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Diazepam Depresses the Ventilatory Response to Carbon Dioxide

To the Editor:—In their recent article,[1] Bailey *et al.* once again raise the question of whether diazepam causes significant depression of the hypercarbic ventilatory response. In 1982, we used the dual isohypercapnic method to measure the time course of ventilatory depression after diazepam, 0.4 mg/kg iv, and found that the slope of the ventilatory response to hypercarbia was significantly depressed for at least 25 min.[2] In a second study,[3] we used Read's rebreathing method and found that diazepam, 0.4 mg/kg, reduces the slope of the ventilatory response to carbon dioxide from 2.41 to 1.30 $l \cdot min^{-1} \cdot mmHg^{-1}$ ($P < 0.001$) within 5 min.

Why, then, were Bailey and his colleagues unable to demonstrate this statistically and clinically significant depression of ventilatory drive? First, their diazepam dose (0.1 mg/kg) is relatively low for young, healthy volunteers. In fact, recommended doses for endoscopic procedures range from 0.15 to 0.3 mg/kg. Clearly, larger doses should be used in fit, young volunteers to predict the effect of clinical doses in elderly or frail patients, who may be more susceptible to diazepam's adverse effects.[4] A second consideration is the statistical analysis of the results. While the authors are to be commended for avoiding the "multiple *t*-test trap," their use of Bonferroni adjusted *t* tests may have been overly conservative. Indeed, had the authors used a more appropriate test, such as the Newman-Keuls or Dunnett's test, the *P* value for ventilatory depression at 5 min would almost certainly have decreased from 0.0508 to less than 0.05. Then, of course, the authors would have written a different paper: "Diazepam decreases the ventilatory response to carbon dioxide." This is but another example of "absence of evidence is not evidence of absence."[5]

Before the authors may state, "The results of this study demonstrate that diazepam, as a 0.1 mg/kg iv bolus, did not depress the ventilatory response to CO_2 . . . ,"[1] they must perform a power analysis to determine the probability of a type II error. Because such an analysis would certainly show that this probability is high (in view of the *P* value of 0.0508), I believe that Bailey's study is best interpreted as confirming our earlier findings of ventilatory depression after iv diazepam.

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In reply:—Dr. Gross questions our findings and interpretation in the article, "Variability of the respiratory response to diazepam." He makes two suggestions in support of his contention that diazepam does depress the ventilatory response to carbon dioxide.

First, Dr. Gross suggests our dose (0.1 mg/kg) was too low and that larger doses (0.4 mg/kg) should be used. Our intention was not to study anesthetic induction doses of diazepam, but rather the sedative doses frequently used for local standby or regional anesthesia or as supplements in general anesthesia. We, therefore, thought a study of the effects of 0.1 mg/kg to be clinically relevant. Nevertheless, others have also found that higher doses of diazepam (0.15 and 0.29 mg/kg iv) do not produce significant depression of the ventilatory response to CO_2.[1,2] Interestingly, variability of response is also seen in some subjects in those studies.

Dr. Gross also questions our statistical approach. He is incorrect in his assumption that we used Bonferroni adjusted paired *t* tests as the basis for our statement that at

no time did diazepam produce statistically significant decreases in the ventilatory response to CO_2. As stated in "Materials and Methods," we used a form of multivariate analysis for repeated measures to show no change in the slope of $\dot{V}_E/PET_{CO_2}$ after diazepam. That test statistic was F 4, 20 = 1.6013, $P = 0.2129$. As the joint hypothesis was not rejected, Bonferroni adjusted paired t tests were not used. The P value 0.0508 represents a simple t test without Bonferroni adjustment. Admittedly, this is not pointed out and has perhaps led Dr. Gross to misinterpret our findings. Therefore, contrary to what Dr. Gross suggests, the P value for ventilatory depression at 5 min should, if anything, be larger, not smaller. Therefore, we believe our conclusions and title should remain the same to emphasize the significant variability of the respiratory response to diazepam.

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Partial Expiratory Limb Obstruction by a Foreign Body Abutting upon an Ohio® 5400 Volume Monitor Sensor

To the Editor:—Obstruction of the expiratory limb of an anesthetic circuit is a rare but potentially lethal occurrence. Such obstructions are associated with incomplete pre-use circuit checking,[1] inappropriate circuit assembly,[1,2] the presence of a foreign body,[1,3–6] or anesthetic apparatus placed in the expiratory limb.[1,7] We wish to describe an episode of expiratory limb obstruction by an accidentally created foreign body abutting upon an Ohio® 5400 Volume Monitor Sensor.

An otherwise healthy patient was to undergo mediastinal node biopsy under general anesthesia. Prior to induction, an Ohmeda Modulus® II anesthetic circuit and ventilator, assembled by a previous operator, were tested for leaks and alarm function *via* thumb occlusion of the patient connector with the mask attached. Both inspiratory and expiratory valves had appropriate movement with positive pressure, and both nitrous oxide and oxygen flow meters demonstrated flow. After induction adequate positive pressure ventilation *via* mask was obtained with no inspiratory or expiratory obstruction noted. Following tracheal intubation, breath sounds were equal bilaterally with manual ventilation. Subsequently, the ventilator was engaged, whereupon 10–15 cmH_2O of positive pressure was noted in the circuit during the expiratory phase. The expiratory limb was immediately disconnected from the Ohio® 5400 Volume Monitor Sensor. A disc of clear plastic was seen partially obstructing the expiratory limb, abutting upon the patient side of the volume monitor sensor (fig. 1). It was removed, and the circuit was reassembled, with no further expiratory obstruction being present.

FIG. 1. Plastic disc abutting upon volume monitor sensor in expiratory limb.