A comparitive study between dexmedetomidine and bupivacaine versus bupivacaine in caudal block in pediatric abdominal surgeries

Thesis

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Abstract

In this study it was demonstrated that Combined general and single shot caudal epidural block is a safe and acceptable anesthetic technique for pediatrics undergoing major abdominal surgeries and the addition of dexmedetomidine (2 µg/ kg) to caudal bupivacaine 0.25% at 1 ml/kg significantly promoted analgesia after anesthetic recovery in children aged 6 months to 6 yrs., undergoing major abdominal surgeries without increasing the incidence of side-effects.

Keywords

ACLS-DVP- Bupivacaine- Abdominal-Dexmedetomidine

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LIST OF ABBREVIATIONS

ACLS	Advanced Cardiac Life Support
ASA	The American Society Of Anesthesiologists
ASRA	The American Society of Regional Anesthesia
CNS	Central Nervous System
CPR	Cardiopulmonary Resuscitation
CVS	Cardiovascular System
DBP	Diastolic Blood Pressure
DVT	Deep Venous Thrombosis
GA	General Anesthesia
ICU	Intensive Care Unit
IL	Interleukin
LA	Local Anesthetics
LAST	Local Anesthetic Systemic Toxicity
MAP	Mean Arterial Blood Pressure
MODS	Multi-organ Dysfunction Syndrome
NCI	National Cancer Institute
NRM	Nucleus Raphe Magnus
PE	Pulmonary Embolism
PICU	Pediatric Intensive Care Unit
PRAN	Pediatric Regional Anesthesia Network
PSIS	Posterior Superior Iliac Spine
RAS	Reticular Activating System
SBP	Systolic Blood Pressure
SIRS	Systemic Inflammatory Response Syndrome
TEA	Thoracic Epidural Anesthesia
TNF α	Tumor Necrosis Factor Alpha

Introduction

In contrast to adult practice, the majority of regional anaesthesia in children and infants is performed under either deep sedation or general anaesthesia. Prospective and retrospective safety studies support the notion that performing regional anaesthesia under general anaesthesia is safe practice [1-4]. Caudal block is one of the most commonly used paediatric regional anesthetic techniques for postoperative analgesia. Caudal block is performed in children undergoing surgery of the lumbosacral to midthoracic dermatomal levels with anticipated moderate-to-severe postoperative pain, its popularity originates in part from easily palpable landmarks and relative ease of placement [5]. The main disadvantage of caudal anaesthesia is the short duration of action after a single injection of local anesthetic solution. Even long-acting local anesthetic drugs such as bupivacaine provide only 4–8 h of analgesia [6]. The use of caudal catheters to administer repeated doses or infusions of local anesthetic solution is not popular, partly because of concerns about infection. Prolongation of caudal analgesia using a single-shot technique has also been achieved by the addition of various adjuvants. Epinephrine was the earliest adjunct drug used, followed by opioids in mid 80's [7], followed by introduction numerous agents, including ketamine, α_2 agonists and other agents e.g. midazolam and tramadol [8].

In a recent systematic review Schnabel and colleagues[9] assessed the efficacy and safety of the combined use of clonidine and local anesthetics in comparison with caudal local anesthetics alone in twenty randomized controlled trials (published between 1994 and 2010) including 993 patients. They demonstrated longer duration of postoperative analgesia in children receiving clonidine in addition to local anesthetic. Furthermore, there were a lower number of patients requiring rescue analgesics in the clonidine group. The incidence of complications (e.g., respiratory depression) remained very low and was not different to caudal local anesthetics alone.

