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SEIZURES AFTER CAUDAL EPIDURAL ANALGESIA – A CASE REPORT.

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ABSTRACT

Background: Neuroexcitation by opioids is a reported phenomenon. Many cases are reported to have seizures after the parenteral administration of opioids. Extradural administration of morphine causing seizures in the adult patient has been reported. In the current literature seizures caused by caudal morphine in the pediatric age group is nil.

Case presentation: We present a case of a 5-month-old baby who underwent open pyeloplasty under general and caudal anaesthesia. The baby was given 200 micrograms of preservative-free morphine as an additive for caudal analgesia. Around 5 hours after the caudal administration of morphine, the baby had seizures in the postoperative period. Despite antiepileptic treatment, the seizure recurred. All investigations including the neurosonogram were found to be normal. The time frame in which the seizures occurred was the first 12 hours of caudal morphine administration, which points towards neuroexcitation by morphine. And the baby needed no further antiepileptic prophylaxis when the action of morphine ceased.

Conclusion: Opioid administration in caudal space should be used cautiously and in a monitored environment only. Whenever possible avoid caudal morphine in daycare and minor cases.

Keywords: Caudal, morphine, seizures, postoperative period.

List of abbreviations
PICU – pediatric intensive care unit

INTRODUCTION

The caudal epidural block is one of the most common central neuraxial anaesthetic techniques used in children. Various additives are used to improve the duration of action and quality of analgesia of the caudal block (1). Although the addition of caudal opioids has been shown to provide sustained analgesia, their use can result in troublesome side effects, including nausea, vomiting, pruritis, urinary retention, and late respiratory depression. A rare complication of extradural morphine analgesia is seizures. There are limited case reports on seizures by caudal morphine (2). We report the case of a 5-month-old baby who developed clonic seizures 5 hours after caudal administration of morphine.

CASE PRESENTATION

A 5-month-old baby weighing 6 kg, was posted for elective open pyeloplasty. The baby was born full-term by vaginal delivery, he cried soon after birth. Antenatal scans had shown urinary tract dilatation but were not associated with any other congenital anomaly. After birth, within 5 months he developed severe left hydronephrosis due to pelvic ureteric junction obstruction, and left kidney function was found to be 38%. The baby had attained normal developmental milestones, for his age. There were no signs of growth retardation and he was vaccinated up to his age. Blood investigations including renal functions were within normal limits.

On the morning of surgery, the baby was premedicated with syrup Trichlorophos orally. After ensuring 4 hours of nil per mouth status of breastfeeding, he was taken to the operation theatre where inhalational induction was done using sevoflurane, oxygen, and nitrous oxide gas mixture, and an intravenous line was secured. The trachea was intubated after muscle relaxation with atracurium. Under all aseptic precautions, caudal space was identified in the left lateral position under general anaesthesia, using a 20G Tuohy needle and confirmed with 2 ml of normal saline, which was injected freely to caudal space after negative aspiration of blood or CSF. The epidural catheter was threaded through the Touhy needle and fixed at 8 cm on the skin. The epidural catheter was fixed. 5 ml of 0.2% of ropivacaine with 200 microgames of preservative-free morphine was given through the epidural catheter. The baby was positioned in the right lateral position and surgery proceeded through the left subcostal incision. Ringer lactate with added dextrose was the intravenous fluid given. Body temperature was well preserved throughout the surgery. The surgery took 3 hours and it was uneventful. After confirming adequate respiratory efforts, we extubated the baby on the table. The baby was wide awake, pain-free, and comfortable. The baby was shifted to the pediatric intensive care unit for monitoring. The epidural catheter was kept in situ for ropivacaine infusion in PICU.

After one hour of reaching PICU, the baby had clonic seizures of the left lower limb which lasted for 1 min. Seizures got subsided with intravenous lorazepam 0.6mg and oxygen was continued through a facemask. The baby was breathing adequately, saturation was maintained and the vitals were stable. He was observed for further seizures. Blood sugar, serum electrolytes – sodium, potassium, calcium, magnesium, arterial blood gases, and body temperature were checked. As all the investigations were found to be within normal limits, the baby was monitored for further events. After around 2 hours, the baby woke up from lorazepam sedation, was active, and playing. Around 1 hour later baby again had generalized seizures which lasted for one minute. A loading dose of levetiracetam was given. Neuro sonogram and EEG, Echocardiogram was taken, and found to be normal. As the baby had 2 episodes of seizures, we decided to hold further epidural analgesia. A maintenance dose of levetiracetam was added. Around one hour later the baby woke up, he was active and playful. He was breastfed and kept in PICU for overnight monitoring. He had no more episodes of seizures. The epidural catheter was removed the next morning, and the baby was shifted to the room. He did not require further antiepileptic medications. He was discharged home on the 4th day of surgery. The follow-up visit in urology OPD was found normal.

