Research Article

Comparing the effect of adding dexmedetomidine versus dexamethasone to bupivacaine in pediatric caudal analgesia.

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Abstract

Background and aims: Different additives have been reported to prolong the duration of caudal anesthesia in pediatrics. Although these drugs successfully increased the duration of the block, many of them were associated with undesirable adverse effects. Dexmedetomidine is a potent as well as highly selective α2 adrenergic receptor agonist. Dexamethasone has been found to effectively increase the duration of an epidural block in adults, with no resulting side effects. Aim of the study: We aimed at comparing the effect of adding dexmedetomidine versus dexamethasone to bupivacaine in caudal block in pediatric patients undergoing infraumbilical operation. **Patients and Methods:** This was a prospective randomized double-blinded and controlled study that included 75 children, aged 2–8 years, American Society of Anesthesiologists physical status I and II, undergoing elective infraumbilical surgeries such as herniotomy, orchidopexy, hypospadias repair. Patients were randomized to receive a mixture of dexmedetomidine 0.2 mg/kg added to 1ml/kg bupivacaine 0.25% (group A), a 1ml/kg bupivacaine 0.25% (group B) or a mixture of dexamethasone 0.2 mg/kg added to 1 ml/kg bupivacaine 0.25% (group C). In the postoperative period, pain was assessed using a modified Objective Pain Scale (mOPS) score until 24 h after surgery and rescue analgesia (I.V paracetamol 15 mg/kg) was administered when mOPS score 4 or more was recorded. The primary outcome measure was the time to first analgesic requirement. The number of analgesic doses required in the first 24 h after surgery, residual motor block, sedation scores, intraoperative and postoperative hemodynamic variables, postoperative nausea and vomiting (PONV), and other adverse effects were recorded. **Results:** The demographics and hemodynamics were comparable among the studied groups. The dexmedetomidine group and dexamethasone group were less in pain score, prolong the duration of analgesia and less in number of patients required analgesia compared to control group. More sedation was present in the dexmedetomidine groups. Minor complications were recorded in the post-anesthesia care unit in group A. **Conclusions**: Both caudal dexmedetomidine and caudal dexamethasone added to local anesthetics are good alternatives in prolongation of postoperative analgesia compared to caudal local anesthetic alone.

Keywords: Dexmedetomidine, Bupivacaine, caudal anesthesia, dexamethasone, pediatric, postoperative analgesia.

Introduction

Caudal analgesia is the most commonly performed regional technique in the pediatric age group[1]. It is a safe and simple technique, with a high success rate, allowing early extubation, ambulation, decreased the risk of chest infections, decreased postoperative analgesic requirements, and early discharge[2]. The major drawback of a single-shot caudal block is its limited duration of action[3]. Various additive drugs have been combined with the local anesthetic injected into the caudal space in an attempt to prolong the duration of the block. In a recent survey of pediatric anesthesiologists in the UK, 76.7%. of them reported using caudal additives[4].

It is known that dexamethasone has anti-inflammatory and analgesic action by inhibition of transmission in nociceptive C - fibers and neural discharge. When given as an additive in peripheral nerve blocks or in intrathecal anesthesia, it prolongs the duration of anesthesia[5].

Dexmedetomidine is α2 agonists that interact with local anesthetics by possible mechanisms. First, by blocking Aδ and C fibers as a consequence of an increase in potassium conductance in isolated neurons, thus intensifying local anesthetic conduction block, second by causing local vasoconstriction, thus decreasing local anesthetic spread, and removal around neural structures. This effect is mediated by drug action on postsynaptic α2 receptors; spinal α2 adrenergic agonists may also induce analgesia by activating spinal cholinergic neurons resulting acetylcholine release[6].

Patients and Methods

After obtaining approval from Ethical Committee of Elminia University Hospital, a written informed consent was obtained from all the parents of the children who participated in this study. This prospective, randomized, double-blinded and controlled study was conducted in Anesthesiology and Intensive care department, El-Minia University Hospital, during the period from October 2016 to May 2017. The study involved 75 children of American Society of Anesthesiologists (ASA) physical status I and II, aged 2–8 years, undergoing elective infraumbilical surgeries such as herniotomy, orchidopexy, hypospadias repair.

Patients included were randomized before induction of anesthesia using computer-generated randomization numbers into three equal groups 25 patients in each and allocation was undertaken using sealed envelopes assignment by anesthetist not involved in clinical management or data collection and who also prepared the anesthetic mixtures and drew up them in similar coded sterilized bottles of equal volumes and supplied to the investigator for caudal block in a double blinded fashion. The protocol was opened after the study was completed. Maximum injected volume 20 ml

Group [A] Patients received a mixture of 2 µg/kg dexmedetomidine in 1 ml/kg bupivacaine 0.25%.

