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EDITORIAL

Good news for Spanish neonates!☆

¡Buenas noticias para los neonatos españoles!

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There is no longer any doubt that sick new-born, and in particular premature-born, infants suffer immediate, but also long-term negative effects as a result of the pain and stress they experience during their hospital stay. It was first shown by Anand and Hickey[1] in the late the 1980s that the outcome after cardiac surgery performed on new-borns was much improved if an opioid was added to the traditional anaesthesia with muscle-relaxant and nitrous oxide alone. This led to an awareness of the necessity to treat and prevent pain in new-borns in order to avoid medical complications, and also to a great number of studies in the subject of neonatal pain.

From this early research stems the knowledge of the acute consequences of untreated pain in new-born infants, namely cardiorespiratory, hormonal and metabolic changes, which are increasing the risk of cerebral haemorrhage and postoperative morbidity.[1]

Subsequent research in the following years also suggested that untreated neonatal pain could have long-term effects such as affected perception and processing of pain in these individuals, both in toddler- and child-years but also later in life, as adolescents and grown-ups.[2] For instance, boys who where circumcised showed more pain at vaccination 4–6 month later, and preterm born adolescents had more ''tender-points'' and lower pain threshold than their full-term peers.

A recent review by Valeri et al.[2] analysed 13 studies about long-term effects of neonatal pain. In infants born extremely preterm, greater numbers of painful procedures were associated with delayed postnatal growth, poor early neurodevelopment, high cortical activation, and altered brain development. In infants who were born very preterm, greater numbers of neonatal painful experiences were associated with a poor quality of cognitive and motor development at 1 year of age and changes in cortical rhythmicity and cortical thickness in children at 7 years of age. Also lower IQ at school age can be related to the number of painful procedures in infancy.

It can be argued that it is not possible – or meaningful – to differentiate between the effects of pain and those of other stressors, like the prematurity and illness themselves, or the separation from the mother. This is true, but the greatest impact of these recent studies is that they have quantified the amount of painful events the infant has been subjected to, and linked a higher number of this to a more negative outcome. They also clearly demonstrate, by using new neuroimaging technologies like fMRI, NIRS and DTI, that changes in the brain can be seen both on the functional and the structural side.[2]

An important focus of the research has always been to find methods to prevent and alleviate the pain. This can be done with environmental, behavioural and pharmacological interventions, in combination with adequate pain assessment.[3] International and regional/national guidelines give the same message in this aspect: as a base the neonates should be guaranteed an environment as stress-free as possible. This means reducing the light, the sound and the activity around the bed-space as much as possible. Painful procedures should be performed only when absolutely necessary and the infant should be helped into a position where it can

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contain and regulate itself, i.e. by being tucked, having the opportunity so suck and be given sweet solution in the mouth before any painful procedure. In addition to that, pharmacologic treatment should be given whenever deemed necessary by pain assessment or by knowledge of how painful the procedure is. It should be noted that sedative medication is not enough and may instead mask the ability to show pain signs.[3]

Mechanical ventilation is a common and severe kind of stressor in neonatal care. It includes both the placement of an endotracheal tube, suctioning of mucus through and around that tube and often forcing the infant to breathe with an involuntary rate, decided by the ventilator and not the infant itself. It is therefore important to provide ventilated infants with sufficient pain- and stress-relief. It has been suggested that a pre-emptive ''umbrella'' with opioid-infusion should be given to ventilated infants, to reduce the risk of neurological sequel. The large multi-centre NEOPAIN-trial, however, could not show this protecting effect. Instead there was a slightly increased risk of intra-ventricular haemorrhage, periventricular leucomalacia or neonatal death in the morphine-group.[4] Animal studies have demonstrated endotoxic effects of many analgesic drugs. For the present being, there is no rationale for recommending a general prescription of pre-emptive opioids for all ventilated infants. Pharmacological treatment should be given on individual indications, and the dose and duration should be re-evaluated on a regular base. Instead extra effort should be made to provide environmental and behavioural support and to perform scheduled pain assessments on infants receiving mechanical ventilation.

Despite this knowledge of the negative impact both of pain and of excessive analgesic use, several studies have shown that we perform many painful procedures every day in our neonatal intensive care units, often without sufficient pain relief. In the recent French EPPIPAIN-study the infants experienced on average 75 painful procedures during their NICU-stay, whereof almost 80% without specific analgesia.[5] The same situation is seen in other epidemiological studies from countries around the world. Things have been better over the last decades but we are still not there.

In the light of this, the NeoOpioid-project (www.neoopioid.eu) started, with the support of the European Commissions 7th framework programme for research, and coordinated by Karolinska Institutet, Stockholm, Sweden. A substantial part of NeoOpioid was the EUROPAIN-study which was conducted with an observational, longitudinal and prospective design (www.europainsurvey.eu). EUROPAIN collected data on over 6000 infants in 18 European countries, with the opportunity for countries and regions to do their own designated studies as part of the larger project. This was done in Spain by Alejandro Avila et al.[6], and the results from an almost total-investigation of Spanish NICUS are presented in this volume of Anales de Pediatria. The findings showed that almost half of the infants admitted to intensive care received sedative and/or analgesic medication. It was also obvious that there was significant variability between Spanish neonatal units in relation to the guidelines for sedation and analgesia. Though a much higher proportion is preferred, the results are similar to those from other studies. The findings can therefore serve as a base for developing national Spanish guidelines in accordance with international guidelines[3] and state-of-the-art knowledge about pain and its effects.[2] With this in mind, the present study must be seen as good – but not perfect – news for Spanish neonates. It also opens up for future collaborative research within the EUROPAIN-network. With Europe as a base, large trials and epidemiological studies can be performed, with better use of resources and faster accomplishment of goals for the study.

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