DISCUSSION

Many drugs including anaesthetics and analgesic agents have been reported to cause seizure-like activity in patients. (3,4). Epileptic seizures are the clinical manifestations of the excessive altered activity of neurons in the cerebral cortex. (5). Opioids are one group of anaesthetic agents that have been reported as causing “seizures” (3). Opioid administration may result in neuroexcitation, including nystagmus, extremity flexion, myoclonus, and seizures. (6). The neuroexcitatory phenomena produced by opioids are not fully studied. Changes in the central catecholamine concentrations in the dopaminergic pathways have been proposed as possible reasons. Other suggested mechanisms include an opioid-induced increase in glutamine-activated currents or an increase in the release of excitatory neurotransmitters. (7). In animal studies, EEG epileptic seizures have been reported in response to morphine, meperidine, fentanyl, and alfentanil (8-10).

Three explanations have been proposed to explain the nature of opioid-induced muscle activity. (4). The first explanation is that opioids may block cortical inhibitory pathways, thus allowing lower

centres to express excitability resulting in clonus. The second explanation suggests that opioid-induced motor activity represents a form of exaggerated muscle rigidity that may sometimes resemble seizures. Thirdly opioid-induced abnormal motor activity may represent subcortical seizures which are unlikely to be detected by surface EEG recordings. (11). The pro-seizure effect of morphine is mediated through selective stimulation of mu and kappa opiate receptors but not the activation of the delta receptor system. (12)

Animal investigations have suggested that the pro convulsant action of morphine is mediated through the 3-glucuronide morphine metabolite. (13) or nitric oxide produced by the constitutive nonspecific nitric oxide synthase (14). Multiple receptor systems are involved in triggering opioid-induced seizures, including opioid, adrenergic, and glutamatergic receptors (15-16), or by opioid antagonism of inhibitory gamma-aminobutyric acid (GABA) neurotransmission. (17).

Epileptic seizures have epileptiform discharges that usually, but not always can be recorded by a scalp electroencephalogram (EEG). Because not all forms of epileptic seizures are associated with electrical discharges that can be detected by scalp electrodes. Depth epidural electrodes may be needed for picking those discharges (7). Opioids may have the potential to induce epileptic seizure activity in nonepileptic patients in areas that are poorly accessible to monitoring with surface electrodes. (7). In our case, we used surface electrodes, which did not pick any epileptiform discharges in EEG.

The cervical and intracranial spread of morphine injected into the lumbar extradural space in man and have observed a time lag of approximately 6 hours for the drug to reach the brain stem and the fourth ventricle (21). The poor lipid solubility of morphine with its consequential restriction to CSF implies a high concentration of the free drug in the CNS. Thus, the high concentration and CNS irritating properties of morphine may have been enough to initiate a seizure in a patient whose trigger threshold was already low. The onset of seizures in our patient was around 5 hours from the time of administration. The time lag is consistent with the known kinetics of morphine in CSF (18,19). The baby had no more seizures when the duration of action of caudal morphine ceased.

Our patient did not have any factors known to induce postoperative seizures in the pediatric age group like hypoglycemia, hyperthermia, hypercarbia, acidosis, hypocalcemia, hyponatremia, and hypomagnesemia. The surgical stress, morphine-induced neuroexcitation, and low seizure threshold of the young age might have caused 2 episodes of seizures during the postoperative period. When used in large doses, the preservative sodium bisulfate used in morphine ampoules may cause myoclonus and seizures. (11). In our patient, we used preservative-free morphine in the caudal space. The biphasic effect of morphine was shown in studies (20,21) low dose morphine got an antiseizure effect and high-dose enhanced spontaneous seizure activity. The conditions under which morphine acts as a proconvulsant rather than an anticonvulsant agent are, as yet, not understood. (20) In our patient, we used 200 micro gm of morphine which is 33microgm per kg for the baby. The safe dose of caudal morphine is 30 to 60 micrograms per kg and our dose falls on the lower side.

We deferred the costly investigations like magnetic resonance imaging of the brain as the baby had no further seizures. Various side effects like sedation, respiratory depression, and pruritis were reported with caudal morphine in the pediatric age group. There are a few case reports about seizures caused by extradural morphine in adults (2), but not in the pediatric population. We report this case because of its rarity.

CONCLUSION

Whether morphine induces epileptic seizures in nonepileptic patients remains uncertain. But there is no reason to avoid its use in the general population provided usage in a monitored environment. Caution is indicated in patients with a documented history of epilepsy. The addition of morphine in the caudal block greatly improves the comfort of pediatric patients. We prefer caudal morphine in major cases with supraumbilical incisions where postoperative pain control is essential and try to avoid daycare surgeries. But to lessen, the unnecessary side effects of caudal morphine we suggest the usage of a lower dose and postoperative monitoring.

AUTHOR AGREEMENT AND CONTRIBUTIONS

Salini collected the entire data, wrote the case report, acquired the references, and verified and drafted the case report.

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Nil

DECLARATIONS

Consent has been obtained from the parents for publication of the case report.
No Competing interests in this case.

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