attributed to hydroxyurea, a recent addition to the therapeutic regimen for hypereosonophilia. Hydroxyurea causes hemopoietic depression involving leukopenia, megablastic anemia and thrombocytopenia and blocks DNA synthesis through action on ribonucleoside diphosphace reductase.[7]

The etiology of the embolization and a laboratory test to predict the thrombotic tendency of the hypereosinophilic patient is unknown. Therefore, extreme difficulty was anticipated in achieving adequate anticoagulation during cardiopulmonary bypass. However, in our case, the absence of clot seemed to correlate with a therapeutically prolonged ACT. When our patient's ACT was near the normal value (less than 160 s), thrombosis was evident despite heparin administration and prolonged PTT and TT.

The ACT is a nonspecific test that detects deficiencies of any procoagulant other than factor VII[8] which correlates with the concentration and the semilogarithmic disappearance of heparin in the blood.[9,10] An ACT value of less than 300 s indicates insufficient heparin during a surgical procedure; more than 600 s indicates overheparinization.[10]

We recommend the ACT be carefully monitored in patients with hypereosinophilic syndrome. In our particular case, the ACT seemed to reflect the degree of anticoagulation though this cannot be explained theoretically. In view of the clinical embolization that may occur with hypereosinophilic syndrome, the need for additional heparin may be necessary and dose titrated by ACT monitoring.

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Prevention of Rigidity during Fentanyl–Oxygen Induction of Anesthesia

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Induction and maintenance of anesthesia with high-dose fentanyl and oxygen has been shown to cause minimal changes in cardiovascular dynamics in patients with mitral valvular disease[1] and in those undergoing surgery for myocardial revascularization.[2] Stanley and Webster[1] found that 10 μg/kg did not significantly change any cardiovascular variable studied and that 20 μg/kg produced a significant decrease in heart rate and mean arterial pressure without affecting stroke volume, cardiac output, central venous pressure, or peripheral vascular resistance. One of the frequently reported disadvantages of fentanyl is the development of chest and abdominal wall rigidity. In a series of 359 patients, 285 (79.4 per cent) developed this complication[3] following an infusion of 8.8 μg/kg administered over a period of 1 min, resulting in slight to total inability to inflate the chest. More recently, Comstock *et al.*[4] using 200 μg/min fentanyl reported a high incidence of rigidity associated with hypercarbia and Kentor *et al.*[5] using 50 μg/kg infused over 60 s reported 100 per cent occurrence of rigidity. Stanley,[1] infusing 50–200 μg/kg fentanyl reported no incidence of rigidity. Lunn *et al.*[2] using 300 μg/min fen-

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tanyl reported a small reduction in chest wall compliance which did not impair ventilation.

In view of these conflicting reports and our clinical impression that rigidity frequently occurs, we designed the following study 1) to establish the incidence of rigidity with high-dose fentanyl–oxygen induction of anesthesia, 2) to assess the efficacy of a simultaneous infusion of pancuronium in preventing rigidity, and 3) to compare the hemodynamic effect of intravenous fentanyl alone to that of fentanyl with a simultaneous infusion of pancuronium.

Materials and Methods

The protocol was approved by the Committee to Review Grants for Clinical Research and Investigation Involving Human Beings at the University of Michigan. Twenty ASA Class III and IV patients of either sex undergoing elective open heart surgical procedures were studied. All patients were premedicated with 0.15 mg/kg morphine, im, and 6 μg/kg scopolamine one hour prior to arrival in the operating room. Prior to induction of anesthesia two peripheral venous lines were placed, a radial artery cannulated, and a Swan-Ganz catheter floated into the pulmonary artery via the internal jugular vein. The study was conducted in a double-blind fashion and the patients randomized into one of two groups. Group 1 (n = 10) consisted of seven patients undergoing coronary artery bypass procedures and three patients for valve replacement. These ten patients received 25 μg/ml fentanyl infused at a rate of $3 \mu g \cdot kg^{-1} \cdot min^{-1}$ to a total dose of 2,500 μg. Group 2 (n = 10) was composed of six patients undergoing coronary artery bypass procedures, three patients for valve replacement, and one patient for closure of ventricular septal defect. These ten patients were given an infusion of fentanyl identical to that given to Group 1 plus a simultaneous infusion of 100 μg/ml pancuronium infused at a rate of $12 \mu g \cdot kg^{-1} \cdot min^{-1}$ to a total dose of 10 mg. The patients remained unstimulated until the total doses had been administered, then endotracheal intubation was performed. Throughout the period of study the arterial pressure, pulmonary artery pressure, heart rate, and electrocardiogram were continuously recorded on a Gould® 4 channel recorder and ventilation was assisted or controlled manually with 100 per cent oxygen. If difficulty with ventilation occurred, airway obstruction was ruled out by the staff anesthesiologist and the subjective diagnosis of rigidity was confirmed by a second observer who was unaware of the composition of the infusion. The rigidity was treated with a bolus injection of 10 mg pancuronium.

The patients were interviewed within 24 h of extubation and again between 48 and 72 h after extubation. On each occasion they were directly asked if they recalled any sensation of choking, of muscular weakness or stiffness, or difficulty in breathing. They were also asked if they recalled tracheal intubation or surgical stimulus.

