Paediatric Emergence Agitation: Management Options

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Abstract

Emergence Agitation (EA) is a common postoperative problem especially in children. It is more common in paediatric age group especially with low blood gas solubility inhalational agents like Sevoflurane and Desflurane. Other factors contributing to increase EA are head and neck surgeries, preoperative anxiety and pain. It increases the risk of postoperative physical trauma to patient like surgical site bleeding, psychological trauma to parents and delayed recovery. Various drugs have been described to decrease EA. In this review article, here we have discussed the management options of EA including non-pharmacological and pharmacological options.

Keywords: Emergence agitation; Dexmedetomidine

Introduction

Eckenhoff et al. [1] first described Emergence Agitation (EA) in early 1960s. Sikich and Lerman [2] have defined EA as “a disturbance in a child’s awareness of and attention to his/her environment with disorientation and perceptual alterations including hypersensitivity to stimuli and hyperactive motor behaviour in immediate postanesthesia period”. It is a common postoperative problem especially in children. Its incidence is reported to be from 10%-50%, may be as high as 80% [3].

Risk factors: Various risk factors are associated with EA including low blood soluble inhalational anaesthetics like Sevoflurane, Desflurane [4,5], paediatric age group, preoperative anxiety [6], eye or head and neck surgeries [7], pain, and rapid awakening. Complications: EA has been documented to increase postoperative complications like significantly increased risk for physical trauma to patient like bleeding from surgical site, psychological trauma to the parents and delay in discharge from the Post Anesthesia Care Unit (PACU) [8].

Management of EA

Scales to Measure EA

Comparing studies have been difficult due to lack of a uniform definition of EA and the lack of a universal assessment scale. Sikich and Lerman [2] developed the Pediatric Anesthesia Emergence Delirium (PAED) scale consisting of five psychometric items for evaluating ED in pediatric patients. PAED scale consists of five psychometric items (1. the child makes eye contact with the caregiver 2. the child’s actions are purposeful 3. the child is aware of his/her surroundings 4. the child is restless 5. the child is inconsolable) (Table 1) incorporating cognitive and agitation assessments. They reported a sensitivity of 0.64, specificity of 0.86 and area under ROC to be 0.77 at a PAED Score of 10. Recently, PAED score >12 has been shown to provide a greater sensitivity and specificity than a PAED Score=10 [9].

Non-Pharmacological Methods

Various non-pharmacological methods have been used to decrease EA. Parental presence is used to allay anxiety and regional anaesthetic blocks like sub-tenon blocks have been documented to decrease EA [7].

Pharmacological methods

various drugs are used for treatment of post operative EA.

Premedication

Midazolam

It is one of the most commonly and popularly used premedication. It possesses potent anxiolytic, amnestic, sedative-hypnotic, anticonvulsant, and skeletal muscle relaxant properties. Its anterograde amnesic property is useful for premedication before surgery to inhibit unpleasant memories. However, it is known to cause dose dependent side effects such as paradoxical reaction, amnesia, restlessness, cognitive impairment and respiratory depression [10].

Cox et al. [11] showed that children premedicated with 0.5 mg/kg oral midazolam 20-30 minutes before surgery is effective in reducing anxiety and facilitates parental separation, with minimal effects on recovery times.

Various routes of administration of midazolam premedication have been tried- oral, intranasal- drops and spray, rectal.

Lejus et al. [12] compared intranasal (0.2mg/kg) versus rectal midazolam (0.3mg/kg) in 93 children aged 8 months-12 years and concluded that intranasal drug should be reserved when there is no alternative, due to poor tolerance and rectal administration should not be used in older children.

In a study, Shrestha et al. [13] administered oral premedication with injectable midazolam mixed in syrup paracetamol, and concluded it as

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
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<tbody>
<tr>
<td>0</td>
<td>No agitation</td>
</tr>
<tr>
<td>1</td>
<td>Minimum score</td>
</tr>
<tr>
<td>2</td>
<td>4 not at all</td>
</tr>
<tr>
<td>3</td>
<td>3 just a little bit</td>
</tr>
<tr>
<td>4</td>
<td>2 Quite a bit</td>
</tr>
<tr>
<td>5</td>
<td>1 Very much</td>
</tr>
<tr>
<td>6</td>
<td>0 - Extremely</td>
</tr>
</tbody>
</table>

Table 1: Pediatric Anesthesia Emergence Delirium Scale (PAEDS) [8].

