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Postoperative nausea and vomiting after surgery for prognathism: Not only a question of patients' comfort. A placebo-controlled comparison of dolasetron and droperidol

Swen N. PIPER[1], Kerstin RÖHM[1], Joachim BOLDT[1], Peter KRANKE[2], Wolfgang MALECK[3], Rudolf SEIFERT[4], Stefan SUTTNER[1]

[1] *Department of Anaesthesiology and Critical Care Medicine (Head: Prof. Dr. J. Boldt), Klinikum Ludwigshafen, Germany;* [2] *Department of Anaesthesiology and Critical Care Medicine (Head: Prof. Dr. N. Roewer), University of Würzburg, Germany;* [3] *Department of Anaesthesia (Head: Dr. S. Widjaja), Spital Menziken, Switzerland;* [4] *Department of Maxillofacial Surgery (Head: Priv.-Doz. Dr. Dr. H. Umstadt), Klinikum Ludwigshafen, Germany*

SUMMARY. Introduction: **The aim of this study was to evaluate the efficacy of dolasetron and droperidol (DHB) for preventing postoperative nausea and vomiting (PONV) in patients undergoing surgery for prognathism.** Material and methods: **In a randomised, placebo-controlled, double-blind trial, the efficacy of 12.5 mg dolasetron i.v. and 1.25 mg DHB was evaluated in preventing PONV in 83 patients undergoing surgery for prognathism. Patients were allocated randomly to one of three groups: group A ($n = 27$) received 12.5 mg dolasetron intravenously (i.v.), group B ($n = 27$) received 1.25 mg DHB i.v. and placebo group C ($n = 29$) received saline 0.9%. If patients complained of retching or vomiting or if patients demanded antiemetics, 20 mg metoclopramide (MCP) i.v. was given. Postoperative nausea, postoperative vomiting, or nausea and vomiting was assessed in the postoperative period at 0–4 h and overall between 0 and 24 h.** Results: **A significant reduction in the incidence of postoperative nausea and/or vomiting was observed in the dolasetron group (33%) when compared with DHB (81%) and placebo (86%) treated patients. No other significant differences between the DHB and the placebo group were found. Dolasetron (11%) significantly reduced vomiting in comparison with the DHB (52%) and placebo group (52%). The use of postoperative MCP per patient was significantly lower in the dolasetron group when compared with both other groups. Dolasetron significantly reduced the postoperative nausea and/or vomiting-score when compared with both other groups. There was no significant difference between DHB- and placebo-treated patients with regard to nausea and/or vomiting.** Conclusion: **Intravenous dolasetron (12.5 mg) is more effective than either intravenous DHB (1.25 mg) or placebo for preventing PONV after surgery for prognathism. It also was significantly superior to either DHB or placebo concerning nausea and vomiting and the need for MCP rescue medication. © 2007 European Association for Cranio-Maxillofacial Surgery**

Keywords: **postoperative nausea and vomiting (PONV), surgery for prognathism, dolasetron, droperidol**

INTRODUCTION

Along with postanaesthetic shivering, postoperative nausea and vomiting (PONV) is one of the main side effects after surgery performed under general anaesthesia (*Piper* et al., 2002a). PONV is a major factor causing patients' discomfort and dissatisfaction regarding office, clinic or hospital experience (*Kovac*, 2005). *Macario* et al. (1999) showed that patients fear PONV more than they do postoperative pain. Apart from the obvious discomfort, PONV may be associated with the risk of aspiration, especially in patients recovering from general anaesthesia or in patients with intermaxillary wiring after oral and maxillofacial surgery (*Palazzo* and *Strunun*, 1984; *Köhler* and *Zöller*, 1988). Many studies have attempted to quantify the incidence of PONV. The incidences reported depend to a large extent on patient and anaesthesia-related factors. The most commonly recognised risk factors are female gender, non-smoking status, a history of previous PNOV and/or motion sickness, the duration of anaesthesia and the use of large amounts of postoperative opioids (*Apfel* et al., 2002; *Maleck* and *Piper*, 2002). An especially high risk group consists of non-smoking females of child-bearing age with a previous episode of nausea and/or vomiting or kinetosis in the patient's history (*Apfel* et al., 2002; *Maleck* and *Piper*, 2002). Although less important, the occurrence of PONV can be influenced by the type of surgery, especially gynaecological, ear, nose and throat, and strabismus surgery has previously been described as particularly emetogenic (*Wang* and *Waite*, 1975; *Graczyk* et al., 1997; *Kontrimaviciute* et al., 2005; *Treschan* et al., 2005). Despite the fact that most of the risk factors are related to an individual disposition towards PONV, a consistent high appearance of PONV has been described in the previous studies following oral and maxillofacial surgery, performed in the seventies and eighties (*Wang* and *Waite*, 1974, 1975; *Tornes*, 1987; *Köhler* and *Zöller*,

1988). It is surprising that newer investigations on this topic are completely lacking, as postoperative vomiting secondary to intermaxillary fixation can be an emergency situation requiring quick release of fixation in some cases (*Goss* et al., 1979; *Frost* and *Frost*, 1983; *Tamari* et al., 1988; *Edgin* and *Orth*, 1997; *Carry* et al., 2001).

Most of the currently used antiemetics including butyrophenones, phenothiazines, dopamine receptor antagonists, anticholinergics and antihistamines have undesirable side effects such as sedation and extrapyramidal symptoms (*Wachta* and *White*, 1992; *Freymond* et al., 2002; *Piper* et al., 2002b). The availability of 5-hydroxytryptamine type 3 (5-HT_3) antagonists has offered a new option in the prevention of PONV without sedative and with negligible centrally acting side effects (*Harter*, 2000; *Korttila* and *Jokinen*, 2004; *Kontrimaviciute* et al., 2005).