Group [B] Patients received 1 ml/kg bupivacaine 0.25% only.

Group [C] Patients received a mixture of 0.2 mg/kg dexamethasone in 1 ml/kg bupivacaine 0.25%.

We excluded patients who had allergy to drugs used, active infectious process at the site of injection, coagulopathy, neurological disorders (active CNS disease, convulsive disorders and, raised intracranial pressure), abnormalities of sacrum, vertebral column and spinal cord.

Careful medical history was taken. General physical examination and local examination to the back and sacrum were carried out. Routine investigations as CBC, coagulation profile and RBS were done.

All patients were fasted according to the ASA guidelines. Then, I.V cannula was inserted and patients were premedicated with atropine 0.02mg/ kg and ranitidine 1mg/kg. General anesthesia was induced using propfol 1mg/kg and atracuruime 0.5 mg/kg followed by the insertion of an appropriately sized endotracheal tube. Anesthesia was maintained using isoflurane 1–2% in 100% oxygen.

After securing ETT, patients were turned to the left lateral position, under complete aseptic conditions, with both legs flexed 90° at hip joints and knee joints. After sterilization to sacral area, a caudal blocks who was performed using a 22-G short beveled needle. Correct placement of the needle was confirmed by the characteristic ‘pop’ felt as the sacrococcygeal membrane was penetrated, followed by a positive ‘whoosh’ test using 0.5 ml of air. After negative aspiration for blood and CSF, the studied drugs were administered into caudal epidural space. During injection any swelling over the sacral area due to extravasations of the drug in soft tissues was ruled out by careful inspection and palpation.

Surgery was started 10-15 min after the block was performed. At the end of surgery, inhalational anesthesia was discontinued and muscle paralysis was reversed by neostigmine (50 mcg/kg) with atropine (0.01mg/kg), then patients were extubated

when awake. After extubation, patients were admitted to post anesthetic care unit (PACU) for 2 hours until complete recovery. If patient complains of pain, I.V paracetamol (15 mg/kg) were given. Any increase in heart rate or blood pressure by more than 20 % of baseline value, and these patients were received fentanyl 1mcg/kg intra-operatively.

Heart rate (HR), systolic blood pressure, diastolic blood pressure, mean arterial blood pressure (MAP), and arterial oxygen saturation (SpO_2) were recorded before induction and then every 5, 10, 15, 20, 30, 45, 60 and every 15 min after induction of anesthesia till the end of surgery. During the intraoperative period, adequacy of analgesia was assessed by hemodynamic stability. An increase of more than 20% in HR or MAP was considered an indication of inadequate analgesia and managed by a bolus dose of intravenous fentanyl 1 mcg/kg, followed by further doses of fentanyl (0.5 mcg/kg) if needed.

After recovery and when they were able to maintain a patent airway, the patients were transferred to the post anesthesia care unit (PACU), where they remained for at least 2 h before being transferred to the ward. Hemodynamic variables (MAP and HR) were recorded on admission to PACU and then every 30 min till the patient was discharged to the ward. Postoperative pain was assessed using a modified Objective Pain Score (mOPS) every 30 min for the first 2 h and at 4, 6, 8, 10, 12, 18, and 24 h postoperatively. This score includes five criteria: crying, agitation, movement, posture, and localization of pain. Each criterion is assigned a score from 0 to 2, with 2 being the worst, to yield a possible total score of 0–10[7]. If the mOPS score was more(³4), rescue analgesia in the form of paracetamol 15 mg/kg I.V was administered. Further boluses of paracetamol 15 mg/kg were administered I.V every 4h if required. Residual motor block and sedation level were also assessed at 30 min and at 1, 2, 4, 6, 8 and 10 h after surgery. Motor block was assessed using a modified Bromage scale consisting of four points [0 = full motor strength (flexion of knees and feet), 1 = flexion of knees, 2 = little movement of feet only, 3 = no movement of knees or feet][8]. The sedation score was assessed using a fourpoint scale (1, alert and aware; 2, asleep, arousable by verbal contact; 3, asleep, arousable by physical contact; and 4, asleep, not arousable)[9]

Adverse effects: all adverse events associated with induction or during maintenance of anesthesia or during recovery including nausea or vomiting. If needed, PONV were treated by ondansetron 0.1 mg/kg intravenous. Any other complications including itching, urine retention (no voiding of urine for 6h postoperative), respiratory depression (respiratory rate≤ 10 breaths/min), or bradycardia (HR decreased >20% of baseline), hypotension (MAP decreased >20% of baseline) and desaturation were recorded.

Statistical analysis

A sample size of 25 patients in each group was determined to provide 95% power for two-tail‘t’ test at the level of 5% significance using G Power 3.19.2 software. We calculated that 25 patients in each group will be needed to detect an intergroup difference in the average time to first rescue analgesic of at least 20% (0.05, =B.0).