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postoperative pain, and it required additional analgesic requirement, was found to be ineffective to completely abolish EA, had no effect on tonsillectomy in adult patients, but in this study very high dose of gabapentin was chosen [25].

Gaba sympathetic and opioid sparing effects is shown to decrease EA. Karamaz et al. [19] showed that oral premedication with relatively high dose ketamine reduced the incidence of EA in children undergoing adenotonsillectomy after desflurane anesthesia without delaying recovery. It was shown to have pre-emptive analgesic effects, reducing the incidence of EA [20]. In contrast, low-dose ketamine (0.5 mg/kg) was found to be ineffective to completely abolish EA, had no effect on postoperative pain, and it required additional analgesic requirement, during painful ophthalmic surgery [21].

Ketamine

Ketamine, N-methyl-D-aspartate receptor antagonist, with analgesic, amnesic and opioid sparing effects is shown to decrease EA. Karamaz et al. [19] showed that oral premedication with relatively high dose ketamine reduced the incidence of EA in children undergoing adenotonsillectomy after desflurane anesthesia without delaying recovery. It was shown to have pre-emptive analgesic effects, reducing the incidence of EA [20]. In contrast, low-dose ketamine (0.5 mg/kg) was found to be ineffective to completely abolish EA, had no effect on postoperative pain, and it required additional analgesic requirement, during painful ophthalmic surgery [21].

**Dexmedetomidine**

It is a highly specific alpha 2 receptors (α2:α1=1600:1) than clonidine (α2:α1=200:1). It has anxiolytic, sympatholytic, and opioid sparing effect that can reduce the dose of hypnotics, opioids, analgesics, and anesthetics required without causing any clinical respiratory depression.

Various routes of administration of dexmedetomidine have been tried- oral, intranasal. Kama et al. [22] compared Oral dexmedetomidine and oral midazolam for pre-anaesthetic sedation and postoperative recovery profile in children undergoing strabismus correction surgeries and found that premedication with 3 μg/kg oral dexmedetomidine is superior to 0.5 mg/kg oral midazolam. In another study, Cimen [23] showed that 1 μg/kg intranasal dexmedetomidine is more effective than buccal administration and has better levels of sedation, parental separation and mask acceptance.

**Gabapentin**

Initially was developed as anticonvulsant. Recently, Salman et al. [24] conducted a randomized study in children undergoing tonsillectomy and adenoidectomy after sevoflurane anesthesia using gabapentin as premedication at a dose of 15 mg/kg orally. They concluded it decreases EA and also 24 hour analgesic requirement. It is shown to induce analgesia by binding and inhibiting presynaptic voltage dependent calcium channels, thereby decreasing calcium influx and inhibiting release of neurotransmitters, mainly glutamate, from primary afferent nerve fibers which synapse on and activate pain responsive neurons in spinal cord [25]. However, the beneficial effects of reduced opioid intake seem to be nullified by the side effects seen during 5 days after tonsillectomy in adult patients, but in this study very high dose of gabapentin was chosen [25].

**Analgesics**

**Fentanyl**

Fentanyl, a short acting opioid, with sedative and analgesic effects can decrease EA. Cohen et al. [26] reported a decrease in EA in thirty two children (2-7year) undergoing adenoidecomy, under desflurane anaesthesia following fentanyl. However, it was found to increase the extubation time, emergence time and time in PACU and a higher incidence of PONV.

**Ketorolac**

Ketorolac, a Nonsteroidal Anti Inflammatory Drug (NSAID), has been an alternative analgesic to decrease EA. It has been postulated that EA is more with low blood gas soluble agents like sevoflurane, desflurane. It was found that rapid emergence from general anesthesia along with inadequate pain control could have attributed to EA. This was supported by Davis et al. [27], who conducted a double blinded prospective study to see the effects of ketorolac on EA in children premedicated with nasal midazolam (0.2 mg/kg) undergoing bilateral myringotomy. It showed that ketorolac reduced the incidence of EA three to fourfold after myringotomy under sevoflurane or halothane anesthesia. However, recently Kim et al. [28] found that 1 mg/kg ketorolac was not effective in decreasing the incidence of EA in children, 3-7 years of age, undergoing sevoflurane anesthesia. Therefore, they postulated that in high risk children other interventions are required for prevention of EA.

