CASE REPORTS

Anesthesiology
80:457–459, 1994

Prolonged Neuromuscular Blockade after a Single Bolus Dose of Vecuronium in Patients with Acquired Immunodeficiency Syndrome

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FACTORS influencing the onset time and potency of neuromuscular relaxants include drug interactions and disease states.[1] Acquired immunodeficiency syndrome (AIDS) is often associated with neurologic dysfunction[2–4] or myopathy[5] at times secondary to the administration of antiretroviral agents.[6,7] This study was designed to examine the effects of vecuronium in patients with AIDS and to compare these effects with those in normal subjects.

Case Reports

Materials and Methods

After approval from Hospital Committee on Human Research, five patients with AIDS (four men and one woman, ASA physical status 2 or 3) and eight patients serving as the control group (six men and two women, ASA physical status 1 or 2), who presented for elective ear-nose-throat surgery, gave their consent to participate in the open nonrandomized study. The patients with AIDS had a history of one or more episodes of infection, the most common being infection of the respiratory system. They were receiving multiple drugs, including antiretroviral agents (table 1).

Hemoglobin, serum potassium, creatinine phosphokinase, lactate dehydrogenase, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, and total bilirubin were measured preoperatively in both groups of patients. All patients received 1.5–2.5 $mg \cdot kg^{-1}$ hydroxyzine (Atarax) and 1 mg atropine, given orally 60–90 min before induction of anesthesia. Fentanyl 0.5–1 $\mu g \cdot kg^{-1}$ and propofol 3 $mg \cdot kg^{-1}$ were administered intravenously to induce anesthesia. The vocal cords were sprayed with 1% lidocaine, and the trachea was intubated without neuromuscular blocking drugs. Anesthesia was maintained with a mixture of oxygen, nitrous oxide, and isoflurane (end-tidal concentration 0.9–1%). The lungs of all patients were mechanically ventilated, with ventilation adjusted to maintain an end-tidal carbon dioxide near 30 mmHg. Hemodynamic and respiratory parameters were monitored throughout anesthesia. Esophageal temperature was not monitored because oropharyngeal and esophageal lesions are common in patients with AIDS. However, operating room temperature, anesthetic technique, and surgical procedure were similar in both groups.

A nerve stimulator (Bio-industry, France) delivered supramaximal square-wave impulses of 0.2-ms duration in a train-of-four sequence at 2 Hz, every 10 s, *via* surface electrodes placed over the ulnar nerve at the wrist. The force of contraction of the adductor pollicis muscle was measured with a force displacement transducer (Curamètre, France) and recorded on paper. Ten minutes after induction of anesthesia, when stable anesthetic conditions had been obtained and baseline neuromuscular recording had been established, a single bolus dose of vecuronium 0.08 $mg \cdot kg^{-1}$ was administered intravenously. The onset time and the duration of relaxation were recorded. The onset time was defined as the interval between the end of injection of vecuronium and maximum depression of the first twitch (T1) tension. At maximum depression, T1 amplitude was zero. The duration of relaxation was defined as the interval from the maximum depression of the first twitch tension until the first twitch had returned to 25% of the baseline twitch tension. At this point, if the operation had been completed, the residual neuromuscular blockade was antagonized with atropine and neostigmine. Otherwise, anesthesia was continued as above until completion of surgery.

The demographic data (age, weight, and height), laboratory test values, onset time, and duration of neuromuscular block were compared between the two groups by applying Student's *t* test for unpaired observations. The normal distribution of each variable within each group of patients was tested with the Kolmogorof test. Differences were considered significant at $P < 0.05$.

Results

The demographic data of patients are given in table 2. The two groups were similar with regard to age, weight, and height.

Hemoglobin concentration was significantly less in the patients with AIDS compared with the control group ($P < 0.001$). In the AIDS group, the serum lactate dehydrogenase, serum alanine aminotransferase, and aspartate aminotransferase concentrations were greater than those in the control subjects (table 3).

Systolic and diastolic arterial pressures and heart rate did not differ between the two groups preoperatively (140 ± 22 mmHg, 79 ± 7 mmHg, and 95 ± 24 beats/min, respectively, in the AIDS group and

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Received from the Department of Anesthesia and Surgical Intensive Care, Hôpital Bichat, Université, Paris, France. Accepted for publication August 31, 1993. Supported in part by a grant from the Ministry of Health, Greece (AF).

