Wakefulness during the Induction with High-dose Fentanyl and Oxygen Anesthesia

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The purpose of this study was to investigate the state of wakefulness during the induction of anesthesia with high-dose fentanyl using the isolated forearm technique. Ten patients scheduled for elective cardiovascular surgery were premedicated with morphine (0.15 mg/kg) and scoploamine (0.3–0.4 mg) intramuscularly one hour before induction. The induction of anesthesia was performed by intravenous administration of 100 μg/kg of fentanyl in 15 min or over. The pneumatic tourniquet applied on the left upper arm was inflated to 220–240 mmHg after 10 μg/kg of fentanyl was given and then pancuronium was administered. Verbal commands were given to the patient after 25, 50, 75 and 100 μg/kg of fentanyl was administered. Eight patients out of 10 responded to the verbal commands after administration of 25 μg/kg of fentanyl. Six patients also responded after administration of 100 μg/kg of fentanyl and diazepam 5 mg was given to prevent tachycardia and rigidity during endotracheal intubation. Muscle rigidity and tachycardia were noticed in three and four patients respectively. These complications disappeared by diazepam administration.

It was noted that wakefulness frequently occurred during the induction by high-dose fentanyl and oxygen anesthesia. To prevent such wakefulness therefore, it is necessary to use anesthetic supplements which do not cause cardiovascular depression. (Key words: high-dose fentanyl, isolated forearm technique, cardiovascular operation, wakefulness)

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High-dose fentanyl and oxygen anesthesia has been generally used for cardiac surgery because of its minimal cardiovascular depressive effects since Stanley et al. made their report in 1978[1]. Fentanyl used as a sole anesthetic, however, may not always produce amnesia or unconsciousness in the patients[2]. Several cases have been reported in which patients showed awareness and recall during operation under high-dose fentanyl and oxygen anesthesia[3–6].

We unexpectedly found the evidence of wakefulness during the induction of high-dose fentanyl and oxygen anesthesia.

In this study, therefore, the evidence of wakefulness during induction of high-dose fentanyl and oxygen anesthesia was investigated in 10 patients scheduled for elective cardiovascular surgery by using the isolated forearm technique described by Tunstall (1977)[7].

Methods

The subjects of the study were 10 patients

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Table 1. Patient Characteristics

Patient No	Age (yr)	Sex	Weight (kg)	Risk (ASA)	Diagnosis
1	33	F	48	II	Mitral regurgitation
2	40	F	61	II	ASD
3	21	M	56	II	ASD
4	56	M	54	II	Thoracic aneurysm
5	55	M	50	III	Aortic annular micotic aneurysm
6	32	F	56	II	Aortic stenosis and regurgitation + Mitral stenosis
7	40	F	49	II	ASD
8	23	M	59	II	Mitral stenosis and regurgitation
9	52	F	50	II	Mitral stenosis
10	46	M	54	II	Mitral stenosis

classified as ASA II or III and scheduled for cardiovascular surgery (table 1). Their ages ranged from 21 to 56 years, average age 40 years. Approval from the Institutional Ethical Committee of Sapporo Medical College and Hospital was granted for the study, and informed consent was obtained from patients.

The patients were premedicated with 0.15 mg/kg of morphine and 0.3 to 0.4 mg of scopolamine intramuscularly one hour before the induction of anesthesia. In the operating room, electrocardiographic (ECG) monitoring was done, and radial and venous catheters were inserted percutaneously in the right hand under local anesthesia. A pneumatic tourniquet with 13 cm width was wrapped around the left upper arm. A cuff of endotracheal tube (I.D. 8.5, Portex Limited, England) filled with water was placed in the palm of left hand. The pressure produced by compression of the cuff was displayed on a chart of a recorder through a pressure transducer connected to the cuff.

Before the induction of anesthesia, headphones were placed over the patients' ears, and they were trained to squeeze the cuff when a verbal message was given from a tape recorder. The induction of anesthesia was conducted by an intravenous administration of 100 μg/kg of fentanyl in 15 min or over. During fentanyl infusion ventilation by face mask was assisted initially and controlled afterwards. The pneumatic tourniquet on the left upper arm was inflated to 220–240 mmHg after fentanyl infusion of a dose of 10 μg/kg. Following this divided doses of 0.08 mg/kg of pancuronium were administered intravenously. The verbal message from the tape recorder was given to the patient after fentanyl infusion of 25, 50, 75 and 100 μg/kg, respectively. Compression of the cuff in the hand of isolated left forearm was plotted as pressure curves on a recorder.

