Diazepam Prevents Fentanyl-induced Muscle Rigidity

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Although high-dose fentanyl-oxygen anesthesia has been widely used for cardiac surgery[1], the most serious and frequently encountered disadvantage of this technique is the development of truncal rigidity[2]. Fentanyl-induced rigidity has been shown to produce hypercarbia, a potent stimulus of pulmonary vasoconstriction[3]. Kallos et al.[4] reported that in man, increased expiratory muscle activity was present even in the absence of clinically evident rigidity. This caused a reduction of functional residual capacity and total chest compliance.

Neuromuscular blocking drugs relieve the rigidity[5-8]. Anesthetic drugs such as thiopental, enflurane and halothane probably prevent or reduce it[8]. Patient awareness precludes muscle relaxant administration to prevent such rigidity. Even if the above anesthetics were able to prevent or reduce truncal rigidity during cardiac anesthesia, they may produce cardiovascular depression. To prevent awareness, diazepam has been employed as a supplement to fentanyl-oxygen anesthesia. Unlike the above drugs[8,10,11] diazepam causes a very mild degree of ventilatory and cardiovascular depression.

The purpose of this study was to demonstrate if diazepam pretreatment would prevent truncal rigidity during high-dose fentanyl and oxygen anesthesia.

Materials and Methods

Twelve patients scheduled for open heart or myocardial re-vascularization surgery were selected for study. Patient age ranged from 20–70 years (mean 52) and weight ranged from 45–68 kg (mean 57). All patients were free of hepatic, renal or neuromuscular diseases. Premedication consisted of intramuscular morphine hydrochloride 10 mg. and scopolamine 0.4 mg., one hour prior to arrival in the operating room.

Prior to induction of anesthesia, venous lines were placed and a radial artery was cannulated. Induction of anesthesia was begun with a 0.2 $mg \cdot kg^{-1}$ of diazepam intravenously. Concomitantly, the patients breathed 100% oxygen via a semiclosed circle with a carbon dioxide absorption system. After 3 min of diazepam injection, 100 $\mu g \cdot kg^{-1}$ of fentanyl was infused over 2 min. Arterial blood pressure, heart rate and the electrocardiogram were continuously monitored throughout the study. Ventilation was assisted or manually controlled ($F_{I_{O_2}} = 1.0$).

Truncal rigidity was diagnosed when ventilation by the anesthesiologist became impossible. A neuromuscular blocking agent was then administered to facilitate ventilation. Arterial blood gases were measured

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Table 1. The changes in heart rate (HR, beats·min^{-1}), mean arterial blood pressure (mAP, mmHg) and arterial blood-gas analyses (BGA) after fentanyl administration with diazepam pretreatment (Means ± SD)

			BGA			
	HR	mAP	pH	Pa_{CO_2} (mmHg)	Pa_{O_2} (mmHg)	BE (mEq·l)
Awake control	80 ± 20	99 ± 21	7.4 ± 0	38 ± 4.7	77 ± 11	-0.4 ± 1.8
After fetanyl						
50 $\mu g \cdot kg^{-1}$	66 ± 13*	85 ± 17*	7.4 ± 0	39 ± 6.1	423 ± 79*	-1.1 ± 2.2
100 $\mu g \cdot kg^{-1}$	65 ± 13*	84 ± 17*	7.4 ± 0	42 ± 8.0	451 ± 92*	-1.3 ± 2.0

*$P < 0.01$, Student's paired t-test when compared to control values

before diazepam injection (control values) and after administration of 50 $\mu g \cdot kg^{-1}$, 100 $\mu g \cdot kg^{-1}$ of fentanyl.

Data were analyzed using Student's paired t-test.

Results are presented as the mean ± 1 SD with a statistically significant change being considered to have occurred when the P value was 0.05 or less.

Results

The date are summarized in table 1. Chest wall rigidity did not develop to a degree that impaired ventilation. No patient required a neuromuscular blocking agent to relieve the rigidity. Significant hypercarbia after 50 $\mu g \cdot kg^{-1}$ or 100 $\mu g \cdot kg^{-1}$ of fentanyl administration did not occur. However, significant decreases in mean arterial blood pressure and heart rate were seen after fentanyl injection when compared to the control valves.

Discussion

One hazard of high-dose intravenous fentanyl is the incidence of truncal rigidity causing impairment of adequate ventilation[2]. Comstock et al.[3] reported that truncal rigidity occurred in 20 of 21 patients after an average dose of 19 $\mu g \cdot kg^{-1}$ of fentanyl at an infusion rate of 200 $\mu g \cdot min^{-1}$. They reported the necessity to administer a neuromuscular blocker to provide adequate ventilation. After fentanyl-oxygen anesthetic induction, Hill et al.[5] found that 9 of 10 patients became rigid. The average fentanyl infusion was 14 $\mu g \cdot kg^{-1}$ at a rate of 3 $\mu g \cdot kg^{-1} \cdot min^{-1}$. Scamman[12] reported that failure to maintain bag-mask ventilation occurred at a mean fentanyl dose of 17 $\mu g \cdot kg^{-1}$, and infusion rate of 3 $\mu g \cdot kg^{-1} \cdot min^{-1}$. Kentor et al.[13] used a more rapid injection of fentanyl and experienced a 100 per cent incidence of muscle rigidity. In their report, patients developed truncal rigidity after receiving 50 $\mu g \cdot kg^{-1}$ fentanyl, over 60 sec. Pa_{CO_2} increased by 11 mm Hg before paralysis reversed the rigidity.

In the present study, although fentanyl was given in a dose of 100 $\mu g \cdot kg^{-1}$ for 2 min. similar to Kentor's study, we did not encounter truncal rigidity or hypercarbia. Prior administration of diazepam seemed to prevent fentanyl-induced rigidity.

Scamman[12] recently reported that glottic closure secondary to fentanyl-induced rigidity was the major cause of inadequate ventilation during fentanyl-oxygen anesthesia induction. Bailey et al.[7] reported that pretreatment with diazepam did not effect the incidence of rigidity. Our results differ from their findings. Their subjects were scheduled for general, orthopedic or gynecologic surgery without premedication. All received glycopyrrolate IV just prior to anesthetic induction. The diazepam dosage was smaller than in our study. Whether underlying disease, premedication, or the diazepam dosage can modify or attenuate the effects on fentanyl-induced rigidity requires further investigation.

Benzodiazepine-induced muscle relaxation may result from its glycine-mimetic effects

in the spinal cord[14]. Narcotic-induced muscle rigidity probably results from supraspinal effect[15]. However, this hypotheses in regard to fentanyl-induced rigidity cannot completely explain the attenuative effects of rigidity by diazepam.

In spite of possible cardiovascular depression[2,7,16], many anesthesiologists recommend the use of diazepam during fentanyl-oxygen relaxant anesthesia to prevent unfavorable hemodynamic sequences as well as recall[17] and awareness[9]. The results of the present study indicate another beneficial effect of diazepam pretreatment for high-dose fentanyl-oxygen anesthesia.

In conclusion, 0.2 $mg \cdot kg^{-1}$ dose of diazepam administered before high-dose fentanyl can completely prevent truncal rigidity. Prior administration of diazepam may be advisable to prevent both truncal rigidity and awareness during high-dose fentanyl-oxygen anesthesia.

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