LETTER TO THE EDITOR

The Pandora’s Box of Neonatal Analgesia

We thank Dr Allegaert and colleagues for their interest in our report. We share with them the same trust in the great potentiality of remifentanil anesthesia in preterm babies. However, they pose a very challenging question: does the pharmacokinetic approach actually correspond to the best pharmacodynamic result? This question, which refers to the practice of administering anesthesia to preterm babies, allows us to open a "Pandora’s box" full of unknown issues.

Tolerance, hyperalgesia, and withdrawal—real risks in the use of opioids—are produced by mechanisms that remain poorly understood even in adults, suggesting that a receptorial deregulation in pain pathways could be responsible. Therefore, in our clinical practice, we are obliged to extrapolate the data, applying unclear knowledge to an as yet extremely immature physiology.

We suppose, and some evidence appears in the literature, that prolonged use of remifentanil may lead to tolerance, and high doses may also induce hyperalgesia in preterms. Rotation with other opioids in the postoperative period is not easy and burdened by several problems. Long-acting opioids, such as morphine and fentanyl, have a too variable effect in premature babies that can be increased by illness in which hepatic blood flow and intra-abdominal pressure are modified.

In these patients, the risk of underdosing or of a therapeutic gap is high, and long-term effects are probably worse than those induced by overdosing. It seems well established, in fact, that painful experiences in the early stage of life can affect the anatomical neurodevelopment, involving future behavioral and social—emotional outcome. Remifentanil appears to be the more appropriate choice because, as per reasons mentioned above, the more predictable and easy drug should be used.

We agree with our colleagues about the need for focused studies on controversies regarding pain assessment in neonates and preventive drugs. Incidentally, we are not allowed to use such drugs as ketamine that could help in the prevention of pain in premature babies less than 32 weeks because of the well-known possibility of inducing apoptosis in the central nervous system of extremely low birth weight infants.

In view of the above awaiting future insights, we remain convinced about our choice to use remifentanil as the sole opioid during and after major surgery in preterm babies, based on the possibility of an easy titration and contained risks, and ensuring hemodynamic stability and neuroprotection.

References


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