Emergence delirium in children

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Overview
- Definition
- Incidence
- Etiology
- Diagnosis
- Risk factors
- Prevention
- Treatment

Incidence
-> 2-80% ?!

depends on hypnotic agent; age; used criteria and definition

DD pain

True or false
- Een kind dat overstuur in slaap gaat wordt geagiteerd wakker
- Premedicatie met midazolam vermindert postoperatieve agitatie
- Een kind dat geagiteerd wakker wordt heeft pijn
- Aanwezigheid ouders bij inductie vermindert EA
**Definition**
Emergence delirium = disturbance in a child’s awareness of and attention to his environment with disorientation and perceptual alterations including hypersensitivity to stimuli and hyperactive motor behaviour in the immediate postanesthesia period.

**Characteristics**
- Within first 30 minutes after GA
- Brief
- Self-limiting

**Does it matter?**
- Risk of harming surgical repair
- Risk of harming self
- Risk of harming caregivers (nurse, parent)
- Risk of pulling out IV’s, drains, tubes, catheters, dressings…
- Stressful for the environment
- More Nursing resources required

**Pathogenesis**
- ?
- Neurodevelopmental characteristics?
- EEG changes?
- Altered metabolism sevoflurane in brain
- Pain?
Diagnosis

- Core behaviors
- PAED rating scale


Table 3 Chi-square analysis of emergence delirium for vocal, activity, eyes averted or stared, eyes closed, purposefulness, responsivity, and no language

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>n</th>
<th>df</th>
<th>P</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vocal</td>
<td>74</td>
<td>1</td>
<td>1.73</td>
<td>0.20</td>
<td>1.07-2.80</td>
</tr>
<tr>
<td>Activity</td>
<td>74</td>
<td>1</td>
<td>10.11</td>
<td>0.0039</td>
<td>3.97-11.14</td>
</tr>
<tr>
<td>Eyes averted/stared</td>
<td>74</td>
<td>2</td>
<td>17.46</td>
<td>0.001*</td>
<td>11.14-24.24*</td>
</tr>
<tr>
<td>Eyes closed</td>
<td>74</td>
<td>1</td>
<td>11.39</td>
<td>0.002</td>
<td>2.05-6.04-4.04</td>
</tr>
<tr>
<td>Purposefulness</td>
<td>74</td>
<td>1</td>
<td>20.91</td>
<td>0.00348</td>
<td>3.48-13.93</td>
</tr>
<tr>
<td>Responsivity</td>
<td>74</td>
<td>1</td>
<td>9.00</td>
<td>0.01</td>
<td>1.97-5.00-3.99</td>
</tr>
<tr>
<td>No Language</td>
<td>73</td>
<td>1</td>
<td>4.97</td>
<td>0.04</td>
<td>1.95-0.88-4.33</td>
</tr>
</tbody>
</table>

OR, odds ratio; CI, confidence interval.
*Odds ratio could not be computed for this variable as 2 x 3 contingency table (eyes averted or stare outcomes were no, yes, and not applicable because eyes closed).

The scores for each of the five listed behaviors are added to achieve a total scale score. A score of ≥10 makes it highly likely that a child has emergence delirium. For further information, refer to UpToDate content on emergence delirium and agitation in children.

From: Srikant N, Lerman J. Development and psychometric evaluation of the Pediatric Anesthesia Emergence Delirium (PAED) scale. Anesthesiology. 2004;100:1238. Copyright © 2004 American Society of Anesthesiologists. Reproduced with permission from Lippincott Williams & Wilkins. Unauthorized reproduction of this material is prohibited.
Differential diagnosis

- PAIN
- Hypoxia
- Dehydration
- Hypotension
- Hypocarbia or Hypercarbia
- Hypothermia
- Hypoglycemia
- Increased intracranial pressure

Risk factors

- Preschool age
- Anesthetic
- Type of surgery
- Length of anesthesia
- Depth of anesthesia
- Preoperative anxiety
- Preoperative PARENT anxiety

PAIN?

- Observe the child over 5 min after spontaneous eye opening
- Does the child make eye contact with the observer?
- Is the child aware of surroundings?
- Is the facial expression abnormal?
- Is the child irritable?
- Is the child crying?
- Is the child in pain?

All these "YES" - The child has PAIN
Consider pain treatment.
At this point, it is impossible to discriminate between delirium and pain.
Consider pain treatment as the primary option.
Observe children over 5 min.


