MUSCLE RELAXATION IN PATIENTS WITH DUCHENNE’S MUSCULAR DYSTROPHY
Use of Vecuronium in Two Patients

W. BUZELLO AND H. HUTTARSCH

Duchenne’s muscular dystrophy, an inherited X-linked disease, is characterized by severe muscle weakness which is the result of a progressive decrease in the total number of muscle fibres. The disease presents in early childhood, and affects particularly the muscles of the pelvic girdle and thigh [1,2]. Its significance in the management of general anaesthesia has been reviewed in previous articles [3,4]. However, a search of the literature failed to reveal any specific recommendations as to the choice, or dose, of non-depolarizing neuromuscular blocking agents based on evoked twitch recording or on electromyography (EMG). We describe two patients, with particular reference to neuromuscular monitoring and the potential hazards of the use of myoneural blocking drugs in patients with muscular dystrophy.

CASE REPORTS

Patient 1

The significant features of the history of this 4-yr-old boy (98 cm, 16 kg) were motor retardation with inability to lift his head, to crawl, or to achieve a sitting position at the age of 9 months. The diagnosis of Duchenne’s muscular dystrophy was established at that time, based on a marked increase in plasma creatine phosphokinase concentration (4640 u. litre⁻¹), and on muscle biopsy. No halothane contracture test was performed. Hospital admission on the present occasion was for the repair of bilateral inguinal herniae. Premedication consisted of flupromazine 5 mg and pethidine 10 mg i.m., 45 min before the induction of anaesthesia. Anaesthesia was induced with halothane and nitrous oxide in oxygen, administered by face mask. Orotracheal intubation was performed without the aid of a neuromuscular blocking drug. Anaesthesia was maintained with 67 % nitrous oxide and halothane (1–1.5 vol % inspiratory concentration) in oxygen administered through a non-rebreathing system. Neuromuscular transmission was monitored by

SUMMARY

Cumulative 50% and 90% neuromuscular blocking doses of vecuronium were determined in two 4-yr-old boys with Duchenne’s muscular dystrophy. Vecuronium 20 μg kg⁻¹ was required for 50% twitch depression in both patients. The 90% blocking doses were 43 and 57 μg kg⁻¹. Although these data do not indicate a greater than normal sensitivity to vecuronium, the recovery time (75–25% block) of twitch tension was three to almost six times as long as in normal children. The evoked compound EMG, additionally recorded in one patient, reflected almost the same dose–response relationship as twitch tension, yet the EMG recovered faster than the twitch. The present findings do not exclude an increased sensitivity to neuromuscular blocking drugs in a larger population of patients with muscular dystrophy. Thus, the titration of the individual neuromuscular blocking dose with the aid of a nerve stimulator is mandatory. During a previous anaesthetic, cardiac arrest and acute rhabdomyolysis had occurred in one patient. The substitution of suxamethonium by vecuronium, or probably any other non-depolarizing myoneural blocking drug of intermediate or short duration of action, may help to avoid this complication.

WALTER BUZELLO, M.D.; HARTMUT HUTTARSCH, M.D.; University Department of Anaesthesiology, Joseph-Stelzmann-Str. 9, D-5000 Koeln 41, Federal Republic of Germany. Accepted for Publication: April 13, 1987.
VECURONIUM IN DUCHENNE'S MUSCULAR DYSTROPHY

229

TABLE I. Neuromuscular transmission in two patients with Duchenne's muscular dystrophy following incremental i.v. administration of vecuronium. ED\textsubscript{50} and ED\textsubscript{90} = cumulative 50\% and 90\% blocking doses [5], respectively, determined from depression of twitch tension and amplitudes of the evoked compound electromyogram (EMG). \*Extrapolated: 64–37\% block = 12 min

