

Research Article

Variables that may Affect the Traditional Signs of Perinatal Asphyxia: Multicentric Study

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Abstract

Objective: To prove if certain variables related to labour affect the traditional signs of perinatal asphyxia (cardiotocography records, Apgar score and the umbilical artery pH).

Methodology: Observational, multicentric, longitudinal, analytical, cohort study in pregnant women at term admitted to the delivery room of Hospital Universitario Infanta Crsitina, Hospital Universitario de Fuenlabrada and Hospital Universitario Puerta de Hierro.

Results: Of all the variables under scrutiny, the onset of labour, parity, clamping the umbilical cord, gestational age, type of delivery, newborn weight and neonatal resuscitation have a significant relationship with the three signs of perinatal asphyxia.

Conclusions: We show a relationship between the three signs and some of the studied variables, therefore recommending to assess them in the perinatal asphyxia diagnosis.

Keywords: Cardiotocography records; Umbilical pH; Apgar score; Perinatal asphyxia

Introduction

Perinatal asphyxia has a multifactorial origin, which may be produced both during pregnancy or labour. It is defined as a gas exchange detrimental to the foetus, where the level of oxygen in the blood decreases and the levels of CO² increase. If the situation is maintained over time, it results in hypoxemia and, consequently, acidosis, which in the most severe cases might cause irreversible damage to the foetus [1-3]. There is not an agreement on the definition of perinatal asphyxia. Some of the criteria selected by different authors when defining it are [4]: low Apgar scores, acidosis in umbilical cord gas, pathological Cardiotocography (CTG) records, delay in spontaneous breathing, clinical signs of brain damage, etc. The most accepted definition is the one suggested by the American College of Obstetricians and Gynecologists (ACOG), the American Academy of Pediatrics (AAP) and the Committees on Maternal – Fetal Medicine and Fetus and Newborn which determined the 4 criteria that must occur so that the perinatal asphyxia can be considered the cause of neurological deficit (all of the following items must appear) [5-8]

intense metabolic or mixed acidaemia (pH<7.00), persistence of an Apgar score 0-3 over 5 minutes, immediate neonatal neurological sequelae and multi-organ system dysfunction in the immediate neonatal period. As it has already been mentioned, the neonatal and obstetric indicators, such as the Apgar score, the umbilical artery pH and the foetal monitoring or cardiotocography are essential when diagnosing neonatal asphyxia. Their results may be affected by certain variables, such as gestational age, parity, newborn weight, using epidural analgesia, the type of labour, how the labour begins, the type of neonatal resuscitation and cord clamping. The maternal age might modify the results of the perinatal asphyxia signs since it has been proven that pregnant women over 35 have further perinatal and obstetric complications [9]. The same thing happens with the gestational age at the moment of birth, when pathological CTGs tend to be more frequent in advancing gestational age, and the Apgar scores lower in preterm labour [10-12]. The onset of labour might be spontaneous or induced, following medical advice, when the benefits of terminating pregnancy for the mother and the foetus outweigh the potential benefits of continuing it. It leads to two different situations that might result in variations on the type of CTG as well as in the outcome of the other two tests. Using epidural analgesia has been related to foetal head malposition, temperature increase, prolonged labour, more frequent use of oxytocin, an increasing number of instrumental deliveries, higher pH values in the umbilical cord, a growing need of neonatal resuscitation and non-reassuring foetal heart rate patterns, which shows its influence in the signs of perinatal asphyxia [13]. Parity refers to the number of pregnancies a woman had that have resulted in the birth of an infant weighing over 500 g after 20 weeks of gestation. During the second stage of labour, the Spanish Society of Obstetrics and Gynaecology [14] reports that the standard duration in nulliparous women is up to 3 hours, and 2 hours in the case of multiparous. With epidural analgesia, these limits

