Randomized Controlled Trial Assessing the Effectiveness of Midazolam Premedication as an Anxiolytic, Analgesic, Sedative, and Hemodynamic Stabilizer

BACKGROUND:

- Anxiety before surgery can lead to hemodynamic instability, increased anesthetic consumption during surgery, and postoperative pain. Midazolam, a benzodiazepine, is widely used as a premedication before general anesthesia to alleviate anxiety despite the lack of clinical evidence for its use. Adverse effects of midazolam that may decrease its utility include paradoxical reactions, over-sedation, decreased blood pressure, and respiratory depression.

OBJECTIVE:

- Evaluate the effects of using midazolam as a premedication for anesthesia in the areas of anxiety reduction, sedation, hemodynamic stability, and analgesic effects.

METHODS

- **Type of study design:** Randomized, prospective, single-blind
- **Study duration:** 2 days
- **Important inclusion/exclusion criteria:**
    - Inclusion: female, age 20-65 years old, American Society of Anesthesiologists physical exam status I or II, scheduled for elective thyroidectomy
    - Exclusion: central nervous system (CNS) disorders, major cardiovascular disease, chronic pain disorders, peripheral neuropathy, diabetes mellitus neuropathy, nephropathy, hepatopathy, current prescription of any medication affecting the CNS or heart rate (HR), alcohol or drug abuse, pregnancy, contraindications to midazolam premedication.
- **Number of patients enrolled:** 128 randomized, 112 completed the study.
- **Drug regimens/dosages used:** 0.05 mg/kg midazolam plus 0.2 mg glycopyrrolate intramuscular injection or 0.2 mg glycopyrrolate alone.
- **Outcome measures (efficacy and safety):**
    - Anxiety: change in Beck anxiety inventory (BAI)
    - Anesthesia: state entropy (SE), response entropy
    - Hemodynamic stability: heart rate (HR), mean blood pressure (MBP)
    - Analgesia: surgical pleth index (SPI), numerical rating scale (NRS), analgesic drug consumption

- **Power:** 80%
- **Data handling method used:** per protocol

RESULTS

- No improvement in Beck Anxiety Inventory from the day before surgery to 30 minutes after injection was observed in midazolam group compared to non-treatment group
- At time point T1 (pre-induction) heart rate (P=0.003), mean blood pressure (P=0.003), and SPI (P<0.001) were significantly different between groups
- At time point T2 (prior to intubation) relative entropy (P=0.008), state entropy (P=0.012), and SPI (P=0.033) were significantly different
- At time point T3 (intubation) relative entropy (P<0.001), state entropy (p<0.001), heart rate (P=0.020), mean blood pressure (P=0.021), and SPI (P=0.012) were significantly different
- At time point T4 (20 minutes after intubation) relative entropy (P<0.001) and state entropy (P<0.001) were significantly different
- Postoperative pain numeric rating scale and analgesic demand did not differ between groups

STRENGTHS

- Outcome measures were reasonable for the research question

LIMITATIONS

- Single blinding could impact results
- Study only performed in females receiving one type of surgery which may affect anxiety levels and reduces extrapolation of results
- Study was lacking power for primary outcome measures
- No placebo or active control was used in the non-treatment group
- A low dose of midazolam was used
- Not all patient data was included in the analysis
- Outcome measures did not include potential adverse effects of midazolam

CONCLUSIONS

- This study joins many others with regard to providing inconclusive evidence for the use of midazolam for premedication during surgery
- Based on this study one cannot definitively say that midazolam is or is not useful for premedication before surgery

- Even if it does not reduce patient perceived preoperative anxiety, midazolam may reduce physiological responses associated with preoperative anxiety

Jeon S, Lee HJ, Do W, et al. Randomized Controlled Trial Assessing the Effectiveness of Midazolam Premedication as an Anxiolytic, Analgesic, Sedative, and Hemodynamic Stabilizer. Medicine. 2018;97:35(e12187).

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