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Predictors for postoperative nausea and vomiting after xenon-based anaesthesia

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Abstract

Background: In contrast to volatile anaesthetics, xenon acts by antagonism at *N*-methyl-D-aspartate receptors and antagonizes 5-hydroxytryptamine type 3 receptors that mediate nausea and vomiting. Therefore, it is unknown whether the same risk factors for postoperative nausea and vomiting (PONV) after volatile anaesthetics apply to xenon-based anaesthesia.
Methods: With ethics committee approval and written informed consent, 502 consecutive patients undergoing xenon-based anaesthesia were included in a multicentre prospective observational study. Antiemetic prophylaxis was administered at the discretion of the attending anaesthetists. Postoperative nausea and vomiting and need for antiemetic rescue medication were assessed for 24 h after anaesthesia. Multivariate logistic regression analysis was performed to quantify risk factors for PONV and need for rescue medication.
Results: Four hundred and eighty-eight subjects were available for the final analysis. The incidence of PONV in subjects without prophylaxis was lower than expected according to the Apfel Score (28% observed; 42% expected, $P<0.001$). Independent predictors for PONV were (adjusted odds ratio; 95% confidence interval) female sex (1.76; 1.08–2.89), younger patient age (0.82 per 10 yr; 0.69–0.97), and longer duration of anaesthesia (1.36 per hour; 1.17–1.59).
Conclusions: The incidence of PONV was significantly lower than predicted by the Apfel Score. Female sex, younger age, and longer duration of anaesthesia are risk factors for PONV after xenon-based anaesthesia.
Clinical trial registration: German Federal Institute for Drugs and Medical Devices number AL-PMS-01/07GER.

Key words: anaesthetics; antiemetics; risk factors

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Editor's key points

- Risk factors for postoperative nausea and vomiting (PONV) after xenon anaesthesia are unknown.
- Multivariate analysis was used to quantify risk factors for PONV and need for rescue antiemetics in a multicentre prospective trial of xenon anaesthesia.
- Incidence of PONV was lower than predicted for propofol or inhaled anaesthesia.
- Female gender, younger age, and longer duration of anaesthesia were risk factors for PONV.

Postoperative nausea and vomiting (PONV) severely impair patient satisfaction and rank together with pain among the most undesirable outcomes following general anaesthesia.[1] The identification of risk factors for PONV forms the basis for adequate prophylaxis and treatment of patients with a high probability of experiencing PONV. In addition to patient-related risk factors, inhaled anaesthetics induce PONV depending on the duration of exposure.[2 3]

As a noble gas, xenon is chemically inert in physiological conditions and therefore free of metabolites. As a result of its low solubility in blood, it is rapidly eliminated from the body during weaning from anaesthesia.[4 5] Furthermore, xenon antagonizes serotonin type 3 (5-HT_3) receptors that mediate nausea and vomiting during chemotherapy and after general anaesthesia.[2] Taken together, one might assume that the incidence of PONV after xenon-based anaesthesia is rather low, yet Coburn and colleagues[6] described an incidence of PONV of more than 60%. Thus, identification of risk factors could facilitate titration of prophylactic antiemetics during xenon-based anaesthesia. However, with respect to pharmacokinetic and pharmacodynamic differences compared with other inhaled anaesthetics, it is not known whether risk factors for PONV are valid in the course of xenon-based anaesthesia or if prevalent pharmacological prophylaxis is sufficiently effective in this setting. Therefore, our aim was to determine (i) the risk factors for PONV and (ii) the efficacy of routinely administered antiemetic prophylaxis after xenon-based anaesthesia.

Methods

Here we present data from a previously unpublished prospective multicentre study performed to evaluate the safety and efficacy of xenon-based anaesthesia with subjects recruited between April 2009 and February 2011. After institutional review board approval (Ethik-Kommission der Ärztekammer Berlin, study number ETH-019/08, and Heinrich-Heine Universität Düsseldorf, study number 3386) and registration at the German Federal Institute for Drugs and Medical Devices (BfArM, study number AL-PMS-01/07GER), all patients classified as ASA status I–II (age 18 yr or older) undergoing surgery during xenon-based general anaesthesia were eligible for this study after written informed consent was obtained. Patients with elevated intracranial pressure, pulmonary disease, coronary artery disease, and impaired left ventricular function were excluded. Induction and maintenance of xenon-based anaesthesia was conducted at the discretion of the attending anaesthetists.

Assessment of postoperative nausea and vomiting

Subjects were followed for 24 h after extubation by study physicians. The incidence of nausea, vomiting, or both within the 24 h period was assessed by medical chart inspection followed by a personal patient interview and recorded as a binary variable. The requirement for postoperative antiemetic medication ('rescue medication') was assessed from medical charts.

Incidence of postoperative nausea and vomiting and quantification of independent predictors

The observed incidence of PONV was compared with the expected incidence predicted by Apfel Score.[7] The initial Apfel Score was corrected for the administered postoperative opioids. This comparison was performed only in subjects who did not receive antiemetic prophylaxis to determine the unimpeded emetic activity of xenon-based anaesthesia.

We assessed predictors for PONV or rescue medication after xenon-based anaesthesia by logistic regression analysis. A recent, large meta-regression identified female sex, history of PONV or motion sickness, non-smoking status, younger age, duration of anaesthesia, use of postoperative opioids, and certain types of surgery as independent predictors for PONV after propofol or inhaled anaesthetic-based anaesthesia.[8] Therefore, we decided *a priori* to include these variables in the model. The comparison of postoperative opioid consumption was facilitated by calculation of morphine equivalents. In addition, different classes of medical antiemetic prophylaxis and study centres were also included as single binary variables in the model *a priori*. The aim of the next step was to identify further potential predictors by testing remaining variables (height, weight, body mass index, amount of intraoperative fluids, type of intraoperative opioid, and use of regional anaesthesia) for association with PONV or rescue medication by univariate analysis. As no statistically significant associations were found, we did not include these variables in our logistic regression analysis. Variables within the model were tested for collinearity using the *collin* extension of Stata (P. Ender, University of California, Los Angeles, CA, USA). Goodness of fit was assessed using the Hosmer–Lemeshow test with 10 groups.

Effectiveness of medical antiemetic prophylaxis

The effect of prophylactic antiemetics was part of the logistic regression analysis. However, we additionally performed a propensity score-matched analysis so that subjects who did or did not receive prophylactic antiemetics were comparable. To this end, a binary variable was generated indicating whether a subject received medical antiemetic prophylaxis or not. Then, a logistic regression model including sex, age, smoking status, history of PONV or motion sickness, regional anaesthesia, duration of anaesthesia, anticipated postoperative opioid use, and study centre was used to calculate the propensity for receiving medical antiemetic prophylaxis. Finally, subjects with prophylaxis were matched on a one-to-one basis with patients without prophylaxis on the logit of the propensity score using callipers of 0.2 SD of the logit.[9] Univariate analyses were performed to verify that groups were balanced on the variables used for calculation of the propensity score (i.e. that matching was successful). Additionally, standardized differences were calculated to quantify balancing of groups.[10]

The sample size estimation of the underlying study was carried out based on the primary end points depth of anaesthesia and incidences of hypertension and anaesthesia. However, when comparing an overall PONV incidence associated with general anaesthesia of 38%[11] and a previously reported PONV incidence of 27.5% after xenon-based anaesthesia,[12] a minimal sample size of 364 patients would be required. On this basis, we