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increase up to 4 hours for nulliparous and 3 for multiparous. By this token, parity might modify the types of CTG and the perinatal results, since the labour duration is usually different based on the number of previous pregnancies. One of the variables most likely to influence the perinatal results is the type of labour, because, depending on how the labour develops, newborns adapt better or worse to extrauterine life. Regarding the type of cardiotocography record, it would determine the type of labour, bearing in mind that non-reassuring records involve more instrumental deliveries and caesarean births. The moment of umbilical cord clamping after birth is important because this technique is not done uniformly by all the professionals. It can be done in two different ways: early clamping, immediately after birth; or delayed clamping, when the cord has stopped beating or 2 to 3 minutes after birth. Either technique might affect the pH values, since, in the case of delayed clamping, the umbilical circulation keeps on providing oxygen, which both expands the blood volume and corrects the pH. That is why, this variable should be taken into account [15-19]. The newborn weight at the moment of birth is considered normal between 2500 and 4000 grammas for term pregnancies. Foetuses with intrauterine growth restrictions might experience complications during the neonatal period, such as breathing difficulties, polycythemia, perinatal asphyxia, etc. Likewise, macrosomic foetuses are more likely to suffer obstetric trauma and intrapartum asphyxia [20]. Neonatal resuscitation is a set of therapeutic measures aimed at restoring and monitoring human vital signs. This variable would be the one closer to the three signs studied in here, because, depending on the neonatal results, newborns will require one type of resuscitation or another one in order to adapt to extrauterine life [21,22]. The objective of this study is to document how the above-mentioned variables can affect the results of the traditional perinatal asphyxia signs, so that, if their relationship is confirmed, they are taken into account in the diagnosis, since perinatal asphyxia is one of the most worrying problems for professionals specialising in obstetrics, paediatricians and society in general.

Methodology

An observational, multicentric, longitudinal, analytical, cohort study was conducted. Every cohort comprises a fraction of the population under study which has one of the registry types according to the record classification guidelines suggested by SEGO that take place in the second stage of labour to assess the results of the above-mentioned variables. It is a multicentric study carried out in three hospitals of the Community of Madrid. According to their activity, number of beds, technology, human resources, cases dealt with and portfolio of services, they are classified into low, medium or high complexity. Therefore, one hospital within each complexity range was selected: the *Hospital Puerta de Hierro* has high complexity; the *Hospital de Fuenlabrada*, medium complexity; and the *Hospital Infanta Cristina*, low complexity. The study population comprises pregnant women admitted to the delivery room of the three hospitals and who met the following inclusion criteria: pregnant women at term (>37 weeks until 42 weeks) with a minimum CTG period of 20 minutes during the second stage of labour. Women with one of the following conditions were not considered as candidates: records below 20 minutes of CTG, out-of-hospital deliveries, multiple pregnancies, preterm labours (<37 weeks), death before birth and pregnancies where data loss hampers comparison with the rest of the sample. The sample size was worked out based on the total number of deliveries in every hospital in 2014, as well as the pH of umbilical cord in newborns, with a 95% confidence level for a maximum permissible

error of 0.8%. Hence, it was considered that every hospital needed the following records:

- *Hospital Infanta Cristina* with a total of 1814 deliveries: 110 records.
- *Hospital de Fuenlabrada* with a total of 2297 deliveries: 139 records.
- *Hospital Puerta de Hierro* with a total of 3351 deliveries: 203 records.

The variables under study were collected the following way:

- Type of CTG (normal, suspicious and pathological, according to the classification by SEGO).
- Maternal age.
- Type of delivery (eutocic, instrumental and non-elective caesarean).
- Newborn weight.
- Apgar score.
- Type of neonatal resuscitation (0 or no resuscitation, I or removing secretions, II or applying indirect oxygen, III or providing intermittent positive pressure, IV or intubation, and V or administering medication).
- Spontaneous or induced onset of labour.
- Parity.
- Arterial pH of the umbilical cord.
- Weeks of gestation at the moment of birth.
- Use or lack of use of epidural analgesia.
- Umbilical cord clamping.
- Type of hospital.

The data obtained was stored in the electronic database Microsoft Excel 2010 and it was analysed later using the statistical package SPSS [23,24]. In all cases, it was analysed beforehand if the relationships existing among the variables depended on the type of hospital. A p-value equal to or less than 5% ($p \leq 0.05$) was considered significant.