So far there are no controlled studies evaluating the efficacy of preventing PONV using 5-HT_3 antagonists in patients undergoing surgery for prognathism. Hence this study was designed to compare the efficacy of dolasetron and droperidol (DHB), two commonly used antiemetic drugs, for the prevention of PONV in this group.

MATERIAL AND METHODS

After approval by the local ethics committee and written informed consent, 83 patients, classified as *American Society of Anesthesiologists* (ASA) physical status 1 or 2, undergoing elective surgery for prognathism were studied. The classification from the ASA was introduced by *Saklad* (1941) and was revised in 1963 with the number of classes being reduced from seven to five (*American Society of Anesthesiologists*, 1963): ASA I: healthy patient, ASA II: mild systemic disease, ASA III: severe systemic disease, ASA IV: severe systemic disease that is a constant threat to life, and ASA V: moribund patient.

The study was performed over a 5-year period (1999–2004) as this kind of operation is infrequent in this hospital. Patients with respiratory, cardiac, hepatic (aspartate aminotransferase $> 40\ U\,l^{-1}$, alanine aminotransferase $> 40\ U\,l^{-1}$), or renal insufficiency (creatinine $> 1.4\ mg\,dl^{-1}$), febrile patients ($>37.5\ ^{\circ}C$), and patients taking long term corticosteroids or drugs with known antiemetic activity within 24 h of surgery were excluded. Other exclusion criteria consisted of severe obesity (>50% above ideal body weight; men ideal body mass index = 0.5 kg/m^2 + 11.5; women ideal body mass index = 0.4 kg/m^2 + 0.03 age + 11), a history of nausea and vomiting within 24 h prior to surgery, use of any drug within 30 days prior to surgery, known alcohol or drug abuse. All patients fasted for at least 6 h prior to anaesthesia, and received premedication with 7.5 mg midazolam orally 30–45 min prior to surgery. Induction of general anaesthesia was standardised including fentanyl ($3\ \mu g\,kg^{-1}$), propofol ($2\ mg\,kg^{-1}$), and *cis*-atracurium ($0.15\ mg\,kg^{-1}$). An endotracheal tube was inserted nasally and anaesthesia was maintained with 3.0–9.0% (inspired concentration) desflurane supplemented by nitrous oxide (60%) in oxygen according to the patients' need. A nasogastric tube was inserted and suction applied to empty the stomach of air and secretions. Mechanical ventilation (Julian®, Dräger, Lübeck, Germany) was performed in all patients with a positive end-expiratory pressure (PEEP) of 5 mbar and adjusted to maintain end-expiratory CO_2 between 4.3 and 4.8 kPa. At the end of surgery, the nasogastric tube was suctioned and removed, and the patients were extubated.

Patients were allocated randomly to one of three regimens, receiving either 12.5 mg dolasetron intravenously (i.v.) in group A ($n = 27$), 1.25 mg DHB i.v. in group B ($n = 27$), or saline 0.9% i.v. as placebo in group C ($n = 29$). All study drugs were diluted to an adjusted volume of 20 ml and administered i.v. at the end of surgery in a double-blind fashion. Randomisation was performed with closed envelopes containing the study assignment opened after inclusion in the study. After surgery and extubation, patients were transferred to the intensive care unit (ICU). Patients were observed for 24 h postoperatively. On arrival at the ICU, 30, 60 min and 4, 24 h postoperatively the patients were asked about occurrence of nausea and vomiting using the following scale: 0 = no nausea, 1 = nausea, 2 = retching, 3 = single vomit, and 4 = multiple vomiting. If values of 2 or more within this scale were reached or if patients specifically demanded antiemetics, 20 mg metoclopramide (MCP) was given i.v. Postoperative pain was monitored using a visual analogue scale (VAS were 0 = "no pain" and 10 = "worst pain imaginable"). Pain was treated with intravenous doses of the opioid piritramide (increments of 3.75 mg) or diclofenac (100 mg) given rectally. The postoperative enquiry of patients and the evaluation of patients' PONV-score were carried out by an anaesthesiologist who was unaware of the patients' drug assignment.

For all patients the individually expected incidence of PONV was calculated using the individual and anaesthesia-related risk factors of the risk score of *Koivuranta* et al. (1997) to predict the occurrence of PONV and vomiting, respectively. This score has been validated repeatedly (*Eberhart* et al., 2000; *Apfel* et al., 2002) and includes risk factors such as female gender, history of PONV secondary to general anaesthesia, non-smoking, history of motion sickness and duration of general anaesthesia > 60 min (*Koivuranta* et al., 1997).

Statistical methods

Demographic data, duration of surgery and anaesthesia, intraoperative blood loss and fluid balance, recovery time between end of anaesthesia and extubation were analysed with Student's *t*-test. The incidence of PONV and vomiting were analysed with Fishers' exact test. The ranked sum test of *Raatz* (1966) was used to compare pain- and PONV-scores. The Raatz-test is a modified rank order test to be used for values that fall into classes (e.g. school notes or scores). Postoperative consumption of piritramide, diclofenac and MCP was analysed with repeated measures analysis of variance (ANOVA) for repeated measurements, and with Bonferroni correction for multiple comparisons.

An incidence of PONV was expected in the placebo group of at least 50% and a reduction of the incidence