

TITLE: SLOW INJECTION OF MIDAZOLAM DOES NOT REDUCE THE RISK OF HYPOXIA
AUTHORS: L.E. Teller, M.D., C.M. Alexander, M.D., J.B. Gross, M.D.
AFFILIATION: Departments of Anesthesiology, Univ. of Pennsylvania, Phila., PA 19104 & Univ. of Connecticut, Farmington, CT 06032

Introduction: Midazolam may cause ventilatory depression and hypoxia during conscious sedation.¹ We performed the present study to determine if this risk is related to the rate of midazolam administration.

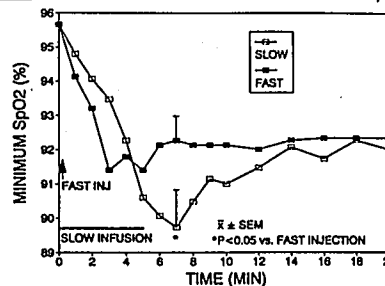
Methods: Thirty patients, ASA I and II, consented to participate in this IRB-approved study. Monitored variables included oxygen saturation (S_{pO_2} -Ohmeda 3700 with ear probe), ventilatory rate (CO_2 detection via nasal cannula), and awareness (0-unarousable to 4-wide awake). At time 0, we began administration of midazolam 0.1 mg/kg i.v. over 15 s (fast) or by infusion over 5 min (slow). If S_{pO_2} (room air) decreased below 92%, we provided graded interventions: 1-verbal command, 2-light tap, 3-trapezius squeeze, 4-jaw lift, 5-supplemental O_2 , 6-assisted ventilation, 7-endotracheal intubation. We analyzed the data over two time periods 0-5 min (during infusion) and 5-20 min (post-infusion) using 2-way ANOVA and the protected LSD test for continuous variables and the Kruskal-Wallis test for categorical variables. $P < 0.05$ indicated significance.

Results: During the first 5 min, patients in the "fast" group were significantly more sedated than those in the "slow" group ($P < 0.001$); once patients in the "slow" group had received their complete dose of midazolam (i.e., time > 5 min) sedation scores were

similar between groups. During the first 5 minutes S_{pO_2} did not differ between groups; however, after the infusion was complete, patients in the "slow" group had significantly lower S_{pO_2} than those in the "fast" group ($P < 0.005$, figure). The degree of intervention necessary to treat hypoxemia did not differ between groups during the first 5 min; thereafter, more interventions were necessary in patients who received midazolam by infusion ($P < 0.05$). No patients required supplemental oxygen, positive pressure ventilation or intubation. Neither respiratory rates nor the length of respiratory pauses differed between groups during either of the two time periods.

Discussion: Our findings suggest that careful monitoring rather than slow administration rates are crucial for the safe use of midazolam. When detected early, midazolam-induced hypoxemia is readily treated. All patients receiving midazolam, regardless of injection rate, should be monitored by oximetry.

Reference: ¹Gastrointest Endosc 36:26-29, 1990



Title: OXYGEN SATURATION FOLLOWING ADMINISTRATION OF BUPRENORPHINE OR MORPHINE DURING THE POSTOPERATIVE PERIOD

Authors: M. Fischler, M.D., C. Basdevant, M.D., M. Gauthé-Feissel, M.D., L. Raffin, M.D., M. Spérandio, M.D.

Affiliation: Department of Anesthesiology, Hôpital Foch, 92151 Suresnes, France

Buprenorphine (BUP), a potent agonist-antagonist opioid, can be used as an analgesic during the postoperative period. The risk of respiratory depression associated with BUP has not been studied as it has been for morphine (MOR) (1). This prospective study was carried out to compare oxygen saturation (SpO_2) after administration of equianalgesic doses of BUP or MOR (2).

Methods. After institutional approval and informed consent, 50 patients, ASA I and II, admitted in the recovery room after general surgery were included in this randomized study. If they were normoxic ($SpO_2 > 95\%$) without oxygen supplementation since 15 min, they received either 10 mg MOR or 0.3 mg BUP IM when needed (first analgesic requirement). SpO_2 was continuously monitored during two hours after injection using a Nellcor N-200 pulse oximeter connected to a PC computer. A specific program was used for real-time data analysis. For each patient the cumulative time spent in each following SpO_2 range (96-100%, 91-95%, 86-90% and $\leq 85\%$), the number and duration of oxygen desaturation episodes were indicated. No oxygen supplementation was given unless SpO_2 was lower than 80%. Data are expressed as mean \pm SD and were analyzed using Chi Square and Mann-Whitney tests. P value < 0.05 is considered as significant.

Results. 26 patients received BUP and 24 MOR. Groups were comparable regarding to demographic data, fentanyl dose administered during surgery (292 ± 142 mcg in the BUP group, 288 ± 145 mcg in the MOR group) and interval between the fentanyl last injection and that of BUP or MOR

(168 ± 74 min in the BUP group, 175 ± 44 in the MOR group).

SpO_2 was recorded during 3681 min in the BUP group and 3161 min in the MOR group. 8 patients of the BUP group and 7 of the MOR group did not experience any oxygen desaturation episode. The time spent in each range of SpO_2 was different for the 2 groups ($p < 10^{-5}$): 74.3 % of the time in the BUP group and 84.3 % in the MOR group in the range 96-100%, 25.2 % and 15.2 % respectively in the range 91-95 %, 0.4 % for both groups in the range 86-90%, 0.05 % for both groups for values of $SpO_2 < 85\%$. The mean number of episodes was 18.2 ± 9.9 in the BUP group and 8 ± 7.7 in the MOR group in the range 91-95 % ($p < 0.01$), 2.8 ± 2.3 and 2 ± 1.2 in the range 86-90% (NS), 1.3 ± 0.5 and 1 in the range $< 85\%$ (NS). The mean durations of oxygen desaturation episodes were short: 3 min ± 2.26 in the BUP group and 1.55 ± 1.29 in the MOR group in the range 91-95 % (NS), equal to or less than 1 min for the other ranges.

Discussion. Administration during the postoperative course of 0.3 mg BUP or 10 mg MOR produces significant oxygen desaturation episodes. Whereas MOR respiratory depression is easily reversed by naloxone, BUP is characterized by a very limited reversal effect of naloxone as demonstrated in human volunteers (3) and, therefore, it must be used with caution.

References.

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