A Comparison of Midazolam and Zolpidem as Oral Premedication in Children.

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Introduction

Anxiety associated with pediatric surgical procedures can be stressful for patients and parents/guardians

Oral midazolam is the most investigated, commonly used, and well-accepted premedication in the pediatric patient

However, oral midazolam may not always be effective:
  - Found to be of benefit only 57% of the time at parental separation and 71% at the time of induction
  - Paradoxical reactions to midazolam premedication can be associated with agitation rather than sedation

Zolpidem is a short-acting nonbenzodiazepine hypnotic drug of the imidazopyridine class that potentiates GABA by binding to the same receptors as benzodiazepines.
  - Oral availability
  - Quick onset of action (~15 minutes)
  - 2-3 hours duration

We sought to compare zolpidem to midazolam for pediatric premedication.

Methods

Departmentally funded, prospective randomized double-blinded clinical trial (NCT02096900), designed to compare the effectiveness of oral midazolam and zolpidem for premedication

ASA class I-II pediatric patients between 2 and 9 years old scheduled for surgery of at least 2 hours duration and at least 23 hours postoperative admission were included in the study

Exclusion criteria:
  - Any contraindication to preoperative sedation
  - Known allergy or sensitivity to the study medications
  - Lack of legal representative consent
  - Weight >95th percentile or <5th percentile, according to the current CDC growth chart

Randomization was done on a 1:1 basis, with 0.5mg/kg midazolam (based on prior investigations in children for premedication) or 0.25mg/kg zolpidem (based on prior investigations in children for sleep) administered orally to the child

Sample size was calculated to require 80 participants total, with a planned interim analysis at 40 participants

The primary outcome measured was the between group difference in patient anxiety at the time of separation using the Modified Yale Preoperative Anxiety Scale (mYPAS).

Evaluators were trained and inter observer agreement verified prior to study initiation

Secondary outcomes included mYPAS change and mask acceptance at induction

We sought to compare zolpidem to midazolam for pediatric premedication.

Results

One procedure was canceled in each group, so interim analysis was performed using the remaining 19 participants in each group

- There were no significant demographic differences between the groups (Table 1)
- All patients were awake at the time of separation
- There was no significance between group difference in:
  - Anxiety at separation evaluation using mYPAS.
  - Change in mYPAS

Figure 1

- 11 (57.9%) zolpidem patients had increased mYPAS at separation compared to 7 (36.8%) midazolam patients, but this did not reach significance (difference -21.1%; -48.7 to 10.6%; p=0.19).

Conclusions

- At interim analysis, the current data supports our null hypothesis in that there is no significant difference in anxiety at separation between midazolam and zolpidem
- Enrollment will be continued to ascertain if the larger number of zolpidem patients who had increased mYPAS reaches significance.

References