Regarding the ethical considerations, the study complied with the International Legislation on Data Protection and the current Spanish legislation [25]. It was also approved by the Ethics and Research Committees of the three hospitals where it was implemented.

Results

The descriptive analysis of the sample provided us with a total of 452 CTGs, being 54.5% of them normal; 31.4%, suspicious; and 14.2%, pathological. The average maternal age was 31.3 (SD 5.5.) and the average weeks of gestation were 39.2 (SD 1.2.). Parity was 54.4% nulliparous, 35.6% primiparous, 6.9% secondiparous, 2.2% with three deliveries and 0.9% with four. Regarding the type of delivery, 69% were eutocic; 16.2%, instrumental; and 14.8%, caesarean. The umbilical cord was clamped early in 74.6% of the deliveries and was delayed in 25.4% of the cases. The onset of labour was spontaneous in 53.3% of women and induced in 46.7%. Pregnant women who opted for epidural analgesia were 90.5%, whereas 9.5% used another type of analgesia or no analgesia at all. As far as the newborns are concerned, their mean weight was 3260.7 grammes (SD 447.4). 81.2% did not

require any resuscitation manoeuvres; 11.7% needed resuscitation type I; 5.5% resuscitation type II; 0.9% resuscitation type III and 0.7% resuscitation type IV. The average umbilical artery pH was 7.26 (SD 0.09) and the Apgar scores at 1 minute after birth stated that 96.2% of newborns did not have neonatal depression at the moment of birth; 3.1% had moderate depression and 0.7% a severe one. At 5 minutes after birth, 99.6% of the newborns did not have neonatal depression and only 0.4% had moderate depression. The multivariate analysis revealed that maternal age and epidural analgesia do not have a statistically significant relationship with any of the three signs under study. However, the onset of labour is related to the CTG type, regardless of the type of hospital, showing that pregnant women with a normal CTG are 2.1 times more likely to start labour spontaneously, in contrast to pregnant women with a pathological CTG. The differences between the parity and cardiotocography records are significant, so for every additional delivery, it is 1.6 times more likely to have a normal CTG than a pathological or suspicious one, regardless of the hospital. The existing relationship between the type of umbilical cord clamping and the umbilical artery pH was also verified. It was noted that the average umbilical artery pH is higher in early clamping than in the delayed one, regardless of the type of hospital. However, the cord clamping and the type of CTG are related differently depending on the hospital, since the staff in the *Hospital Puerta de Hierro*, according to the protocol, only clamp the cord early, whereas in the *Hospital Infanta Cristina* and *Hospital de Fuenlabrada* it differs. In both places, pregnant women with suspicious or pathological CTGs frequently require early clamping, while those with a normal CTG usually undergo delayed clamping in *Hospital Infanta Cristina*, but the type of clamping is similar in the *Hospital de Fuenlabrada*. The gestational age has a statistically significant relationship with the umbilical artery pH, regardless of the type of hospital, so that, for every week over the gestational age, the average umbilical artery pH of the newborn decreases 0.1 units. The same thing happens with the type of CTG, representing this relationship in Figure 1. The three indicators under study have a statistically significant relationship with the type of labour, regardless of the hospital. Regarding the CTG, pregnant women with eutocic deliveries are 2.9 times more likely to show normal CTGs compared to those with caesarean births; however, no significant differences have been found between instrumental and caesarean deliveries. Likewise, the umbilical artery pH (Figure 2) and the Apgar test at one minute (Figure 3) and five minutes after birth (Figure 4) show a significant relationship. Significant differences were only found between the newborn weight and the type of CTG, regardless of the hospital. The average weight of children born of women with a normal CTG is higher than that of children born of women with a suspicious CTG. Among pregnant women with a pathological CTG, there were no differences regarding the other two types of cardiotocography records. Finally, there were statistically significant differences between neonatal resuscitation and the three signs of perinatal asphyxia, regardless of the hospital. As far as the umbilical artery pH is concerned, when advanced resuscitation manoeuvres are required, the average value of the umbilical cord pH decreases. In the Apgar test at one and five minutes after birth, the lower the score, the higher the type of neonatal resuscitation needed. The same applies to the types of CTG, declaring that among pregnant women with a suspicious CTG, it is 4.5 times more likely to need neonatal resuscitation in newborns, contrary to women with a normal CTG; and the offspring of women with pathological CTG are 5.3 times more likely to need neonatal resuscitation manoeuvres than those of pregnant women with a normal CTG.