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Key words: Infection: acquired immunodeficiency syndrome. Muscle relaxants: vecuronium.

Table 1. History of the Disease, Concurrent Treatment, and Recovery Time to 25% of T1 in Each AIDS Patient

Patient	History of the Disease	Concurrent Treatment	Time to T1/T0 = 25% (min)
1	*Pneumocystis carinii* pneumonia*	Didanosine, folinic acid, ofloxacin, pyrimethamine, metronidazole, bromazepam	102
2	Repeated lung infections, hepatomegaly, cholestasis	Zidovudine, sulfadiazine	67
3	*Pneumocystis carinii* pneumonia,* Hodgkin's disease of tonsils, pneumococcus pneumonia*	Didanosine, ceftazidime, amikacin, pristinamycin, vancomycin	22
4	*Pneumocystis carinii* pneumonia,* tuberculosis,* myalgias	Didanosine, dapsone, pyrimethamine	78
5	Cerebral toxoplasmosis (operated), bronchitis	Didanosine, folinic acid, dapsone, pyrimethamine, phenobarbital	65

* Treated.

140 ± 17 mmHg, 75 ± 12 mmHg, and 95 ± 14 beats/min in the control group). After intubation and before injection of vecuronium, systolic and diastolic pressures were significantly lower in the AIDS group than in the control group (systolic 102 ± 13 compared with 120 ± 8 mmHg, $P < 0.01$, and diastolic 54 ± 7 compared with 65 ± 9 mmHg, $P < 0.05$). Heart rate was significantly higher in the AIDS group when compared with that of the controls (97 ± 10 and 82 ± 11 beats/min, respectively, $P < 0.05$). When the maximal response to vecuronium was observed, the systolic and the diastolic pressures did not differ significantly between the AIDS and control groups (systolic 111 ± 24 and 113 ± 9.1 mmHg, respectively, and diastolic 63 ± 11 and 59 ± 9 mmHg) and neither did the heart rate (97 ± 16 and 80 ± 13 beats/min, respectively). When 25% recovery of the first twitch stimulus occurred, the AIDS and control groups did not differ significantly with regard to the systolic (120 ± 17 and 111 ± 10 mmHg, respectively) and diastolic (66 ± 15 and 59 ± 8 mmHg) arterial pressures and heart rate (82 ± 15 and 71 ± 10 beats/min).

The onset time of neuromuscular blockade produced by vecuronium in patients with AIDS was twice as long as in the control group (3.4 *vs.* 1.5 min; $P < 0.001$). The rate of recovery of the twitch tension to the 25% of baseline also was significantly prolonged in the AIDS group compared with that in the control group (69 *vs.* 32 min; $P < 0.01$) (table 3 and fig. 1).

Discussion

The onset time of neuromuscular blockade produced by vecuronium in our control group was less than that found by other investigators.[8] This difference may be attributed to the different methodology in the induction of anesthesia as well to the train-of-four stimulation, factors enhancing the onset of blockade.[9,10] In patients with AIDS the onset time of vecuronium effect was significantly longer than the onset times in the control group. The significant reduction in systolic blood pressure and the rapid infusion of crystalloids in the AIDS group may account for the this difference in onset times.

The duration of the effect of vecuronium in the AIDS group was twice as long as that in the control group. Peripheral neuropathy associated with AIDS[2-4] and with

Table 2. Age, Body Weight, and Height in the AIDS and Control Groups

	AIDS Group (n = 5)	Control Group (n = 8)
Age (yr)	28.8 ± 2.2	33.4 ± 12.8
Body weight (kg)	56.0 ± 8.3	62.0 ± 4.8
Height (cm)	169.8 ± 8.4	170.7 ± 5.8

Values are mean ± SD.