Preschool age

<table>
<thead>
<tr>
<th>Variable</th>
<th>Preschool</th>
<th>School</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>3 ± 1</td>
<td>8 ± 1</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>18.9 ± 3.4</td>
<td>33.8 ± 3.3</td>
</tr>
<tr>
<td>Duration of anesthesia (min)</td>
<td>28 ± 4</td>
<td>28 ± 6</td>
</tr>
<tr>
<td>Depth of anesthesia</td>
<td>13 ± 3</td>
<td>12 ± 2</td>
</tr>
<tr>
<td>Incidence of delirium on emergence</td>
<td>1/50 (2%)</td>
<td>1/50 (2%)</td>
</tr>
</tbody>
</table>

Values are mean ± SD. Time to sedation and time to emergence after sevoflurane anesthesia were significantly less than after halothane anesthesia in each age group (P < 0.05). P = 0.001; P = 0.001 for halothane vs. sevoflurane in each age group. The incidence of delirium on emergence was most prominent in preschool boys. The incidence of delirium on emergence was significantly higher in preschool children than in school-aged children. P = 0.001. P = 0.001 for preschool vs. school-aged children.

Anesthetics

**propofol vs sevoflurane**

<table>
<thead>
<tr>
<th>Study/Ref (s)</th>
<th>Agitation (n)</th>
<th>Cross ratio and 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Need, et al. (10)</td>
<td>150/499</td>
<td>0.59 (0.41 - 0.86)</td>
</tr>
<tr>
<td>Lizard et al. (11)</td>
<td>60/1540</td>
<td>0.93 (0.29 - 3.10)</td>
</tr>
<tr>
<td>Gokten, et al. (12)</td>
<td>60/760</td>
<td>0.47 (0.26 - 0.87)</td>
</tr>
<tr>
<td>Roets, et al. (13)</td>
<td>522/1154</td>
<td>0.33 (0.14 - 0.78)</td>
</tr>
<tr>
<td>Olivera et al. (14)</td>
<td>4/16</td>
<td>0.44 (0.02 - 10.78)</td>
</tr>
<tr>
<td>Nikolov, et al. (15)</td>
<td>515/5015</td>
<td>0.10 (0.06 - 0.16)</td>
</tr>
<tr>
<td>Ofem, et al. (16)</td>
<td>655/2100</td>
<td>0.71 (0.47 - 1.05)</td>
</tr>
<tr>
<td>Cohen, et al. (17)</td>
<td>127/629</td>
<td>1.00 (0.55 - 1.84)</td>
</tr>
<tr>
<td>Fuentes, et al. (18)</td>
<td>127/9268</td>
<td>0.19 (0.09 - 0.42)</td>
</tr>
<tr>
<td>Ramirez, et al. (21)</td>
<td>3/187</td>
<td>1.37 (0.16 - 11.29)</td>
</tr>
<tr>
<td>Brown, et al. (22)</td>
<td>89/5101</td>
<td>0.34 (0.14 - 0.83)</td>
</tr>
<tr>
<td>Toming, et al. (23)</td>
<td>169/2091</td>
<td>0.75 (0.50 - 1.17)</td>
</tr>
<tr>
<td>Deng, et al. (24)</td>
<td>5/150</td>
<td>0.33 (0.07 - 1.50)</td>
</tr>
<tr>
<td>Peters, et al. (25)</td>
<td>610/1110</td>
<td>0.55 (0.36 - 0.84)</td>
</tr>
</tbody>
</table>

**Type of surgery**

When pain is prevented or adequately treated, the type of surgical procedure probably does not affect the risk of ED.

The incidence of ED after a pain-free procedure (MRI) = surgical procedures where pain was controlled

**Length of anesthesia**

<table>
<thead>
<tr>
<th>Procedure</th>
<th>n</th>
<th>Age (mean, SD)</th>
<th>Anx (mean, SD)</th>
<th>EA</th>
<th>Logistic regression</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRI</td>
<td>290</td>
<td>36.0 ± 11.1</td>
<td>36.0 ± 11.1</td>
<td>0.29</td>
<td>0.964 (0.884 - 1.053)</td>
</tr>
<tr>
<td>No surgery</td>
<td>270</td>
<td>36.3 ± 11.1</td>
<td>36.3 ± 11.1</td>
<td>0.29</td>
<td>0.964 (0.884 - 1.053)</td>
</tr>
</tbody>
</table>

**Effects of sevoflurane vs other general anaesthesia on emergence agitation in children**

Sevo better | Sevo worse

**Length of anesthesia**

- EA is not associated with length of time under deep anesthesia
Depth of anesthesia

Figure 2. Mean Pediatric Assessment of Emergence Delirium (PAED) score over time. Error bars denote 95% confidence interval of mean PAED score for each group. PACU = postanesthesia care unit.

Frederick, Heather; Wofford, Kenneth; CRNA, PhD; de Lisle Dear, Guy, MB, FRCA; Schulman, Scott. A Randomized Controlled Trial to Determine the Effect of Depth of Anesthesia on Emergence Agitation in Children. Anesthesia & Analgesia. 122(4):1141-1146, April 2016.

