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IMPACT OF DEXMEDETOMIDINE ON OPIOID AND BENZODIAZEPINE DOSING REQUIREMENTS IN CHILDREN

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BACKGROUND
- Dexmedetomidine is a potent and selective alpha2-adrenergic agonist which has sedative, analgesic, and anxiolytic effects.
- In adults, dexmedetomidine has been shown to decrease opioid dosing requirements when utilized for pain and sedation management.
- We hypothesized that similar to adult data, the addition of dexmedetomidine to standard pain and sedation management protocols may reduce the overall opioid and benzodiazepine dosing requirements in children after cardiac surgery.

OBJECTIVES
- Thirty six patients in each group were included.
- No difference between groups.

RESULTS
- Total daily opioid dosing requirements were reduced 37% in the dexmedetomidine group versus the comparison group.
- Patients in the dexmedetomidine group had higher midazolam dosing requirements.

METHODS
- Study Design
  IRB approved retrospective cohort study
- Data Source
  Computer generated lists were used to randomly select both case (DEX) and comparison (COMP) subjects.
  Dosing information was collected via medication administration records for the duration of anesthesiologist management.

Patient Population
- Patients included were pediatric cardiovascular surgery patients who were admitted to the intensive care unit post-operatively.
- Exclusion criteria:
  - Patients greater than 18 years
  - Cardiovascular surgery patients whose operative procedure was not performed for repair or palliation of a congenital heart defect
  - Dexmedetomidine patients who did not have dexmedetomidine initiated within 24 hours of surgery.

Pain and Sedation Management
- Standard pain management and sedation protocol managed by pediatric anesthesiologist in all patients.
- Therapeutic options and dosing were dependent on patient’s airway status.
  - Mechanically ventilated
  - Continuous fentanyl infusion
  - As needed (PRN) IV morphine
  - PRN IV midazolam
  - +/- dexmedetomidine
  - Spontaneously breathing
  - PRN IV morphine
  - PRN IV midazolam
  - +/- dexmedetomidine

Data Analysis
- Total cumulative doses of fentanyl, morphine, and midazolam were determined.
- For equal comparison, opioid dosing was standardized by using equipotent morphine doses.

<table>
<thead>
<tr>
<th>Baseline Demographics</th>
<th>No</th>
<th>Dexmedetomidine</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>(n = 36)</td>
<td></td>
</tr>
<tr>
<td>Age* (months)</td>
<td></td>
<td>50.9 (0.85 – 207.4)</td>
<td>44.9 (0.13 – 233)</td>
</tr>
<tr>
<td>Weight* (kg)</td>
<td></td>
<td>18.5 (3.2 – 104)</td>
<td>16.4 (2 – 99)</td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td>21 (58%)</td>
<td>20 (56%)</td>
</tr>
<tr>
<td>Bypass</td>
<td></td>
<td>35 (97%)</td>
<td>34 (94%)</td>
</tr>
<tr>
<td>Intubated</td>
<td></td>
<td>26 (72%)</td>
<td>20 (56%)</td>
</tr>
<tr>
<td>RACHS-1, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td>4 (11%)</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>9 (25%)</td>
<td>10 (28%)</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>22 (61%)</td>
<td>21 (58%)</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>11 (3%)</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Continuous Infusions
- Fentanyl
  - Administered to 18 (50%) in the DEX group and 14 (38%) in the COMP group
  - DEX group required fewer days of therapy 4.8 vs. 8.9 (p = 0.004)
- Midazolam
  - Not utilized in any patient
- Dexmedetomidine
  - Mean initial infusion: 0.34 ± 0.1 mcg/kg/hr
  - Maximum infusion: 0.44 ± 0.17 mcg/kg/hr
  - Bolus doses administered to 8 patients (22%)
  - Average length of infusion: 2.4 ± 1.9 days

DISCUSSION
- When compared to a historical control population, dexmedetomidine administration to children within 24 hours after surgery for congenital heart disease, was associated with a 37% reduction in total daily opioid dosing requirement, although not statistically significant.
- Decreased opioid use may also result in decreased PICU days and decreased incidences of opioid withdrawal, both of which impact overall length of stay and associated healthcare costs.
- Trending towards statistical significance, a reduction in continuous fentanyl infusion requirements was also observed.

- In our study, cumulative midazolam dosing requirements were higher in patients who received dexmedetomidine, although not statistically significant.
- This could be explained by limited upward dexmedetomidine dose titration and may signify that the dexmedetomidine doses were not optimized to achieve desired sedation outcomes.