TITLE: COMPARISON OF MIDAZOLAM AND PROPOFOL IN COMBINATION WITH ALFENTANIL FOR TOTAL INTRAVENOUS ANESTHESIA

AUTHORS: J. Vuyk, M.D., P.J. Hennis, M.D., Ph.D., A.G.L. Burm, Ph.D., J.W.H. de Voogt, M.Sc. and Joh. Spierdijk, M.D., Ph.D.

AFFILIATION: Dept. of Anesthesiology, University Hospital of Leiden, Leiden, The Netherlands

Both propofol and midazolam are suitable for use in total intravenous anesthesia (TIVA). We compared the hemodynamics of induction, the alfentanil and naloxone requirements and the speed of recovery of TIVA with propofol/alfentanil (P) and midazolam/alfentanil (M).

Methods. With institutional approval and informed consent, 20 patients, aged 18-45 yr, ASA I, scheduled for lower limb surgery were randomly assigned to either group P or M. Premedication was with temazepam 10 mg P.O. Anesthesia was induced and maintained with either propofol 2 mg/kg in 5 min followed by 9 mg kg^{-1} h^{-1} for 30 min followed by 4.5 mg kg^{-1} h^{-1} until skin closure or midazolam 0.42 mg/kg in 5 min followed by 0.125 mg kg^{-1} h^{-1} until skin closure. After a loading dose of 50 μg/kg alfentanil (ALF) infusion was started at 50 μg kg^{-1} h^{-1}. Vecuronium 0.1 mg/kg was given for muscle relaxation. After intubation of the trachea the lungs of the patients were ventilated with O_2/air (FiO_2 = 0.3). During surgery, when blood pressure increased > 15 mmHg above the preoperative value, heart rate exceeded 90 bpm in absence of hypovolemia or when other autonomic or somatic signs occurred a bolus of ALF 7 μg/kg was given and the infusion rate increased by 25 μg kg^{-1} h^{-1}. The infusion rate was reduced by 25 μg kg^{-1} h^{-1} in absence of these signs for 15 min, and stopped 10 min before skin closure. If, 10 min after skin closure patients did not breathe adequately (ET_{CO2} > 6 vol.%, TV < 7 ml/kg, RR < 10/min), naloxone 40 μg was given every 2 min. Preoperatively and 5, 30, 60, 120, 240 min postoperatively patients performed a p-deletion and a blocks test[1]. Data were assessed for normality using the Shapiro Wilk test. Further statistical evaluation was done by repeated measures ANOVA, linear regression, paired and unpaired t-test or Mann Whitney U test where appropriate. P < 0.05 was considered significant.

Results. Patient characteristics and duration of surgery were comparable in both groups. In both groups blood pressure decreased significantly and to a similar extent during induction. The total dose of ALF was similar in both groups, 10.0 ± 4.3 mg in group P and 12.6 ± 7.6 mg in group M. No patient in group P and 9 patients in group M needed naloxone (average dose 130 ± 70 μg). This difference was highly significant (P < 0.001). Postoperatively the blocks test score recovered to 90% of the control score at 78 ± 23 min in group P and at 215 ± 37 min in group M (P < 0.001). For the p-deletion test the times were 56 ± 9 min and 245 ± 36 min respectively (P < 0.001).

Discussion. The hemodynamic responses to propofol/ALF were similar to that of midazolam/ALF. However, recovery was significantly faster and the incidence of respiratory depression less in patients given propofol/ALF. The latter combination is preferable for TIVA.

Reference

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Title: **THE INFLUENCE OF RECTAL CISAPRIDE ON MORPHINE INDUCED GASTRIC STASIS**

Authors: M.T. Kluger FCAnaes, H.Owen FFARACS and J.L. Plummer PhD

Affiliation: Department of Anesthesia and Intensive Care, Flinders Medical Centre, Bedford Park, 5042, South Australia, AUSTRALIA.

INTRODUCTION This study was designed to assess the efficacy of a rectal formulation of cisapride in reversing the effects of morphine on gastric motility. Pulmonary aspiration of gastric contents remains an important cause of anesthetic mortality[1]. Opioids administered preoperatively have been shown to significantly delay gastric emptying[2] and may predispose to an increased risk of inhalation of gastric contents perioperatively. Cisapride, a gastric prokinetic drug, has been shown to reverse morphine induced gastric stasis when given I.M.[2].

METHODS After informed consent and Ethical Committee approval forty patients, aged 18-65 years, were randomly assigned to four treatment groups; A: placebo suppositories only, B: placebo suppositories plus morphine 10 mg I.M., C: cisapride 30 mg suppositories plus morphine 10 mg I.M. and D: cisapride 60 mg suppositories plus morphine 10 mg I.M. Patients received morphine 60 mins after insertion of the suppositories. Acetaminophen (1.5g) was administered orally with 50 ml of water 80 min after the suppositories. This provided an indirect marker of gastric emptying. Venous blood samples were collected at 15 min intervals for a period of 3.25 hrs and analysed via HPLC methods for cisapride and acetaminophen concentrations.

Indices of gastric emptying examined were, area under the plasma acetaminophen-time curve from 0-40 min ($AUC_{0-40\ mins}$), maximum acetaminophen concentration (A_{max})and time to A_{max} (T_{max}). Peak plasma cisapride concentration was also measured (Cis_{max}). Groups were compared by one factor analysis of variance . A priori contrasts were used to assess effect of morphine (Gp A vs. B, C & D), effect of cisapride in preventing morphine induced gastric stasis (Gp B vs. C & D) and dose related effect of cisapride (linear trend over Gps B, C & D).

	GROUPS			
	A	B	C	D
A_{max}(mcg/ml)	28.4 (7.4)*	19.0 (9.0)	21.6 (12.6)	20.3 (12.7)
T_{max}(mins)	29.5 (12.3)*	59.5 (41.8)	40.0 (29.2)	53.3 (44.6)
$AUC_{0-40mins}$	635.1 (253.1)	439.0 (387.9)	543.3 (364.9)	467.5 (395.1)
Cis_{max}(ng/ml)	0.00	0.00	49.2 (23.4)	56.8 (27.6)
	Mean (S.D.)	*$p < 0.05$* vs Gps B,C &D		

RESULTS Demographic data for all groups were not significantly different. Patients receiving morphine had significantly impaired gastric emptying. Reversal of opioid induced gastric stasis was not achieved with 30 or 60 mg of cisapride rectally.

CONCLUSONS Plasma levels of 100 ng/ml have previously been reported as effective in reversing gastric stasis[2], whereas those around 50 ng/ml are ineffective. In this study, even at the 60 mg dose, blood cisapride concentrations were below 100 ng/ml; thus the lack of demonstrable effect may be due to the delivery characteristics of this formulation.

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REFERENCES

1. *Mortality Associated with Anaesthesia* 1980: Nuffield Hospital Trust.
2. *British Journal of Anaesthesia* 1987; 59: 536-39