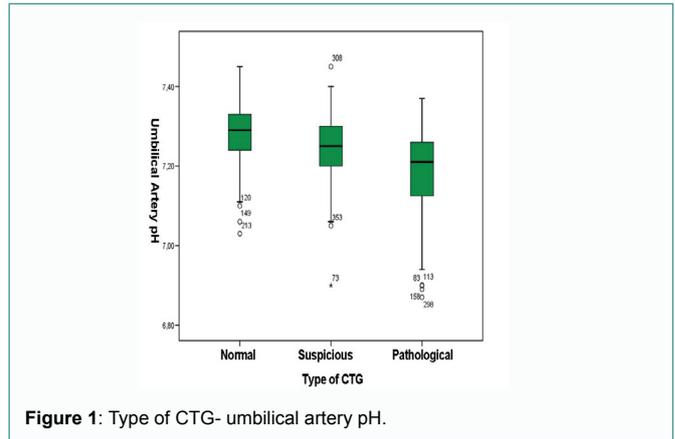


Figure 1: Type of CTG- umbilical artery pH.

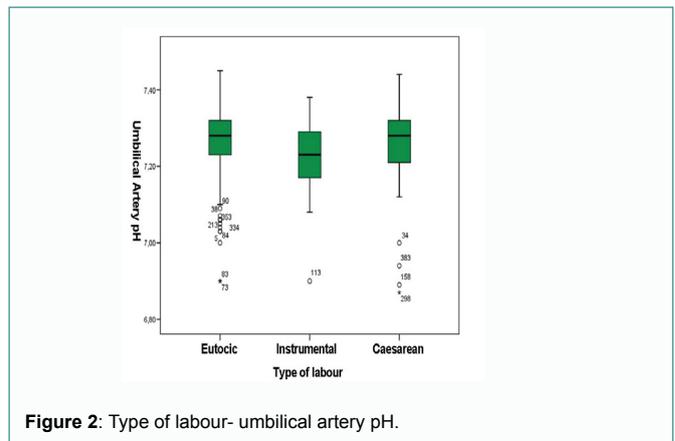


Figure 2: Type of labour- umbilical artery pH.

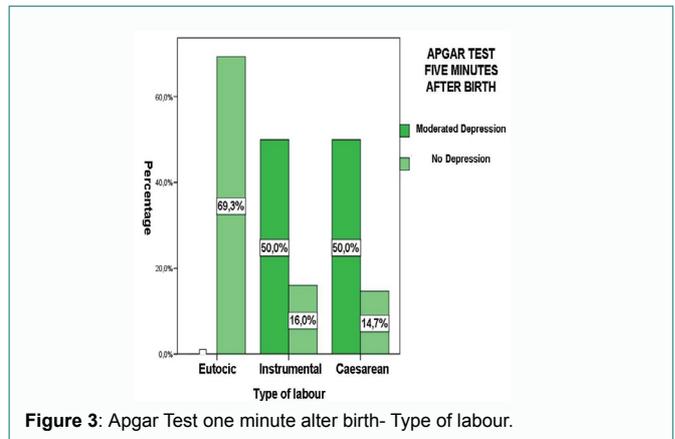


Figure 3: Apgar Test one minute alter birth- Type of labour.

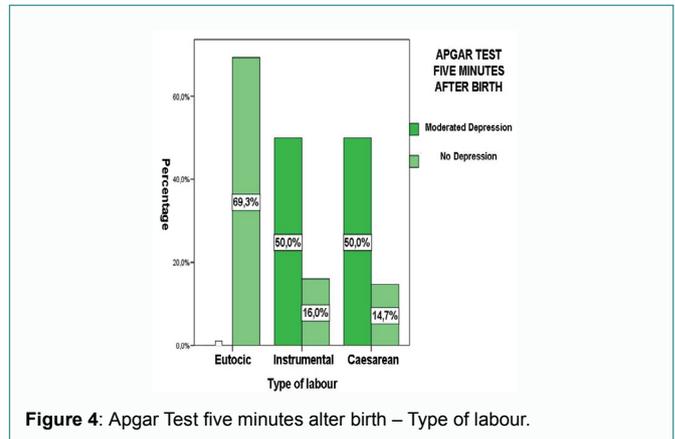


Figure 4: Apgar Test five minutes alter birth - Type of labour.