In animals, Dexmedetomidine had been identified to possess an eight fold greater affinity for α_2 adrenergic receptors than clonidine and much less α_1 adrenergic effects [10]. Evidence

showed that neuroaxial dexmedetomidine produces antinociception by inhibiting the activation of spinal microglia and astrocyte [11], decreasing noxious stimuli release of nociceptive substances [12] and further interrupting spinal neuroglia and regulating the nociceptive transmission under chronic pain condition [13]. Thus dexmedetomidine might be an interesting adjuvant for neuroaxial anesthesia and analgesia to decrease both intra and postoperative anesthetic and analgesic requirements. However the potentially increased risk of bradycardia, hypotension and neurotoxicity should be considered. In paediatric population intravenous dexmedetomidine had been extensively used during various procedures ranging from sedation to complex cardiac intervention with great safety [14]. Evidence regarding dexmedetomidine as an adjuvant to local anesthetics among pediatric population is lacking, however preliminary results had demonstrated that addition of dexmedetomidine to local anesthetics had been associated with prolonged motor and sensory block, hemodynamic stability, and reduce demand of rescue analgesics [15-18]

Invasive complex abdominal surgeries induce a combination of local response to tissue injury and generalized activation of systemic metabolic and hormonal pathways via afferent nerve pathways and the central nervous system. The local inflammatory responses and the parallel neurohumoral responses are not isolated but linked through complex signaling networks, some of which remain poorly understood. The magnitude of the response is broadly related to the site of injury (greater in regions with visceral pain afferents such as abdomen and thorax) and the extent of the trauma. The changes include alterations in metabolic, hormonal, inflammatory, and immune systems that can be collectively termed the stress response. Integral to the stress responses are the effects of nociceptive afferent stimuli on systemic and pulmonary vascular resistance, heart rate, and blood pressure, which are a combination of efferent autonomic response and catecholamine release via the adrenal medulla. Therefore, pain responses, cardiovascular responses, and stress responses need to be considered as different aspects of a combined bodily reaction to surgery and trauma [19]. Logically obtunded pain responses would be associated with less neuro-hormonal responses, and logically prolongation of such obtunded response in the immediate postoperative period would be of additional value. Thus the question is as follows: whether addition of dexmedetomidine to local anesthetic

solutions during single caudal epidural block among paediatric patients undergoing complex abdominal surgery would be superior to local anesthetic solution alone?

Overview of regional anesthesia in pediatric patients

Regional anaesthesia is a cornerstone of modern paediatric anaesthesia. combining general and regional anaesthesia provide superior and long-lasting analgesia without risk of respiratory depression. Furthermore, regional anaesthesia techniques have shown to attenuate peri-operative stress response, allow early tracheal extubation after major abdominal or thoracic surgery, decrease the ICU stay and allow rapid recovery of gastro-intestinal function [20-25].

During early phase of regional anesthetic techniques, the safe doses of Local anesthetics (LAs) had not been determined and, as a result of this, numerous case reports were published of LA toxicity, including both convulsions and cardiovascular complications. However, after an initiative by the Patient Safety Foundation, safe dosing guidelines for the use of bupivacaine in newborns, infants and children were issued by Berde [26]. With widespread adherence to these recommendations, reports of systemic toxicity from overdose of LA have almost disappeared [27].

The risk of complications associated with the use of regional anaesthesia in children has been a concern, as the vast majority of the blocks are performed with the child anaesthetized. In a seminal publication that prospectively studied > 20 000 blocks, Giafré et al. found paediatric regional anaesthesia to be very safe [1]. The Pediatric Regional Anesthesia Network [4] constructed a centralized database to collect detailed prospective data on all regional anesthetics performed by anesthesiologists at the participating centers. Data were uploaded via a secure Internet connection to a central server. Data were rigorously audited for accuracy and errors were corrected. All anesthetic records were scrutinized to ensure that every block that was performed was captured in the database. Intraoperative and postoperative complications were tracked until their resolution. Blocks were categorized by type and as single-injection or catheter (continuous) blocks. A total of 14,917 regional blocks, performed on 13,725 patients, were accrued from April 1, 2007 through March 31, 2010. There were no deaths or complications with sequelae lasting >3 months.

