Title: THE EFFECT OF MIDAZOLAM PRETREATMENT ON ALFENTANIL-INDUCED MUSCLE RIGIDITY

Authors: T.J. Sanford Jr. M.D., N.T Smith M.D., M.B. Weinger, M.D., J.L. Benthuysen M.D*., N. Head, B.S.

Affiliation: Department of Anesthesiology, University of California, San Diego, Veterans Administration Medical Center, San Diego, University of California, Davis*.

Introduction: Opioid-induced rigidity occurring during anesthesia induction with fentanyl and its analogs is considered to be one of the side effects of these potent drugs. A screening study using a previously described model of alfentanil (A) induced rigidity[1] and a saline pretreatment, reported that several drugs including diazepam(D) 5mg and methcarbamol(MC) 1-3 gms administered prior to induction of anesthesia significantly reduced the severity of opioid-induced muscle rigidity.[2] However, D was administered 9-10 minutes prior to induction and MC needed to be administered by infusion beginning 15 minutes before induction. At the time of the screening study it was felt that midazolam (MDZ) would be a better pretreatment drug because of its rapid onset and short duration and could be administered just prior to induction. However, neither MDZ nor A was not released at the time of the original study. We now present results which confirm the effectiveness of MDZ as a pretreatment agent to attenuate or prevent opioid- induced rigidity.

Methods: After institutional approval and informed consent 6 male patients ranging in age from 48-54 years old scheduled for elective surgery were studied. All studies were monitored by the attending anesthesiologist assigned to each particular patient. This anesthesiologist was not a member of the study team. Each patient was monitored with the following: arterial and central venous pressure lines, bilateral bifrontal-occipital electroencelphalogram, beat-to-beat cardiac output. Electromyographic (EMG) activity was recorded from 5 different muscle groups: biceps(B), intercostal(IC), abdominal(ABD), gastrocnemius(G), and quadriceps(Q). In addition, each patient had a pulse oximeter placed on the hand opposite from the arterial line and a transcutaneous oxygen (Tc02) electrode placed on the left upper chest below the clavicle. All data were recorded on a Hewlett Packard 8 channel strip-chart recorder and a Vetter E tape recorder. EMG data was analyzed by conversion to the root-mean-square method of power analysis. EMG data were compared to 9 previously obtained saline pretreatment controls.[1]

Before induction each patient received an intravenous fluid bolus of 7cc/kg of lactated ringers solution over 5 minutes. Following a 5 minute period of preoxygenation by mask, MDZ 2.5mg was administered i.v. One minute later anesthesia was induced with alfentanil 175µg/kg given over one minute. Following induction patients were observed and monitored for signs of muscle rigidity, hemodynamic instability, oxygen desaturation, or rapid decreases in Tc02 values. The duration of the observation period was up to 4 minutes after the completion of alfentanil infusion. At the end of the observation period or if muscle rigidity was severe, muscle relaxants (pancuronium 0.04mg/kg and metocurine 0.02 mg/kg) were administered and ventilation with 100% oxygen by bag and mask was begun. Patients were then intubated orally and the anesthetic was continued at the direction of the attending anesthesiologist. Results of this MDZ group were compared to the saline pretreatment model.[1] All data was analyzed using two way ANOVA, followed by a Newman-Keuls analysis.

Results: There was no difference in patient demographics. Patients pretreated with MDZ had significantly attenuated muscle rigidity following A administration when compared to the saline pretreatment group in the B, ABD, and IC muscle groups.(figure 1-3) Attenuation of rigidity approached significance in the G group(fig 4), but not in the Q group. However, there is a decrease in rigidity protection that occurs with time as the peak effects of MDZ wear off. One patient had moderately severe rigidity 3 minutes after A infusion when ventilation by bag and mask was attempted.

Discussion: Our results demonstrate that MDZ administered one minute prior to A induction is a clinically feasible method to attenuate the muscle rigidity associated with potent opioid induction. This study further confirms the impression that two groups of muscles can be delineated in describing muscle rigidity: central (IC and ABD) and peripheral (G,Q). MDZ had a significant protective effect the groups that most concern the anesthesiologist. When compared to D,MDZ pretreatment compared favorably in terms of central muscle group protection, but the effects of MDZ wore off, quite promptly. Although D appeared to protect all muscle groups it needed to be administered 5-10 prior to induction,[1] whereas, MDZ can and should be administered closer to the time of induction.

References

1. Benthuysen JL, Smith NT, Sanford TJ, et al. Physiology of alfentanil-induced rigidity. Anesthesiology 64:440-446, 1986.
2. Blasco TA, Smith NT, Sanford TJ, et al. A clinical study of the effects of various pretreatment agents on alfentanil-induced rigidity: EMG data. Anesthesiology 63:A380, 1985.

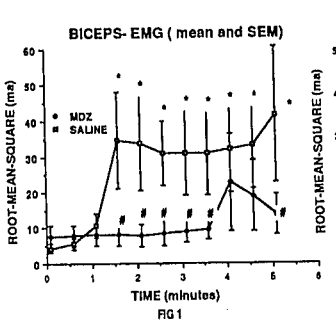

FIG 1

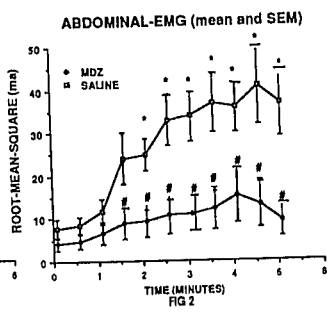

FIG 2

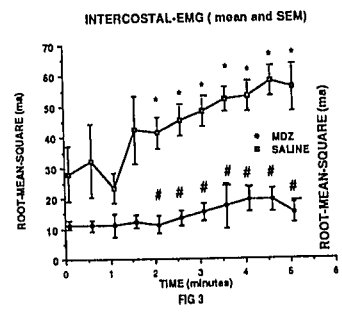

FIG 3

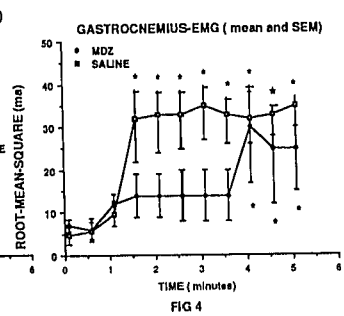

FIG 4

*=p<.05 from control
#= p<.05 MDZ vs Saline