In order to compare the hemodynamic response during the study period, measurements were recorded at the intervals shown in table 1 and the measurements compared to control values using Student's paired t test. For comparison between the groups, Student's unpaired t test was used. To compare the incidence of rigidity χ^2 test was used.

Results

There was no significant difference between the groups as regards age, weight, or length of time of induction. The mean (±SD) total doses administered before intubation were 35.53 ± 10.38 μg/kg fentanyl and 0.14 ± 0.04 mg/kg pancuronium. The mean length of time of induction was 11.85 min (range 7.75–20.83 min).

Of the ten patients who received fentanyl alone, nine became rigid; of the ten who received fentanyl and pancuronium none became rigid ($\chi^2 = 16.364$, $P < 0.001$). The mean dose at which rigidity occurred was 14.56 μg/kg ± 4.17 SD.

Table 1. Hemodynamic Parameters (Means ± SD)

	Fentanyl/Pancuronium			Fentanyl Only*		
	MAP (torr)	MPAP (torr)	HR (beats/min)	MAP (torr)	MPAP (torr)	HR (beats/min)
Pre-induction (control)	90 ± 15	31 ± 18	76 ± 23	97 ± 16	27 ± 17	70 ± 22
Fentanyl, 7.5 μg/kg	90 ± 16	32 ± 18	76 ± 25	92 ± 17†	27 ± 15	62 ± 21†
Fentanyl, 15 μg/kg Or at the Time of rigidity	84 ± 12	32 ± 18	82 ± 28	88 ± 22	31 ± 17†	66 ± 22
1 min later	81 ± 10	31 ± 18	81 ± 23	90 ± 15	28 ± 13	82 ± 28
2 min later	85 ± 13	30 ± 17	83 ± 22	91 ± 17	28 ± 13	80 ± 24
3 min later	85 ± 13	30 ± 18	82 ± 21	92 ± 20	26 ± 12	78 ± 22
End of induction	89 ± 15	31 ± 18	86 ± 19†	87 ± 20	25 ± 13	82 ± 24

MAP = mean arterial pressure; MPAP = mean pulmonary arterial pressure; and HR = heart rate.

* Data are shown only for the nine patients who became rigid.
† $P < 0.05$ compared to preinduction values.

On comparing the hemodynamic response at the time intervals shown in table 1 with preinduction values, it was noted that in the nine patients who received fentanyl alone and became rigid, there was a significant increase in mean pulmonary arterial pressure (MPAP) at the time of rigidity and there was a significant fall in mean arterial pressure (MAP) after 7.5 μg/kg fentanyl had been administered. In the group who received the combination infusion there was no change in MPAP or in MAP throughout the period of study. When comparing heart rate with control values in the group who received fentanyl alone, there was a significant decrease in rate after 7.5 μg/kg had been infused, and in the group who received fentanyl and pancuronium there was a statistically significant increase in heart rate at the end of induction (table 1). When the hemodynamic responses were compared between the groups there was no significant difference at any time point.

On postoperative questioning no patient had any recall of muscle weakness or stiffness, difficulty with secretions, a sensation of choking, nor difficulty with breathing, nor had they any recall of tracheal intubation or surgical stimulation.

Discussion

We have clearly demonstrated a high incidence of rigidity with a fentanyl infusion of 3 $\mu g \cdot kg^{-1} \cdot min^{-1}$. This agrees with the findings of earlier investigators[3-5] but conflicts with the report of Stanley and Webster.[1] A possible explanation of this may be that Stanley administered succinylcholine at a mean dose of fentanyl of 11 ± 3 μg/kg whereas we did not observe rigidity until a mean dose of fentanyl of 14.6 ± 4.2 μg/kg had been given. Although the diagnosis of rigidity was made subjectively we had no difficulty in reaching such a diagnosis as adequate controlled ventilation became impossible until the bolus of pancuronium became effective. Fentanyl rigidity has been shown to produce hypercarbia[4,5] which is a potent stimulus for pulmonary vasoconstriction and this might account for the significant increase in MPAP observed at the time of rigidity.

Obviously one of the criticisms of a concomitant infusion of a muscle relaxant is the possibility of a patient being aware while being paralyzed. Stanley found that patients were unresponsive to pin prick stimulus of the chest wall after 11 μg/kg fentanyl. Lunn, *et al.*[2] reported unresponsiveness to verbal command at a mean dose of 18 μg/kg fentanyl with a range of 13–22 μg/kg. When recognized amnesics such as diazepam or scopolamine were omitted, Knight *et al.*[6] found 50 per cent of patients were amnesic to visual stimuli at a mean dose of 6–7 μg/kg fentanyl. The differences in mean levels at which unresponsiveness is observed may be related to the criteria for assessing unresponsiveness or to the patient population and will be influenced by the addition of known amnesics and additional therapy.

Following premedication with morphine and scopolamine we found none of the patients had recall of muscle weakness nor rigidity. Provided ventilation is assisted or controlled, we would suggest that by a simultaneous infusion of fentanyl and pancuronium, rigidity can be eliminated without compromising the hemodynamic stability associated with high-dose fentanyl induction of anesthesia.

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