**Intravenous**

**Ketamine**

Ketamine, with analgesic, amnesic and opioid sparing effects is shown to decrease EA. Won Ju Jeong et al. [29] studied the effect of Ketamine in ophthalmic surgery in sixty children (2-8years), following Desflurane anesthesia. They concluded that 1 mg/kg Ketamine effectively reduces anxiety, postoperative pain and scores of EA without delay in discharge. Recently, Lee et al. [30] compared iv ketamine 0.25 mg/kg and 0.5 mg/kg and reported the similar decrease in incidence of EA due to combined analgesic and sedative effect. However, less pain score was noted with the higher dose of ketamine, that suggested that an increase in ketamine dose was effective in analgesic action, but increasing its dose did not affect the incidence of EA.

**Propofol**

Propofol is a short acting sedative- hypnotic agent. It has also been used to decrease EA with decreased nausea and vomiting. Aoud et al. [31] conducted a study in 80 children (2-6yr) receiving 1 mg/kg propofol at end of surgery for prevention of EA undergoing strabismus surgery during sevoflurane anesthesia. They concluded that single dose of propofol at end of surgery after sevoflurane discontinuation decrease incidence of EA without delaying patients discharge. However, Cohen et al. [32] reported that propofol 2mg/kg when used at the beginning of surgery did not decrease EA, probably due to its shorter duration of action and reduced serum level post-operatively, insufficient to effectively decrease EA.

**Ketofol**

Ketofol is a sedative-hypnotic agent and ketamine, a phencyclidine derivative, provides analgesia and amnesia. So combining low dose ketamine offsets the cardiorespiratory depression caused by propofol while providing adequate analgesia, sedation and better haemodynamics [33]. Sherry et al. [34] used ketofol in a randomized study to assess its efficacy and safety to control EA in 90 children (3-6 years) undergoing adenotonsillectomy after sevoflurane based anesthesia. They were randomly assigned to receive 10 ml normal saline, 1 mg/kg propofol in 10 ml saline or ketofol as 1mg/kg propofol and 0.25mg/kg ketamine in...
The OPS scale includes haemodynamic change, emotional factors (crying, agitation, and movement), and localisation of pain. Sikich and Lerman [2] developed the Pediatric Anesthesia Emergence Delirium (PAED) scale consisting of five psychometric items for evaluating ED in pediatric patients. PAED scale consists of five psychometric items (1. the child makes eye contact with the caregiver 2. the child’s actions are purposeful 3. the child is aware of his/her surroundings 4. the child is restless 5. the child is inconsolable) incorporating cognitive and agitation assessments. The EA score consists of five grades (1= sleeping, 2= awake and calm, 3= irritable and crying, 4= inconsolable and crying, and 5= severe restlessness and thrashing). Severe EA cut-off points were defined as a 5-point EA score of 4 and above, PAED score 11 and above, and 6 for OPS. They observed that the mean values of maximum EA, maximum PAED, and maximum OPS score were significantly lower in Group FD than in Group F at all time intervals up to 20 minutes with p<0.001. The severity of EA (FD- 12.8% VS F- 74.5%, p<0.01) and frequency of rescue analgesia was significantly lower in group FD than group F (p<0.001) (12.8% vs. 74.5%, p<0.001). They concluded that intraoperative low dose infusion of Dexmedetomidine effectively reduces EA in children undergoing strabismus surgery following anaesthesia with Desflurane.

In another randomized, placebo-controlled study, by Guler et al. [41] iv dexmedetomidine (0.5 µg/kg) and placebo were compared for the reduction of emergence agitation following sevoflurane used for anesthesia in 60 unpremedicated patients (3-7 years) undergoing adenotonsillectomy. Agitation behaviour and pain postoperatively were assessed using a 5-point scale (1= sleeping, 2= awake/calm, 3= irritable, 4= inconsolable, crying, 5= severe disorientation, thrashing, restlessness). Pain and agitation scores were better among patients in the dexmedetomidine group (p<0.05). However, emergence time and time to extubation were significantly long in the group, along with lower heart rate and blood pressure (p<0.005) upon extubation and recovery compared with placebo.

Conclusion

EA is a common postoperative problem with EA ranging upto 80% [4,5]. Various strategies have been used to decrease its incidence, such as pharmacological or non pharmacological methods. However, the most convenient and efficacious method and drug is still debatable.

References


Table 2: Various drugs used in EA are given below.

<table>
<thead>
<tr>
<th>Premedication</th>
<th>Hydroxyzine-Midazolam</th>
<th>Ketamine</th>
<th>Dexmedetomidine</th>
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<tbody>
<tr>
<td>Analgesics</td>
<td>Fentanyl</td>
<td>Ketorolac</td>
<td>Ketamine</td>
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<td>Intravenous</td>
<td>Propofol</td>
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<tr>
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