Preoperative anxiety

A Child’s View during Induction of anesthesia

Figure 2. Relationship between preoperative anxiety and emergence delirium symptoms. mYPAS = modified Yale Preoperative Anxiety Scale.


Preoperative anxiety: No

Preoperative parent anxiety: yes

- The higher the level of maternal salivary amylase; the more severe the child’s pre-op anxiety AND the more severe the post-op ED

- Maternal heart variability just before surgery significantly correlated with the emergence behavior of children undergoing GA

Risk factors:
- Preschool age
- Anesthetic (sevoflurane/desflurane)
- Type of surgery
- Length of anesthesia
- Depth of anesthesia
- Preoperative anxiety
- Preoperative PARENT anxiety

Prevention:
- Non-pharmacological
- Pharmacological
Prevention: non-pharmacological

Strategies to reduce preoperative anxiety
- Parental presence at induction

**Table 2. Scores of quality of mask induction and emergence behavior.**

<table>
<thead>
<tr>
<th></th>
<th>Midazolam (n=19)</th>
<th>PPIA (n=20)</th>
<th>Midazolam + PPIA (n=19)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mask induction</td>
<td>2 (1–3)</td>
<td>3 (2–3)</td>
<td>2 (1–3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Emergence behavior</td>
<td>4 (2–5)</td>
<td>4 (2–5)</td>
<td>3 (2–4)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are median (range). PPIA, parental presence during induction of anesthesia.
*Different from the PPIA group (P= 0.05).
†Different from the other groups (P= 0.05).


Prevention: non pharmacological

- Family-centered preparation


Pharmacological

Prevention

- Transition to propofol at the end of surgery

Prevention

IV Midazolam at the end of surgery

<table>
<thead>
<tr>
<th>Midazolam 0.03 mg/kg</th>
<th>Midazolam 0.05 mg/kg</th>
<th>Saline (n = 30)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of patients with emergence agitation</td>
<td>6 (16%)</td>
<td>5 (16%)</td>
<td>15 (45%)</td>
</tr>
<tr>
<td>SOE score</td>
<td>10 (31%)</td>
<td>9 (31%)</td>
<td>15 (45%)</td>
</tr>
<tr>
<td>No of patients with postoperative emergence delirium</td>
<td>27 (57%)</td>
<td>7 (24%)</td>
<td>28 (80%)</td>
</tr>
<tr>
<td>SOE score</td>
<td>14 (43%)</td>
<td>17 (50%)</td>
<td>15 (45%)</td>
</tr>
</tbody>
</table>

Data are presented as numbers of patients (percentages, median change, or mean ± SD). Multiple comparisons using Bonferroni’s (n = 6) were obtained as described.

Cho EJ, Yoon SZ, Cho JE, Lee HW. Comparison of the effects of 0.03 and 0.05 mg/kg midazolam with placebo on prevention of emergence agitation in children having strabismus surgery. Anesthesiology. 2014 Jun;120(6):1354-61.

Intraoperative opioid administration

Dexmedetomidine: emergence time

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Dexmedetomidine</th>
<th>Placebo</th>
<th>Risk Ratio</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>All NA, 2013</td>
<td>10.9</td>
<td>10.7</td>
<td>1.41%</td>
<td>0.23 (0.06, 0.78)</td>
</tr>
<tr>
<td>Emb T, 2009</td>
<td>12.7</td>
<td>12.2</td>
<td>1.04%</td>
<td>0.76 (0.19, 3.09)</td>
</tr>
<tr>
<td>Gil G-Ramón, 2013</td>
<td>7.2</td>
<td>6.9</td>
<td>1.06%</td>
<td>0.85 (0.24, 2.94)</td>
</tr>
<tr>
<td>Guler G, 2009</td>
<td>9.3</td>
<td>9.2</td>
<td>1.04%</td>
<td>0.76 (0.20, 2.77)</td>
</tr>
<tr>
<td>Guler G, 2005</td>
<td>9.3</td>
<td>9.2</td>
<td>1.04%</td>
<td>0.76 (0.20, 2.77)</td>
</tr>
<tr>
<td>Guler O, 2005</td>
<td>9.3</td>
<td>9.2</td>
<td>1.04%</td>
<td>0.76 (0.20, 2.77)</td>
</tr>
<tr>
<td>Inashvili, 2004</td>
<td>8.2</td>
<td>7.5</td>
<td>1.08%</td>
<td>0.76 (0.20, 2.77)</td>
</tr>
<tr>
<td>Ipekci, 2004</td>
<td>8.6</td>
<td>8.1</td>
<td>1.06%</td>
<td>0.85 (0.24, 2.94)</td>
</tr>
<tr>
<td>Leclercq, 2006</td>
<td>8.0</td>
<td>7.4</td>
<td>1.06%</td>
<td>0.85 (0.24, 2.94)</td>
</tr>
<tr>
<td>Li G, 2012</td>
<td>12.0</td>
<td>11.7</td>
<td>1.03%</td>
<td>0.76 (0.20, 2.77)</td>
</tr>
<tr>
<td>Meng Q, 2012</td>
<td>14.5</td>
<td>13.7</td>
<td>1.03%</td>
<td>0.76 (0.20, 2.77)</td>
</tr>
<tr>
<td>Meng Q, 2015</td>
<td>15.5</td>
<td>14.8</td>
<td>1.03%</td>
<td>0.76 (0.20, 2.77)</td>
</tr>
<tr>
<td>Oh A, 2011</td>
<td>9.2</td>
<td>8.2</td>
<td>1.08%</td>
<td>0.76 (0.20, 2.77)</td>
</tr>
</tbody>
</table>

