of labor) (Table 4). Considering this analysis, only type of analgesia and cervix dilation differed significantly between years (p<0.001). Lower doses of analgesic combined with opioid and earlier epidurals were administered in 2015.

Parameters	2015		2014		Total		p
	n	%	n	%	n	%	
High concentrations	391	29.6	482	36.6	873	33.1	<0.001*
Low+opioid	929	70.4	835	63.4	1764	66.9	
≥ 3cm	1061	93.3	1439	97.7	2500	95.8	<0.001*
<3cm	76	6.7	34	2.3	110	4.2	
Eutocic	1026	69.5	1053	68.6	2079	69	0.609
Instrumented	451	30.5	482	31.4	933	31	
Spontaneous	1063	83.2	1070	81.5	2133	82.3	0.261
Induced	215	16.8	243	18.5	458	17.7	
<1 h	65	5.5	82	6.8	147	6.2	0.21
1-5 h	632	53.7	655	54	1287	53.8	
10-May	332	28.2	355	29.3	687	28.7	
15-Oct	99	8.4	86	7.1	185	7.7	
>15	49	4.2	35	2.9	84	3.5	
No ambulation	1462	96.8	1526	97	2988	96.9	0.758
Yes	49	3.2	48	3	97	3.1	
*Statistically significant difference							

Table 4: Descriptive data amongst years. Differences analysed with Chi-Square test.

In order to investigate if the causes of 2015's lower Apgar values rely on the bigger number of early EA or lower concentrations administered, year, type of analgesia and cervix dilation were sequentially introduced on a multivariable regression (Table 5). Differences on Apgar scores between years stopped being statistically significant (p=0.089).

Parameters	Univariable			Multivariable		
	OR	95% C.I.	p	OR	95% C.I.	p
2015 *vs.* 2014	1.77	1.18-2.65	0.006*	1.51	0.94-2.45	0.089
High *vs.* Low +opioid	0.82	0.51-1.30	0.388	1	0.60-1.67	0.955
<3cm *vs.* ≥ 3cm	1.82	0.77-4.26	0.171	1.86	0.78-4.43	0.162
*Statistically significant difference-univariable method, **Statistically significant difference-multivariable method.						

Table 5: Logistic regression-year, type of EA and cervix dilatation.

Discussion

Identifying modifiable risks factors that negatively influence Apgar scores is of major interest to improve perinatal medical care and clinical outcome.

The fact that even after exclusion of cesarean sections and twins, global prevalence of low Apgar scores found in this study represents 3.8% of deliveries is an important feature. This value is substantially higher than the ones described in studies performed by other developed European countries, some of which did not include these exclusion criteria [2,19].

On individual analysis, year and team that performed the delivery had a statistically significant impact on the occurrence of deliveries with AS5th<7 (p=0.006 and p<0.001, respectively), whereas on multivariate method, only Team 4 presented lower 5th minute Apgar scores (p=0.043). According to this regression, year of delivery did not exhibit a statistically significant result (p=0.164). Nonetheless, given that the sample was considerably reduced after exclusion of missing cases, caution is required when interpreting multivariable logistic regression.

When both years were compared in terms of obstetrical and anaesthetic variables surprisingly lower doses of analgesic combined with opioid and earlier epidurals (in terms of cervix dilatation) were administered in the year with lower Apgar scores (2015). These results do not match with what is postulated by recent literature that advises precocious administrations as soon as requested by women and lower doses of analgesics combined with opioid to reduce the amount of motor blockade. When those variables were inserted sequentially in the multivariate model, differences on Apgar scores between years were no longer relevant (p=0.089). Despite more precocious epidurals and lower concentrations were used since 2014, this result means they are not the probable cause of 2015's Apgar scores drop.

According to this analysis, other factors might be influencing Apgar scores in 2015 other than analgesic concentration and cervix dilation when EA was administered. However, detailed analysis of those factors is beyond the scope of this investigation

As already stated, the team that conducts the delivery remains statistically relevant after multivariable logistic regression (p=0.043). Many factors concerning infant's state or delivery itself can contribute to this result.