Table 3. Blood Values, Liver Function Tests, and Neuromuscular Blockade in the AIDS and Control Groups

	AIDS Group (n = 5)	Control Group (n = 8)
Hemoglobin ($g \cdot dl^{-1}$)	11.2 ± 1.2*	15.2 ± 0.8
K^+ (3.6–5 mM)	4.0 ± 0.35	3.9 ± 0.45
Creatinine (<120 μM)	95 ± 21	92 ± 20
CPK (<200 $IU \cdot l^{-1}$)	70 ± 55	91 ± 44.3
LDH (<450 $IU \cdot l^{-1}$)	641 ± 213*	290 ± 50
ALAT (<40 $IU \cdot l^{-1}$)	46 ± 25†	18.6 ± 8
ASAT (<40 $IU \cdot l^{-1}$)	43 ± 32†	16 ± 5.0
Alkal. phosph. (<123 $IU \cdot l^{-1}$)	736 ± 1255	66 ± 15.2
Total bilirubin (20 μM)	6.5 ± 2.4	10.8 ± 3.8
Neuromuscular blockade		
Onset time (min)	3.4 ± 0.5*	1.5 ± 0.5
Range	3.1–4.0	1.1–2
Recovery to T1/T0 = 25% (min)	67 ± 29‡	32 ± 6
Range	22–102	21–38

Values are mean ± SD.

CPK = creatinine phosphokinase; LDH = lactate dehydrogenase; ALAT = alanine aminotransferase; ASAT = aspartate aminotransferase.

* $P < 0.001$ compared with the control group.

† $P < 0.05$ compared with the control group.

‡ $P < 0.01$ compared with the control group.

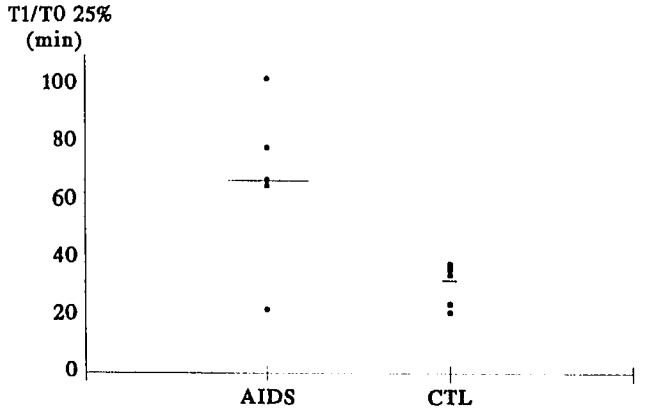

Fig. 1. Individual values (circles) and mean values (horizontal bars) of 25% recovery of the first twitch (minutes) in the acquired immunodeficiency syndrome (AIDS) patients and in the control patients (CTL). T1/T0 = of T1 to T0 (control). T1/T0 25% = time for the T1 to recover to 25% of the control (T0).

didanosine therapy[6] may interfere with the effect of vecuronium. The fibromyalgia syndrome described in these patients[5] or the myopathy due to treatment with zidovudine[7,11] may have altered the response to vecuronium in the AIDS group. Patient 5 (table 1), who had myalgias and arthralgias, exhibited prolonged neuromuscular blockade (78 min).

Prolonged neuromuscular blockade occurred in three of the four patients treated with didanosine (patients 1, 4, and 5). Patient 3 (table 1), in whom the duration of blockade was short, in addition to didanosine received amikacin, an antibiotic reported to prolong neuromuscular blockade.[12]

Hepatitis and elevations in hepatic aminotransferases are complications of both didanosine therapy[6] and human immunodeficiency virus infection.[13] Two of the five patients in the AIDS group had moderately increased alanine aminotransferase and aspartate aminotransferase concentrations, which do not explain the prolonged neuromuscular nondepolarizing blockade. On the contrary, in patient 1, who exhibited the longest blockade (102 min), all liver function tests were normal, except for a slight increase in alkaline phosphatase.

Our study was limited to the 25% recovery measurements because prolongation of anesthesia was not justified by the duration of the surgical procedure. Evaluation of the prolonged neuromuscular blocking effect of vecuronium in patients with AIDS is complex because of the systemic nature of the disease and the concurrent drug use. All of the patients in our AIDS group were receiving multiple drug treatments. Questions regarding the duration of effect of muscle relaxants not dependent on liver and renal function, such as atracurium, remain open to investigation.

We conclude that the neuromuscular effect of a single bolus dose of vecuronium may be significantly prolonged in patients with AIDS. The reasons for this prolonged effect are unclear.

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