Total (95% CI): 363

Heterogeneity: CH² = 8.56, df = 11 (P = 0.46); I² = 0%

Risk Ratio

Dexmedetomidine: additional analgesia

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Dexmedetomidine</th>
<th>Placebo</th>
<th>Risk Ratio</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emb T, 2009</td>
<td>30</td>
<td>30</td>
<td>16.02%</td>
<td>0.44 (0.21, 0.91)</td>
</tr>
<tr>
<td>Guler G, 2005</td>
<td>7</td>
<td>30</td>
<td>19.77%</td>
<td>0.35 (0.17, 0.71)</td>
</tr>
<tr>
<td>Guler O, 2005</td>
<td>7</td>
<td>30</td>
<td>19.77%</td>
<td>0.35 (0.17, 0.71)</td>
</tr>
<tr>
<td>Guler N, 2013</td>
<td>4</td>
<td>18</td>
<td>17.22%</td>
<td>0.29 (0.12, 0.70)</td>
</tr>
<tr>
<td>Kim NY, 2014</td>
<td>0</td>
<td>20</td>
<td>3.13%</td>
<td>0.20 (0.03, 1.24)</td>
</tr>
<tr>
<td>Polette, GR, 2011</td>
<td>6</td>
<td>23</td>
<td>27.20%</td>
<td>0.39 (0.19, 0.82)</td>
</tr>
<tr>
<td>Polette, SG, 2011</td>
<td>11</td>
<td>28</td>
<td>22.33%</td>
<td>0.39 (0.19, 0.82)</td>
</tr>
<tr>
<td>Salti, 2010</td>
<td>1</td>
<td>39</td>
<td>1.22%</td>
<td>0.06 (0.01, 0.36)</td>
</tr>
</tbody>
</table>

Total (95% CI): 180

Heterogeneity: CH² = 2.97, df = 8 (P = 0.81); I² = 0%

Ketamine?

Figure 1. Recovery mental state in the three groups of patients.
**Prevention: summary**
- Reduce preoperative anxiety
- TIVA or propofol infusion near end surgery
- Midazolam 0.03mg/kg near end surgery
- Intraoperative opioids
- Alpha$_2$ agonists (clonidine 2mcg/kg or dexdor 0.3 - 1mcg/kg IV)
- Ketamine 0.25mg/kg IV near end surgery

**Treatment**
- Support and prevention of harm…
  -> 95% spontaneously resolves in 20’
- Assess for potentially dangerous causes of agitation and for pain!
  - Propofol 1mg/kg IV
  - Midazolam 0.1mg/kg IV
  - Fentanyl (1 to 2 mcg/kg IV) or other opioids
  - Parental presence

**Summary**
- **Risk factors**: preschool-age and inhaled anesthetics
- **Diagnosis**: non-purposefulness, eyes averted, stared or closed, and non-responsivity
- **DD**: Pain and potentially dangerous causes of agitation (ie, hypoxia, hypotension, hypercarbia, hypoglycemia)
- Most effective **preventive measure**: avoid inhalation anesthetics…
- Mostly, resolves over 20 minutes, and requires no treatment other than support and prevention of harm.
True or false

• Een kind dat overstuur in slaap gaat wordt geagiteerd wakker -> onduidelijk
• Premedicatie met midazolam vermindert postoperatieve agitatie -> nee
• Een kind dat geagiteerd wakker wordt heeft pijn -> soms
• Aanwezigheid ouders bij inductie vermindert ED -> afhankelijk van pre-op parental anxiety

Questions?

References

• Mason KP. Paediatric emergence delirium: a comprehensive review and interpretation of the literature. BJA 2017 118 (3): 339-43.
• Kain, Zeve Et Al. Preoperative Anxiety and Emergence Delirium and Postoperative Maladaptive Behaviors. Anesthesia & Analgesia 2004. 99(6):1648-1654,