Advanced cardiopulmonary resuscitation in the newborn: Are there data to justify adopting different protocols for the extremely premature neonate?

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International guidelines on neonatal resuscitation recommend initiation of chest compression, and then adrenaline, in the event of severe bradycardia that does not respond to appropriate ventilation with positive pressure. No separate criteria are established for the resuscitation of extremely premature neonates (EPN)[1]. Nonetheless, the fragility of these infants gives rise to the concern that the use of chest compression or adrenaline (advanced cardiopulmonary resuscitation, ACPR) might bring about an increase in the number of survivors with severe disabling neurological deficits.

Scarce data obtained at the end of the 1980s and in the early 1990s on the evolution of EPN who required ACPR in the delivery room drew a gloomy picture: among the 26 newborns weighing less than 751 g[2-4] or with under 29 weeks gestation at birth[5], there were no survivors free of severe neurological sequelae. However, from the mid-1990s on some studies began to show a different scenario. Survival following ACPR among neonates under 1,000 g increased to 53-78%[6-9], and neurological development was normal for more than half of those children who were followed up[7-9]. This improvement in morbidity and mortality for EPNs following ACPR was paralleled by the general tendency observed in this group of patients during the 1990s, probably reflecting more appropriate obstetric and neonatal management, including the use of prenatal steroids, surfactant and other technological advances, such as new ventilation strategies[10,11].

After 1995 the trend towards improved evolution for EPNs appeared to come to a halt[10], in part owing to the more severe condition of the patients at birth[12]. Has this also been the case among those requiring ACPR in the delivery room? In this issue of *Anales de Pediatría* two studies provide information gathered in the first years of the twenty-first century. Sánchez Torres *et al*[13] found no significant differences in survival at discharge between babies weighing less than 1,000 g requiring ACPR and those that did not (62.5% *vs.* 76.3%); only combined neurological morbidity analysis at discharge revealed significant differences between the groups (46.7% *vs.* 21.6%). In children weighing less than 1,251 g, Deulofeut *et al.*[14] found lower survival among those requiring ACPR (60% *vs.* 85%). However, among those weighing less than 1,001 g their results were comparable to the results of the Spanish study (59% *vs.* 77%). In terms of short-term neurological morbidity, significant differences were found in the group weighing 751 to 1,000 g only for III/IV degree intraventricular hemorrhaging (37% *vs.* 12%), and no differences in mortality or neuro-imaging were found in those weighing less than 751 g. Unfortunately, a high number of children were lost for follow-up, which questions the validity of extrapolating the findings to the population studied.

What results are to be expected for other age-groups of neonates who had ACPR? In a cohort of 26 full-term neonates, 69% survived, of whom 67% were normal at follow-up[9]. Following pediatric ACPR, survival at discharge hovered at around 50%, and more than 80% of babies suffered no worsening of their prior neurological state[15,16]. Among adults only 20-30% survive, of whom around 25% will suffer serious neurological sequelae[17,18]. Thus, the best results for survival are to be expected during the neonatal period —including EPN. Of all those patients resuscitated, symptom-free survival is expected by

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around 45 % of full-term newborns, 40 % of children, 30-45 % of EPNs, and somewhat less than 20 % of adults.

There are certain limitations that must be borne in mind when interpreting the available data. First, all the studies are retrospective. Partly for this reason we know very little about the characteristics of the event. We lack information about what caused the cardiopulmonary arrest, the reasons for undertaking ACPR or its duration, the means used for resuscitation (adrenaline dose, use of other drugs, volume expansion, etc.) or the monitoring of the event. All of these factors may have a significant effect on the results of resuscitation.

In older children and adults the cause that precipitates the arrest is an important prognostic factor[15,16]; it is probable that different etiologies might also affect EPNs in different ways[19]. Furthermore, animal experimental models show that the success of ACPR depends in part on the duration of the arrest prior to the beginning of CPR, its duration and the ability to establish a sufficient flow. The prognosis is better for children with severe bradycardia at the beginning of resuscitation than it is for those who are asystolic[15]. Among infants born at term, persistent asystolia lasting more than 10 minutes in spite of appropriate ACPR is associated with very poor prognosis[2,14]. Although it is likely that EPNs behave in a similar fashion, the particular physiological characteristics of this group may imply differences in times, drug doses and sequences that will have to be evaluated in animal models and prospective clinical studies.

Again, we lack knowledge concerning the attitudes and guidelines in the various centers. It has been noted that an active approach with respect to perinatal management of EPNs increases the survival rate without increasing morbidity at one year of age, while a restrictive attitude leads to greater mortality without reducing the morbidity of the survivors[20]. Differences in the management of these neonates during ACPR may have an influence on the results. Thus, strategies such as control of oxygenation (FiO_2), ventilation (CO_2), inspiratory (PIP) and expiratory (PEEP) pressures, and the monitoring of their effects (pulsoxymetry, capnography, arterial pressure) might help bring about a more favorable evolution. Finally, one of the greatest limitations is the scarcity of follow-up data, which, when available, often cover short time periods and show elevated losses.

The first minutes following delivery are probably not the best moment for deciding on the life or death of an EPN, due to the scarce information on each individual child. Occasionally the clinical data will show no real possibility of the patient responding to treatment (for example, persistent asystolia lasting at least ten minutes in spite of correct ACPR); in such cases discontinuation of CPR is justified. Nevertheless, in most instances it is only possible to establish a general prognosis in the form of percentages that make no provision for the individual characteristics of the resuscitated patient. In this situation of uncertainty, the sick child has the right to be treated if there exists a real hope of life without severe neurodevelopmental disability. Throughout the first days of life, the analysis of the clinical situation and neuroimaging studies will provide relevant information. Although establishing a neurological prognosis for an EPN who survives ACPR may be particularly difficult, in the event of extremely severe brain damage, a multidisciplinary approach in close relationship with the family of the newborn may counsel against maintaining extraordinary therapeutic measures.

Sánchez Torres *et al.* concluded that the increased level of mortality and the risk of severe brain damage traditionally associated with the use of ACPR in EPNs do not appear to be confirmed[13]. These data justify not using different criteria with ENPs when chest compression or the administration of adrenaline is indicated. In addition, they underline the need for (and difficulty of) clinical care that encompasses all the multiple factors at play: the very real presence of the neonate, his or her gestational age, the clinical evolution, the hopes of the parents and our capacity to establish a long-term prognosis. The exclusive use of risk percentages separated from this multivariate picture can become a form of prejudice, which, instead of offering the real infant a balanced treatment, fails to avoid extreme attitudes such as therapeutic overzealousness, or the discontinuation of life-sustaining treatments dictated by times decided by professionals, and not by the evolution of the pathology. More still, given the difficulties and the risk of long-term handicaps that the extremely premature neonate faces, it seems reductive to affirm as the only answer his or her death. It is incumbent upon the attending team and society as a whole to offer the best possible treatment, as well as to assist and support the newborn infant and his/her family.

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