Presurgery sedation and patient experience: comment & response

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COMMENT & RESPONSE

Presurgery Sedation and Patient Experience

To the Editor In a randomized clinical trial by Dr Maurice-Szamburski and colleagues,[1] premedication with oral lorazepam 2 hours prior to arriving in the operating room did not improve patient satisfaction after surgery and was associated with prolonged time to extubation and decreased cognitive recovery compared with placebo or no medication. These results may not indicate that all sedative premedication is unwarranted but may suggest lorazepam is inadequate.

Maurice-Szamburski and colleagues explained why lorazepam was used instead of midazolam for their trial: "The choice of lorazepam was motivated by its use in the largest survey of sedative premedication published to date," referring to a study by Kain et al.[2] There is some discrepancy between this statement and the survey results, in which among adults, the most commonly used sedative premedication was midazolam (>75%), followed by diazepam (7%), and lorazepam (2%).[2] Seven years later, a follow-up survey study by Kain et al[3] found that adult inpatients received midazolam most often (80%), followed by diazepam (3%), fentanyl (2%), and lorazepam (1%).

Lorazepam may have disadvantages compared with midazolam. Midazolam is a short-acting benzodiazepine with an elimination half-life of 2.0 hours to 2.5 hours, whereas lorazepam has a half-life of 10 hours to 20 hours. In a randomized clinical trial that compared midazolam with lorazepam for postoperative sedation, delays in emergence from sedation were observed in the lorazepam group.[4]

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4. Barr J, Zomorodi K, Bertaccini EJ, Shafer SL, Geller E. A double-blind, randomized comparison of IV lorazepam versus midazolam for sedation of ICU patients via a pharmacologic model. *Anesthesiology*. 2001;95(2):286-298.

To the Editor The key purpose of patient premedication with benzodiazepines is preoperative anxiolysis,[1] which allows for safer monitoring and induction of anesthesia. In contrast, the primary outcome parameter of the study by Dr Maurice-Szamburski and colleagues[2] was the patient's perception quantified with a patient satisfaction index (Evaluation du Vécu de l'Anesthésie Generale; EVAN-G)[3] on the first postoperative day. From a clinical viewpoint, a patient's perception on the first postoperative day is not the key parameter to judge the value of premedication.

The more important outcomes were the secondary outcomes measuring preoperative and intraoperative conditions. Anxiety upon arrival in the operating room was significantly lower (visual analog scale scores for anxiety: 35 points for lorazepam group vs

44 points for placebo group; $P = .001$). However, the scores for quality of conditioning and well-being upon arrival in the operating room were not statistically significant. The present study was underpowered to shed light on these clinically important and desired effects of premedication.

In the lorazepam group, the duration of surgery was 11 minutes longer than in the placebo group and postoperative pain was significantly lower. The statistically significant secondary outcome of a prolonged time to extubation can be attributed to lorazepam only if dosages of sedatives and opioids were comparable between the groups, which were not presented in the article.

Because many patients do not want to remember anything about the operation, amnesia is an intended effect of premedication. The increased proportion of patients with amnesia (24% with lorazepam vs 6% with placebo) is a beneficial effect of lorazepam rather than a complication as the authors suggested.

Lorazepam produced clinically desired effects in the study by Maurice-Szamburski and colleagues. The data do not justify the conclusion of the authors that lorazepam lacks any benefit in routine use.

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In Reply If midazolam remains the most prescribed sedative premedication, lorazepam ranks third for outpatient surgery and fourth for inpatient surgery.[1] Midazolam and lorazepam both belong to the benzodiazepine class and share most of their indications. The PremedX study evaluated sedative premedication with lorazepam given orally 2 hours before surgery. Lorazepam was chosen over the more commonly used midazolam because, due to its shorter acting time, midazolam may not have been as potent as lorazepam upon arrival in the operating room.

In the study by Barr et al cited by Dr Fujita, these 2 drugs were the most frequently prescribed drugs for sedation. However, one should be careful about extrapolating results from this intensive care unit study with continuous administration of benzodiazepine and fentanyl up to 72 hours. Although delays in emergence were longer in the lorazepam group, the lengths of administration differed (mean [SD], 36.94 [30.90] hours with midazolam vs 15.02 [3.33] hours with lorazepam).[2]

In response to Drs Heller and Koch, we believe the purpose of premedication is not established. According to anesthetists, there are many different reasons for using sedative premedication.[3] Because sedative premedication primarily concerns patients and their experience,[4] the main outcome of the PremedX study was the patient experience and satisfaction assessed by a validated questionnaire, evaluating both the preoperative, perioperative, and postoperative periods.[5] The EVAN-G mean global index showed no significant differences between the lorazepam, placebo, and no premedication groups in the whole population or in the subgroup of the most anxious patients, those expected to benefit the most from sedative premedication.

Even though anxiety upon operating room arrival was lower with lorazepam than with placebo, it was no different between lorazepam and no premedication (35 [95% CI, 32-38] vs 38 [95% CI, 35-41], respectively, $P = .41$) and was higher comparing placebo with no premedication (44 [95% CI, 40-47] vs 38 [95% CI, 35-41], respectively, $P = .05$), suggesting a nocebo effect of placebo. In our study, anesthetists were unable to distinguish between the lorazepam, placebo, and no premedication groups for quality of patient conditioning. Before invoking underpowering to explain the lack of efficacy, sedative premedication relevance should be questioned.

The randomization of the study was intended to eliminate other sources of variability, such as the dosing of sedatives and opioids. The types of drugs used for the anesthesia protocol were not different between groups.

Lorazepam was associated with a 10-point lower satisfaction score on the attention dimension of the EVAN-G scale. One explanation is that the amnesia from benzodiazepine led patients to forget the attention they received from caregivers, which would not necessarily be beneficial.

Given the results of the PremedX study, we continue to believe that routine sedative premedication with benzodiazepine should not be recommended.

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