Single-injection blocks had fewer adverse events than continuous blocks, although the most frequent events (33% of all events) in the latter group were catheter-related problems. Ninety-five percent of blocks were placed while patients were under general anesthesia. Single-injection caudal blocks were the most frequently performed (40%) [4], they also concluded that Regional anesthesia in children as commonly performed in the United States has a very low rate of complications; comparable to that seen in the large multicenter European studies [4]. From all of the above, we can confidently conclude safety of combined regional and general anesthetic techniques and consider optimal utilization of such anesthetic tool in selected patient population.

Major abdominal surgeries can be likely associated with increased stress response [19]. Stress response is a term used to describe perioperative metabolic and neuro-hormonal derangements, and can further be associated with deleterious postoperative outcome. In a recent systematic review [28] Caudal epidural analgesia was found to be better in both early and late periods in regard to rescue analgesia and adverse effects in children undergoing inguinal surgeries compared to non caudal regional technique. They also explained that reductions in adverse postoperative outcomes can be directly attributed to modulation of pain and stress mediators associated with caudal techniques [28] .

Thus, logically, caudal epidural analgesia would be a very attractive option for operations associated with massive injury and those associated with severe postoperative pain, in attempt to decrease postoperative deleterious effects associated with pain and stress response mediators released, that in some severe cases would produce a picture similar to those with multiorgan dysfunction syndrome (MODS) [29].

It should be also noted that controversial issues regarding caudal epidural in pediatrics still exist, and no sharp conclusive evidence had been demonstrated regarding several debatable topics, including technique, type and volume of anesthetic used, adjuvants to local anesthetic solutions. Moreover, most evidence lack insights regarding major primary outcome variables (e.g. mortality and cost-effectiveness) and available evidence is considered too small (underpowered) to provide certain conclusions.

In the current review we will illustrate the following topics according to best available evidence:

I. **Acute pain: pathophysiological and clinical considerations.**

II. **Pediatric caudal canal block: Anatomical and technical considerations.**

III. **Overview of dexmedetomidine.**

IV. **Caudal epidural blocks in pediatric anesthesia: What is the evidence?**

I. Acute pain: Pathophysiological and clinical considerations:

- *Definition and pathway:*

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. This definition emphasizes that pain is not a predicted physiological response to stimulus nor based on observation, but is always subjective with each individual learning about pain through experiences relating to tissue injury in early life when pain is reported in terms of intensity, location and sometimes quality**.** This is referred to as the sensory- discriminative component of pain. Many people report pain in the absence of tissue injury and this pain may be amplified by psychological, emotional, cognitive and social factors as well as learned behavior [30].

Surgical pain is due to inflammation from tissue trauma (i.e., surgical incision, dissection, burns) or direct nerve injury (i.e., nerve transaction, stretching, or compression) **.**Tissue injury leads to release of inflammatory mediators with subsequent nociceptor stimulation. Pain impulses are then transmitted to the dorsal horn of the spinal cord, where they make contact with second-order neurons that cross to the opposite side of the cord and ascend via the spinothalamic tract to the reticular activating system (RAS) and thalamus. The localization and meaning of pain occurs at the level of the somatosensory cortex [31] Figure 1.

Tissue trauma releases local inflammatory mediators (e.g. histamine, bradykinin, and substance p) that can produce augmented sensitivity to stimuli in the area surrounding an injury (hyperalgesia) or misperception of pain to non-noxious stimuli (allodynia). Other mechanisms contributing to hyperalgesia and allodynia include sensitization of the peripheral pain receptors (primary hyperalgesia) and increased excitability of central nervous system neurons (secondary hyperalgesia) [32]. Surgery-associated tissue injury and peripheral nerve injury sets off a cascade of related events, including nociception and inflammatory reaction ,accompanied by elevated levels of pro-inflammatory cytokines including interleukins(IL-1β and IL-