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OVERVIEW OF SAFETY AND EFFICACY OF CLONIDINE/ BUPIVACAINE COMBINATION IN CAUDAL BLOCK

[1]Shaher Salem Hadi Alqahtani, [2]Taher Mohammed Yaseen Bantan, [3]SHADI Shareef M ALAMMRI, [4]RAED HAMAD ALSULAMI, [5]Anas Saeed Saeed Alghamdi, [6]Albaraa Saeed Alradaddi, [7]Abdulaziz Ibrahim Abdulaziz Alsaab, [8]Abdullah Ahmed Abdullah Alabdali, [9]Abdullatif Ahmad Abdullatif Maimny, [10]Ayman Abdullah Ahmed Abuseer,

[1]Anesthesia specialist non doctor, Maternity and Children Hospital
[2]anesthesia specialist non doctor, King Abdulaziz General hospital
[3]anesthesia technology, King abdulaziz hospital
[4]anesthesia technology, King Abdulaziz General hospital
[5]Anesthesia specialist non doctor, King abdulaziz general hospital
[6]Anesthesia specialist non doctor, King abdulaziz general hospital
[7]Anesthesia specialist non doctor, Maternity and Children Hospital
[8]Anesthesia specialist non doctor, Maternity and Children Hospital
[9]Anesthesia specialist non doctor, Maternity and Children Hospital in makkah .
[10]Anesthesia specialist non doctor, Maternity and Children Hospital in makkah .

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Abstract:
Caudal analgesia is the most frequently utilized regional anesthetic in pediatric surgery for lower abdominal, urological, and lower limb procedures. We did a narrative evaluation of the medical databases PubMed, Embase, and others for all relevant English-language publications published through the beginning of 2022. Clonidine 1 and 2 micro g/kg may be given safely to bupivacaine caudal blockade in small children undergoing ambulatory hernia surgery to increase the duration of analgesia compared to bupivacaine alone.

Corresponding author:
Shaher Salem Hadi Alqahtani,
Anesthesia specialist non doctor,
Maternity and Children Hospital

QR code

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INTRODUCTION:

Postoperative pain treatment is essential for minimizing the biological, functional, and psychological harm caused by the algic process [1]. Caudal epidural anesthesia stands out as a technique for postoperative pain prevention in children because to its technical simplicity and excellent risk-benefit ratio [2]. Bupivacaine is a local anesthetic often administered via the caudal epidural route at doses ranging from 0.125% to 0.175%, as it induces analgesia with a limited duration of roughly six hours [2]. In an effort to increase the quality and duration of the analgesia produced by bupivacaine, the association of other medicines, mechanisms, and other sites of action are evaluated. However, there are disputes over the real analgesic efficacy and occurrence of adverse effects of such combinations [3].

Opioids appear to lengthen the duration of analgesia among the caudal–epidural adjuvant medications, but their usage is limited by side effects such as nausea, vomiting, pruritus, and urine retention [4]. On the other hand, several combinations and dosages of caudal–epidural clonidine have been studied, without any side effects but with varying efficacy. Consequently, disagreement exists regarding the safest and more effective dosage [5].

Diverse techniques are employed to prolong caudal blockage. The standard ratio of epinephrine to local anesthetic is 1:200,000. Plasma levels suggest decreased systemic reabsorption, which is an advantage [6]. In actuality, epinephrine prolongs the analgesic effects of lidocaine, whereas it appears to have little effect on the longer-acting bupivacaine [7]. In addition to prolonging analgesia, the use of opioids involves the risk of respiratory depression [8]. Ketamine causes analgesia following epidural administration and increases the length and quality of analgesia supplied by bupivacaine in caudal blocks [8,9]; however, the potential for neurotoxic consequences following accidental intrathecal delivery restricts its application [10].

A systemic, epidural, or intrathecal infusion of clonidine, an alpha2-adrenergic agonist, results in analgesia without considerable respiratory depression [11]. After neuraxial injection, the analgesic effect of clonidine is stronger, suggesting a spinal site of action and making this mode of administration preferable [12]. Additionally, the addition of clonidine extends the duration of effect of bupivacaine following intrathecal and epidural administration in adults [13]. A mixture of 1 mL of 0.25 percent bupivacaine and 1-2 micrograms per kilogram of clonidine improves the duration and quality of analgesia provided by caudal block in children, although results vary widely, ranging from 16.4 hours for 1 microgram per kilogram [14] to 5.8 and 9.8 hours for 2 micrograms per kilogram [15]. Nonetheless, clonidine has the potential to produce hypotension, bradycardia, and respiratory impairment due to its powerful sedative effects; however, these side effects rarely demand a pharmacological response in adults. In children, however, hemodynamic data from studies that added clonidine to caudal blocks are either unavailable or only cover the intraoperative or postoperative [16,17] periods of time.

DISCUSSION:

A meta-analysis evaluating the efficacy of caudal epidural clonidine based on research published between 1966 and 2011 showed that this medication may improve the duration and quality of analgesia, however the biases of the studies analyzed severely limit this result [11]. In order to improve the dependability of the results, the current study aimed to remove some of these confounding variables. As such, in addition to using the FLACC scale, which is appropriate for postoperative pain evaluation in the examined group [15,16], perform a single unpleasant surgical procedure. Despite the use of a laryngeal mask or tracheal tube for airway access, as was also observed in another trial, no analgesic or opioid was administered intraoperatively, independent of airway management. Similar to a previous study, bupivacaine was chosen at a concentration of 0.166%, as studies indicate that the optimal concentration for caudal epidural use is 0.125 to 0.175%, as opposed to 0.25%, which offers comparable analgesia with less motor blockage [17].