The patients were intubated after fentanyl infusion of 100 μg/kg. When the patient moved at the endotracheal intubation, 0.05–0.1 mg/kg of diazepam was intravenously given. After intubation, the patients were ventilated with 100% oxygen, and the tourniquet was released. The patients were interviewed to confirm the evidence of wakefulness or awareness during anesthesia on the third day after surgery.

Results

Patients appeared well sedated in the operating room except one patient (Case 4) with slight anxiousness. The results of the response of the patient to the verbal messages from a tape recorder are summarized in table 2. Eight patients responded to verbal commands after 25 μg/kg of fentanyl administration. Six patients also responded

Table 2. Results

Patient No	Dosage of fentanyl (μg/kg) 25	50	75	100	Complications
1	+	+	+	+	
2	+	+	+	+	
3	+	+	+	+	Rigidity Tachycardia
4	+	+	+	+	Rigidity
5	+	+	+	+	Tachycardia
6	−	−	−	−	
7	+	+	−	−	
8	−	−	−	−	Tachycardia
9	+	+	−	−	
10	+	+	+	+	Rigidity Tachycardia

+ = response to verbal commands, − = no response to verbal commands

after administration of a dose of 100 μg/kg, therefore supplemental administration of diazepam (0.05 to 0.1 mg/kg) was required until their responses disappeared.

Figure 1 shows an example of pressure curves produced by compression of the cuff after fentanyl infusion of 25, 50, 75 and 100 μg/kg, respectively.

Complications during the induction of anesthesia are summarized in table 2. Muscle rigidity appeared on the isolated forearm in three patients. Tachycardia (more than 120 per min) occurred in four patients. The rigidity and tachycardia disappeared after intravenous administration of 5 mg of diazepam.

There was no significant hypotention following administration of diazepam. In the postoperative interview none of the patients could recall any intraoperative events or dreams.

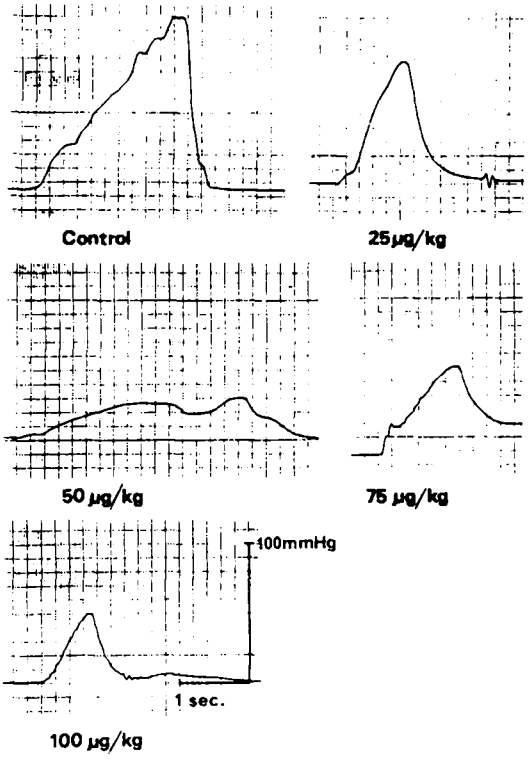

Fig. 1. An example of the pressure curves produced by compression of the cuff placed in the palm of left hand after 25, 50, 75 and 100 μg/kg of fentanyl administration, respectively.

Discussion

Although the analgesic potency of fentanyl is estimated to be about 100 times as strong as morphine, awareness episodes in high-dose fentanyl and oxygen anesthesia have been reported rather frequently[3−6]. The episodes occurred at the sternal incision, the start of cardiopulmonary bypass or after cardiopulmonary bypass. It is presumed that such episodes occurred in low plasma concentrations of fentanyl[8]. Intraoperative awareness certainly is undesirable for the patients undergoing cardiovascular surgery because of eliciting hypertensive crisis during operation[6]