Discussion and Conclusions

Authors that compare maternal age with changes in the cardiocography records do not find a relationship between both variables [26,27]. That is also the case of our study, where we cannot prove a statistically significant relationship between the three types of record in the second stage of labour, the Apgar score and umbilical artery gases, and the maternal age at the moment of birth. This study proves the relationship between the gestational age and the changes in CTGs: the higher the gestational age (in pregnant women at term), the more frequent to find pathological records, as [28,29] state in their studies. On the contrary, there are other studies that find no correlation between these two variables [30]. Regarding the Apgar test, no significant differences were found based on the weeks of gestation. It might be due to the fact that in our sample we only gathered data on gestations at term. A decreasing Apgar score has been described only in preterm newborns, due to their immature central nervous system and musculoskeletal system, in accordance with [31] and [32], as well as in postterm infants, as shown by Salvo [33]. Unlike the reviewed studies [34], in here there is evidence of a relationship between the umbilical artery pH and the weeks of gestation, diminishing the average pH as the gestational age increases. At the outset, we thought that inducing labour might influence the results, since labour is usually longer and it might affect both the gas results and the Apgar scores, but neither in our study nor in the one by López [35] it has been observed. The opposite is true for the types of CTG, where pregnant women with a spontaneous onset of labour are more likely to have normal records, contrary to women who require induction. This result was predictable since induction requires an intervention in the natural labour process, which might lead to changes in the cardiocography records. Nowadays, epidural analgesia stands out among other methods for pain relief during labour, despite not being exempt of risks, as shown in this study, since in every hospital over 78% of the time they make use of the above-mentioned analgesia. There are no significant differences in the use of epidural analgesia in relation to the three variables under study, as it is stated in the articles by Johnson and Van Oudgaarden and Montague [37] and Paternoster and Micaglio and Tambuscia and Braccianti and Chiarenza [38]. The results of this study show that the number of offspring does not affect neither the umbilical artery pH nor the Apgar score. This is a predictable data because the foetal compromise during labour does not depend on maternal parity. However, it has been proven that the higher the number of deliveries, the more frequent it is to have a normal CTG, which might be due to the fact that, as parity increases, deliveries are usually faster. Other studies [39,40] prove that the average umbilical artery pH is higher in normal deliveries than in caesarean births, a predictable relationship since a large number of caesareans are carried out when suspecting a non-reassuring foetal status. However, in our study, this association is not observed, but there are statistically significant changes between the average pH in instrumental labours in contrast to caesareans, where it is lower. Regarding the types of CTG in the second stage of labour, normal CTGs are less common in instrumental and caesarean deliveries than in the eutocic ones, an understandable result because the worse the changes in the foetal heart rate during the second stage of labour, the more necessary to receive obstetric intervention, in agreement with the studies by González and Liu and Liu [41]. There is a lot of literature [42-44] on the relationship between instrumental deliveries and low Apgar scores, since, many times, instrumentation takes place because of acute foetal distress, growth retardation, retroplacental hematomas