A possible explanation relies on inter-observer variability while attributing AS. Elements of the score (tone, color, reflex and irritability) can be subjective and partially dependent on infant's physiologic maturity [5]. Studies reveal that these differences are more prominent in preterm infants and are accentuated in those who require resuscitative measures [10,28]. This means that an otherwise healthy newborn, even without evidence of asphyxia, could have a lower Apgar score only due to prematurity, once tonus and irritability are both physiologically reduced on these individuals [29,30].

To circumvent this problem, a group of investigators created a new AS named Expanded-Apgar (Figure 2). According to the rules of this new Apgar, maximum score can be allocated to either a healthy term or preterm infant without any problems in postnatal adaptation, but also to infants receiving resuscitative or supportive interventions with an adequate response (good chest expansion during ventilation or pink color due to supplemental O_2). Additionally, a score is also attributed to the supportive interventions and resuscitative measures applied [31]. Some studies found a better correlation with perinatal asphyxia using expanded score compared to the conventional scoring system [32, 33].

Apgar Score

Gestational age_____weeks

Sign	0	1	2	1 minute	5 minute	10 minute	15 minute	20 minute
Color	Blue or Pale	Acrocyanotic	Completely Pink					
Heart rate	Absent	<100 minute	>100 minute					
Reflex irritability	No Response	Grimace	Cry or Active Withdrawal					
Muscle tone	Limp	Some Flexion	Active Motion					
Respiration	Absent	Weak Cry; Hypoventilation	Good, Crying					
			Total					

Comments:

Resuscitation

Minutes	1	5	10	15	20
Oxygen					
PPV/NCPAP					
ETT					
Chest Compressions					
Epinephrine					

Figure 2: Expanded-Apgar Score.

These modifications can enlighten dubious points of the score, but cannot avoid variability amongst observers. A recent study found possible solutions to unravel this problem. Significant differences on scores' consistency before and after a simple clarification of some parameters were found, especially on the points with higher degrees of variability–preterm or infants submitted to resuscitative measures [28].

The fact that no other maternal, newborn or delivery variables were related with low Apgar scores is another relevant result of this study.

Association between prematurity and low birth weight with inferior neonatal outcome is described in several publications [1,3,14,34]. Lack of lung maturation and the need for artificial ventilation can be pointed as explanations why premature infants receive lower Apgar scores. In those studies, attribution of a lower index just because of prematurity was not accounted for and possible inter-observer inconsistencies were discarded.

Despite the fact that maternal obesity has been linked to adverse perinatal events and mortality in several publications, such result was not found on this investigation [1,3,4,14]. The sample analyzed in this study had a high prevalence of obese mothers and the mean BMI was in pre-obesity range (29.9 kg/m^2). This result can be due to the multifactorial character of this variable. Maternal age, parity, socioeconomic status and educational level were already pointed as possible confounders.

Relation amongst extremes in maternal age and adverse neonatal events was already demonstrated, nevertheless, some controversial still subsists regarding this matter. Other socioeconomic factors such as a higher educational level in women older than 41 years old can mitigate the risk of possible neonatal complications [1,4,14,35-37].

Regarding parity, several bibliographic contradictions are found. Some studies report nuliparity as risk factor due to extension of second stage of labor, while others determine that having more than 6 live births increases the risk of breech delivery [34,38].

This study reveals limitations common to many retrospective studies. The initial sample was representative of two consecutive years, however, due to missing cases, after logistic regression the number of cases decreases to 1480. In order to avoid this problem, both an increase in the sample and a better anesthetic record keeping are required.

Conclusion

The relevance of this study relies on the fact that both the team that conducts the delivery (Team 4) and year 2015 presented significantly lower Apgar scores on individual analysis. This link was kept by the variable Team after multivariable logistic analysis, which indicates that it influences the occurrence of deliveries with lower Apgar scores regardless of other variables. The underlining motives of the differences obtained among teams are beyond the scope of this study.

The fact that a higher number of AS5th<7 was observed in 2015 does not seem to be related with increment in number of EA performed earlier and with lower anesthetic concentrations combined with opioid.

Further studies specifically designed to account for demographic, obstetric and analgesic differences among years are required to clarify this subject.

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