It has been proven that clonidine has analgesic effects when delivered via epidural route [18]. Later, it was utilized in paediatric caudal block, and it was discovered that it prolonged analgesia in children [19,20]. Also administered intrathecally [21]. Combining caudal clonidine with bupivacaine at various doses revealed that raising the clonidine dose from 1 g/kg to 2 g/kg did not increase its efficacy [,22]. However, dose-dependent hypotension and bradycardia were observed as adverse effects, with incidence decreasing with 1g/kg [23]. To obtain efficient extension of caudal block with a smaller dose [22] and a lower incidence of hypotension, bradycardia, and respiratory depression [24], we selected Clonidine at a dose of 1g/kg. In addition, Dr. Manickam et al. [25] demonstrated that the addition of 1g/kg clonidine to 0.1% ropivacaine enhanced the

duration and quality of pain relief without causing motor blockade or drowsiness.

Multiple adjuvants have been utilized to increase the duration of bupivacaine's analgesia for caudal analgesia in children. Opioids, ketamine, and midazolam are often utilized drugs [1]. Opioid use is related with an increased incidence of pruritus and postoperative nausea and vomiting [1]. Unlike neuraxial opioids, clonidine extends the duration of analgesia without increasing the prevalence of side effects such as respiratory depression, itching, and urine retention.

A combination of 0.25 percent bupivacaine and 1-2 micrograms per kilogram of clonidine has been shown to increase the duration and quality of caudal block analgesia in children. The duration of analgesia ranges from 6.3 hours to 16.4 hours for 1 g/kg to 5.8 and 9.2 hours for 2 g/kg, despite the fact that results vary greatly. In one trial, children receiving caudal clonidine with bupivacaine experienced analgesia for a mean duration of 20.9 7.4 hours, however this study utilized a clonidine dose of 5 g/kg [26]. The large range in duration of action of clonidine between trials may be attributable to a number of factors, including dose, pre-medication, volatile anesthetic, kind of surgery, rationale for rescue analgesia, pain rating, and statistical analysis [26].

The mean duration of analgesia of clonidine is also extended when it is combined in a dose of 1 – 2 g/kg with caudal S+ ketamine 1 mg/kg [27]. With 1 and 2 g/kg, the duration of analgesia is 22,7 hours and 21,8 hours, respectively.

Several mechanisms have been proposed for the clonidine-induced extension of bupivacaine-induced caudal analgesia. The antinociceptive effect is due to the direct inhibition of nociceptive neurons in the spinal cord by epidural clonidine. Clonidine also interacts with alpha 2 adrenoceptors at spinal and supraspinal locations to generate analgesia by crossing the blood-brain barrier. Clonidine inhibits neurotransmission in A and C peripheral sensory nerve fibres. The last proposed mechanism is pharmacokinetically mediated: clonidine promotes vasoconstriction via -2b adrenoceptors in peripheral vascular smooth muscle [28].

Despite the fact that numerous research has confirmed the analgesic advantages of caudal clonidine as an additive, some studies [29] have demonstrated that there is no such benefit. Some investigations have also demonstrated that the incidence of vomiting is greater with caudal clonidine [30] and that the mean time of awakening from anesthesia is significantly lengthened[31]. None of the clonidine-treated youngsters in our research experienced postoperative vomiting.

Sharpe et al. [31] hypothesized that a little volume of bupivacaine (0.5 mL/kg) may not be sufficient to transport clonidine to the spinal cord, leaving only direct effect on the nerve pathways in the caudal region. These results imply that the addition of 2 g/kg clonidine to low volumes of caudal anesthetics has minimal therapeutic benefit for circumcised youngsters.

Hypotension and bradycardia are the adverse effects of neuraxial administration of clonidine. The antihypertensive effect occurs from stimulation of 2 inhibitory neurones in the medullary vasomotor centre of the brainstem, which reduces nor-epinephrine turnover and sympathetic nerve outflow from the central nervous system to the peripheral tissues. Bradycardia is triggered by an increase in vagal tone as well as a decrease in sympathetic drive [31].

1-5 g/kg of clonidine has been administered to children without clinically significant respiratory or hemodynamic effects. Motsch and colleagues [27] noted that although hemodynamic side effects appear to be less evident in children than in adults, they may be dose-dependent. One incidence of life-threatening apnoea has been recorded following inguinal herniorrhaphy and orchidopexy in a two-week-old term baby [30,31]. Numerous studies have indicated a high prevalence of hypotension and bradycardia in patients receiving clonidine.

CONCLSION:

In recent years, caudal analgesia has been the favored intraoperative and postoperative pain management strategy for lower abdomen and lower limb procedures. This is due to its simplicity, ease of execution, and predictability of blockage level. Several studies conclude that 1 g/kg of clonidine added to 0.25 percent bupivacaine for caudal analgesia and administered as a 1ml/kg mixture in children undergoing sub-umbilical surgery significantly increases the duration of post-operative analgesia compared to 1ml/kg of 0.25 percent bupivacaine alone, with no adverse effects. In children, 1 g/kg of caudal Clonidine is an acceptable and effective adjuvant to caudal Bupivacaine for delivering sustained postoperative analgesia with few adverse effects.

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