and abnormal presentations among others, all of which are related to a low Apgar score at the moment of birth. This information is consistent with the results of the present study. Regarding the umbilical cord clamping compared to the type of labour, it is necessary to reflect on the fact that in caesarean and instrumental deliveries there is earlier clamping. In caesareans, it is always done that way to close the surgical wounds as soon as possible. In the case of instrumental deliveries, because they are done when complications arise during labour, newborns might show worse adaptation and need resuscitation manoeuvres immediately after birth. In agreement with the articles published by López, Lievaart and De Jong and Wilberg and Kallen and Olofsson, our study proves that the average umbilical artery pH is higher with early clamping than with the delayed one, although other studies [45,46] do not show differences in the mean arterial pH concerning the two types of clamping. Regarding the Apgar test at one minute and five minutes after birth, there is no correlation with the type of clamping, as it is the case in other studies. This is a surprising fact, because, generally, when a newborn finds it difficult to adapt to extrauterine life, it is normal to clamp the umbilical cord early, so that neonatal resuscitation manoeuvres can start as soon as possible. As regards the type of umbilical cord clamping and the CTG type, there are differences depending on the type of hospital. In the *Hospital Puerta de Hierro*, they only clamp the cord early because they use active management of the third stage of labour, so the amount of blood and the blood pressure is considerably higher than the physiological one, consequently early clamping is obligatory. This relationship shows that pregnant women with suspicious and pathological CTG frequently have the cord clamped early, whereas in those with a normal CTG, delayed clamping is usually more common. This is an expected result since, after a normal CTG, newborns usually adapt well to extrauterine life, which allows professionals to delay clamping until a few minutes after birth. In our study, the average weight of newborns was 3259 grammas, with no significant differences regarding the umbilical artery pH results. That is the expected outcome, since in the bibliography [47], there are only references concerning the newborns with growth retardation, where there is a higher rate of acidemia, hypoxemia and hypercapnia. The same thing happens with the Apgar score: there are no significant differences related to the weight of newborns, contrary to the findings of the literature, where children with low birth weight or exceptionally large are connected with lower Apgar scores. Nonetheless, there are differences between the newborn weight and the CTG types in the second stage of labour, holding that the average weight of newborns whose mothers had a normal CTG is higher than those with a suspicious CTG, as stated by Odendall and Bruce and Petrie and Davidson in their studies where fetuses with uterine growth retardation, due to their lower supplies, are more likely to develop modifications in CTGs. Perinatal asphyxia is the situation that most frequently requires neonatal cardiopulmonary resuscitation at the moment of birth. When analysing our results, we verify the relationship between neonatal resuscitation and CTGs. It is a logical result because in records with some changes in the foetal heart rate it is likely that newborns have difficulties adapting to extrauterine life and thus require resuscitation manoeuvres, contrary to López and Bucksee and Deka and Padmaja and Dadhwal and Bhatla, who reveal in their studies that there is not a relationship between changes in the Foetal Heart Rate and the need to do neonatal resuscitation. The same applies to the existing relationship between the neonatal resuscitation manoeuvres and the umbilical artery pH, a predictable result where the average pH decreases as more resuscitation manoeuvres are

required. It is normal since newborns with a lower pH probably adapt worse to extrauterine life in their first minutes. Regarding the Apgar scores and the need for neonatal resuscitation, we were expected to find statistically significant differences in their relationship, because the value at one minute after birth reflects the foetal adaptation to extrauterine life and the need of resuscitation manoeuvres, whereas at five minutes, the score shows how effective the above-mentioned measures have been. Among the limitations of the present study, there is the inter-observer variability when interpreting the cardiotocography records, since every hospital has a different observer. As stated by Nielsen and Stigsby and Nickelsen and Nim and Schwartz and Young, mean inter-observer agreement is between 20%-30%, and lower when dealing with pathological or potentially pathological records, as well as when deciding whether a foetus requires intervention [48]. The same applies to the average pH, which depends on the laboratory of each hospital, and the Apgar score, which depends on the person performing it. Based on the delivery, it will be assessed by the nurse/midwife or paediatrician who carries out the neonatal resuscitation. It is important to highlight the external validity of the study, thanks to the registration of a large number of cases and the fact that it is a multicentric study, although it has been proven that results do not depend on the centre. In further research, it would be interesting to include variables such as prematurity, other types of analgesia, maternal pathology (pre-eclampsia, gestational diabetes, epilepsy, intrauterine growth retardation, oligohydramnios...), maternal position in the second stage of labour, etc. in order to add further data to this line of investigation. According to what has been set out above, it can be concluded that the onset of labour, parity, cord clamping, gestational age, type of labour, newborn weight and the type of neonatal resuscitation are related to the neonatal and obstetric indicators under study.

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