Results

This study included 75 children of ASA physical status I and II, aged between 2–8 years divided into three groups, 25 patients in each group.

Seven patients were excluded from the study (two patients from group A, two patient from group B and three patients from group C), as caudal analgesia was inadequate as indicated by increase in heart rate or blood pressure by more than 20 % of baseline value, and these patients were received fentanyl 1mcg/kg intra-operatively and replaced by other patients.

The studied groups were found to be comparable with respect to Patient characteristics such as age, sex, weight, ASA classification and duration and type of surgery.

The duration of analgesia was significantly higher group A (15.2±3.4h) compared to

group B (5±1.8h) and group C (11.4±3.8h) as shown in figure (1). Group A required significantly fewer doses of I.V paracetamol doses than group B and C in the first 24 h after surgery as shown in table (1). The MOPS was statistically significant lower in group A than group B and C. Once MOPS reach ≥4 analgesia in the form of I.V paracetamol (15 mg/kg) was given as shown in figure (2).

The studied groups showed that sedation score was statistically significant higher in group A than group B and C as shown in figure (3) and modified bromage scale was statistically significant lower in group A than group B and C as shown in figure (4).

Hemodynamic variables recorded Intraoperatively and Postoperatively in the PACU were statistically significant difference between baseline value and all subsequent values mainly in group A. Nausea and vomiting occurred in 3 patients in group A (12%), 1n 10 patients in group B (40%), and in 5 of patients in group C (20%), no significant difference between the studied groups. Other complications in the form of bradycardia, hypotension and desaturation occurred in 2 patients in group A with no significant difference between the studied groups. No other complication occurred during the study.

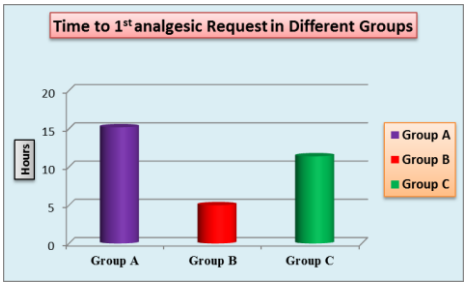

Fig. (1):- Duration of analgesia and Number of paracetamol doses in different groups data presented as mean± SD.

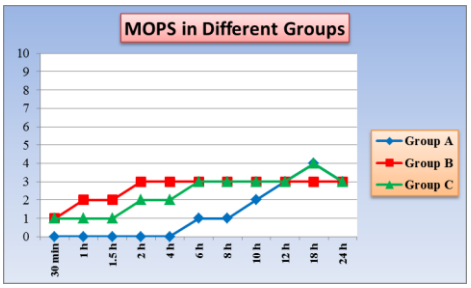

Fig. (2): Modified objective pain score (MOPS) in different groups data presented as mean± SD.

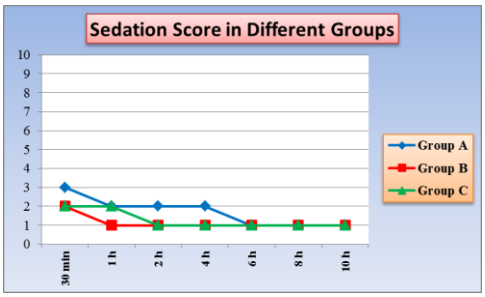

Figure (3): Sedation score in different groups data presented as mean± SD.

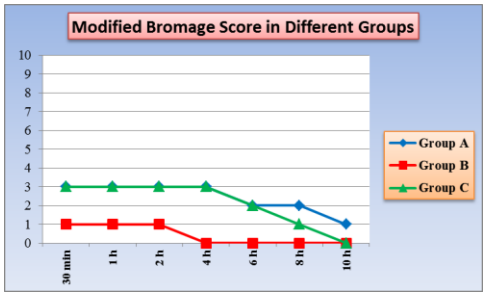

Figure (4): Modified Bromage score in different groups data presented as mean± SD.

Discussion

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. Children with significant postoperative pain may demonstrate anxiety, fright, insomnia which often exacerbate their pain perception rendering the postoperative recovery period an unpleasant and traumatic experience. Other deleterious consequences of pain include sleep disturbance, nausea, vomiting, prolonged hospital stay and parental dissatisfaction[10].

Various additives have been tried successfully till now to increase the duration of caudal block including epine-

phrine, clonidine, dexmedetomidine, neostigmine, ketamine, morphine, tramadol and fentanyl. However they do have their share of undesirable side effects[11].