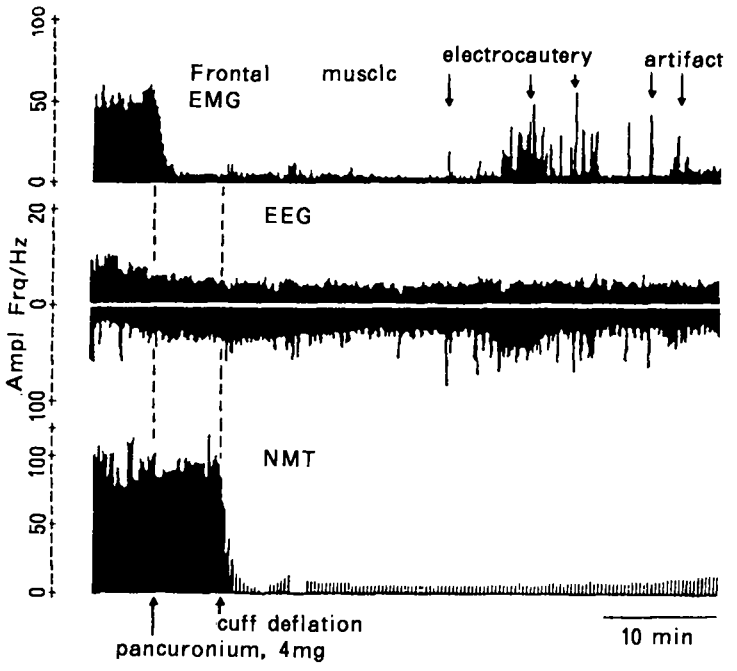

Fig. 2. An example of a frontal muscle EMG, EEG and neuromusclar transmission monitor (NMT) described by Anesthesia and Brain Monitor (DATEX). The highest line shows that a frontal muscle electromyograph decreases after pancuronium administration. The lowest line shows that the muscle action potentials of the abductor digiti minimi after pancuronium administration has no suppression in the forearm isolated by inflation of the cuff, however they show suppression by deflation of the cuff. The monitor therefore shows that the left forearm is isolated from the general circulation by an air inflated tourniquet cuff.

or psychiatric symptoms in the postoperative period[9].

We first found out that many of the patients could respond to verbal commands even when the plasma concentration of fentanyl was increased. In our study, four patients had tachycardia during induction of anesthesia and three of them could respond to verbal command after 100 μg/kg of fentanyl. And then all of these tachycardic episodes resolved after a supplement of intravenous diazepam without significant hypotention.

Incidentally, the term of awareness refers to the situation where a patient remembers either awaking or having an unpleasant dream during operation. On the other hand, the term of wakefulness refers to the situation where a patient indicates awaking behaviors during operation even though he cannot recall the behavior afterwards[7]. There are several case reports of patients with awareness during high-dose fentanyl and oxygen anesthesia[3–6]. However, in our study, we demonstrated that more than half of patients could respond to verbal commands after 100 μg/kg of fentanyl administration by using the isolated forearm technique, and that none of them could recall their experiences of squeezing a cuff afterwards.

It is known that loss of responses to verbal commands[1,3,8,10–12] or pin prick stimulation[1] could be assumed that the patient be in a state of unconsciousness. However, in these reports, loss of response to verbal commands and rigidity of the chest wall often occurred concurrently at a dose of 8–19 μg/kg of fentanyl. Therefore many of patients required neuromuscular blockade in order to provide adequate ventilation prior to unconsciousness[10–12]. This fact shows that patients might be awake during induction after the administration of muscle relaxant.

The method for detecting consciousness would be necessary with administration of muscle relaxant in high-dose fentanyl and oxygen anesthesia.

In 1977, Tunstall introduced the isolated forearm technique which demonstrated a response to verbal commands by preventing spread of relaxant drug into one forearm isolated by an inflated pneumatic tourniquet[7]. This method is useful for detecting wakeful-

ness in a light plane of general anesthesia with administration of a muscle relaxant. Because the sense of hearing is the last to go and the first to return after anesthesia[13].

We investigated the usefulness of this method by using Anesthesia and Brain Activity Monitor (DATEX) before the start of this study. An example is shown in figure 2. Muscle action potentials of the abductor digini minimi in isolated forearm show no suppression after pancuronium administration because of the inflation of pneumatic tourniquet.

To guard against awareness, the addition of anesthetic supplements such as diazepam, scopolamine, or N_2O has been recommended during high-dose fentanyl and oxygen anesthesia[2,4,14]. However, it was known that the addition of one or more of these supplements might produce cardiovascular suppression under high-dose fentanyl and oxygen anesthesia[1,2,8]. In our study, there was no case with significant hypotension following diazepam administration, when it was needed just to abolish consciousness.

In Case 3 and Case 10, muscle rigidity and tachycardia occurred concurrently during fentanyl infusion, but these ceased immediately after the administration of diazepam.

In conclusion, this study clearly showed the appearance of wakefulness during the induction of high-dose fentanyl and oxygen anesthesia by using isolated forearm technique. To prevent and treat the wakefulness of fentanyl anesthesia, it is necessary to give anesthetic supplements without cardiovascular depression, such as a small dose of diazepam.

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