Pharmacokinetic profile and adverse effects occurrence of levobupivacaine during continuous caudal epidural analgesia of neonates

Abstract

The presented thesis aims to verify the safety of levobupivacaine (a local anesthetic, LVB) during long-term administration via caudal epidural analgesia (c-CELA) in neonates. At this age, pain management is complicated. C-CELA is effective in reducing opioid doses, thereby minimizing their adverse effects. The immaturity of metabolic pathways and reduced organ function raise concerns about the potential accumulation and systemic toxicity of local anesthetics (LAST). The literature sparse due to technical and ethical limitations. In the LEVON trial (part of this work), the laboratory technique was adjusted to ensure that blood sampling was safe. From the collected micro-samples (14 patients), the concentrations of total and free LVB were determined, and the results were compared. Higher levels of free LVB are responsible for LAST. No accumulation or signs of LAST were detected, only minor complications related to the use of c-CELA. Free LVB levels were safe and reached equilibrium 6th hour after start c-CELA. Total LVB reached a steady state between the 12th and 72nd hours, with highly variable concentrations (potentially toxic in three patients). The correlation between total and free concentrations was questionable or independent during the first 12 hours (i.e., the free fraction could not be inferred from the total concentration). A proven correlation was observed from the 36th hour, and a direct linear correlation was evident from the 72nd hour. The results suggest that c-CELA is safe in this age group. The more suitable laboratory marker for toxicity and accumulation is free LVB.

Keywords

Postoperative analgesia, neonate, continuous epidural analgesia, free levobupivacaine, total levobupivacaine