Dexmedetomidine is highly selective α2 adrenoreceptor agonist, the analgesic action of intrathecal or epidural dexmedetomidine results from direct stimulation of pre- and post-synaptic α2 adrenoreceptors in the dorsal grey matter of spinal cord thereby inhibiting the release of nociceptive neurotransmitters. This effect correlates with the concentration of dexmedetomidine in the cerebrospinal fluid but not that in the plasma[12].

Dexamethasone is a well-known corticosteroid with strong anti- inflammatory effects, started to be investigated for its analgesic efficacy. Epidurally administered dexamethasone could reduce the incidence and severity of postoperative pain in adults[13].

It is difficult to differentiate responses to pain from emergence agitation, especially in the preschool children. For this reason, we chose to use isoflurane for maintenance of anesthesia as opposed to sevoflurane to avoid the higher incidence of emergence agitation reported with sevoflurane maintenance anesthesia[14].

The results of current study demonstrated that caudal injection of dexmedetomidine 2 mcg/ kg with bupivacaine (0.25%) significantly resulted in decrease in heart rate and blood pressure intraoperatively and significantly prolonged the mean duration of postoperative analgesia and lower analgesic consumption compared with caudal injection of a mixture of dexamethasone 0.2 mg with bupivacaine (0.25%) and with caudal injection of plain bupivacaine (0.25). Also, affecting motor scale up to 10 hours postoperatively and sedation scale up to 8 hours postoperatively more on adding dexmedetomedine to caudal bupivacaine, without any statistically significance in complications.

In agree with the results of this study, Goyal et al., (2016)[6] who used 1 mcg/kg dexmedetomidine on 100 children undergoing elective infraumbilical surgeries. The mean duration of postoperative caudal analgesia in patients in group bupivacaine only was 4.33±0.98h while in patients of group dexmedetomidine + bupivacaine this duration was 9.88±0.90h, without respiratory depression, hypotension or bradycardia. In current study the mean duration of postoperative caudal analgesia in patients in group dexmedetomidine + bupivacaine was 15.2±3.4h, but there was respiratory depression and desaturation in 2 patients postoperative and treated with oxygen only, hypotension and bradycardia in 2 patients intraoperative and treated with atropine, ephedrine and I.V fluids (without any statistically significant difference). It may be due to doubling the dose of dexmedetomidine (1mcg/kg vs 2mcg/kg).

Al-Zaben et al., (2015)[15] who concluded that, a 1 μg/kg dose of caudal dexmedetomidine achieved comparable prolongation of postoperative analgesia to 2 μg/kg dose, with shorter duration of postoperative sedation and lower incidence of other side effects. The duration of postoperative analgesia of 2 μg/kg dose of caudal dexmedetomidine is comparable with the results of current study, but less in sedation score than current study.

Supporting the results of the present study was the results of El-Feky and Abd El Aziz, (2015)[16] who found that the demographics and hemodynamics were comparable among the studied groups. Dexmedetomidine and dexamethasone groups had lower in pain score, prolonged duration of analgesia and lower in number of patients required analgesia compared to control and fentanyl groups. More sedation was present in the fentanyl and dexmedetomidine groups. The fentanyl group showed significant increase in the adverse effect incidence.

In agree with the results of the current study, Choudhary et al., (2016)[17] who used 0.1 mg/kg dexamethasone added for caudal analgesia. They concluded that pain scores measured at 1, 2, 4, and 6 h post-operative, were lower in dexamethasone group as compared to control group. Mean duration of analgesia in control group was 248.4 ±

54.1 min and in dexamethasone group was 478.046±104.57min with P = 0.001. Rescue analgesic requirement was more in control group as compared to dexamethasone group. Adverse effects after surgery were comparable between the two groups. The duration of analgesia was comparable to current study.

The Current study has confirmed the findings of aprevious study performed by Girgis, (2014)[18]. Who used 0.2 mg/kg dexamethasone added for caudal analgesia. He found that dexamethasone group showed a significantly longer time to first analgesic requirement than control group (11.2±3.5 vs. 7.1±3.2 h, P<0.001). The number of oral paracetamol doses required in the first 24 h was significantly less in dexamethasone group. Dexamethasone group showed lower MOPS scores than control group. Modified Bromage scale scores, sedation scores, as well as intra-operative and postoperative hemodynamic variables were comparable in the two groups. Dexamethasone group showed significantly fewer incidences of PONV compared with control group.

Conclusion

The addition of dexmedetomidine 2 μg/kg to bupivacaine 2.5 mg/ml (1 ml/kg) improves post-operative analgesia, decreases analgesic consumption with clinically accepted sedation and less hemodynamic instability compared with the addition of decamethasone 0.2 mg/kg to bupivacaine 2.5 mg/ml (1 ml/kg) administered caudally in infraumbilical surgeries.

Conflict of Interest

No relations with people or organization as regards this work and no any type of financial support.

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