<table>
<thead>
<tr>
<th>Patient 1</th>
<th>Twitch</th>
<th>EMG</th>
<th>Patient 2</th>
<th>Twitch</th>
<th>EMG</th>
</tr>
</thead>
<tbody>
<tr>
<td>ED\textsubscript{50} (\mu g kg\textsuperscript{-1})</td>
<td>20</td>
<td>19</td>
<td>20</td>
<td>57</td>
<td></td>
</tr>
<tr>
<td>ED\textsubscript{90} (\mu g kg\textsuperscript{-1})</td>
<td>43</td>
<td>37</td>
<td>57</td>
<td>37</td>
<td></td>
</tr>
<tr>
<td>Recovery time (75–25% block) (min)</td>
<td>22*</td>
<td>14</td>
<td>40</td>
<td>14</td>
<td></td>
</tr>
</tbody>
</table>

the simultaneous recording of the evoked twitch tension of the left adductor pollicis muscle and the evoked compound EMG of the left thenar eminence in response to supramaximal train-of-four stimulation of the ulnar nerve at the wrist every 15 s. Three 10-\mu g kg\textsuperscript{-1} doses of vecuronium, injected i.v. 30 min after the induction of anaesthesia at 3-min intervals, resulted in a 70\% and 78\% depression of twitch tension and EMG amplitudes (measured from peak to peak), respectively. Neuromuscular transmission was then allowed to recover spontaneously. The boy did well during anaesthesia and surgery, and the trachea was extubated uneventfully 7 min after completion of the 40-min procedure. Almost equal dose–response relationships were calculated from the EMG and twitch tracings, whereas recovery time was 8 min shorter when assessed by the EMG than when determined using the twitch tension (table I).

**Patient 2**

This boy had been anaesthetized repeatedly for closed reduction of bilateral club foot. No complications were reported, when he was 1 yr of age, during the first three anaesthetics which were with halothane and nitrous oxide in oxygen, administered via an anaesthetic face mask or tracheal tube. The fourth procedure was complicated by cardiac arrest with acute rhabdomyolysis, immediately following the i.v. administration of suxamethonium 10 mg. Cardiopulmonary resuscitation was successful; however, the child suffered persisting brain damage. This incident prompted further investigation which, on the basis of an increase in creatine phosphokinase concentration (5918 u. litre\textsuperscript{-1}), neurophysiological examination and muscle biopsy, led to the diagnosis of Duchenne's muscular dystrophy. In addition, the result of an in vitro halothane contracture test (1 vol\%) was consistent with susceptibility to malignant hyperthermia. A right-sided amaurosis and convergent strabismus were noted 1 year after the incident. Two years later (the present occasion) the child (now 4 yr, 99 cm, 19 kg) was anaesthetized for a further attempt to correct his club foot deformity. Premedication was with morphine 4 mg and pentobarbitone 60 mg injected i.m. 1 h before the induction of anaesthesia, which was with thiopentone 100 mg i.v., 67\% nitrous oxide in oxygen via face mask with assisted ventilation, and fentanyl 0.10 mg i.v. in divided doses. Neuromuscular transmission was monitored by means of evoked twitch tension as described above. After stabilization of the recording system, vecuronium was injected i.v. in 12 2.5-\mu g kg\textsuperscript{-1} doses over 25 min. The resulting 83\% twitch depression provided satisfactory conditions for tracheal intubation. Neuromuscular transmission was then allowed to recover spontaneously. Anaesthesia was uneventful, and nasopharyngeal temperature remained constant at 36.8 °C. The tracheal tube was removed 20 min after the completion of surgery. The data on neuromuscular transmission are shown in table I, where the 40-min recovery time is particularly remarkable.

**DISCUSSION**

In normal children, Goudsouzian and colleagues [6] found the cumulative 90\% blocking dose of vecuronium to be 51 ± 16 \mu g kg\textsuperscript{-1} (mean ± SD). The corresponding figures in the present patients were within these limits, indicating that these two patients did not have a greater than normal sensitivity to vecuronium. However, these data do not permit statistical analysis or inter-patient comparison, nor do they generally exclude an increased sensitivity of patients with muscular dystrophy to non-depolarizing myoneural blocking drugs. Increased sensitivity to non-depolarizing blockers might be expected, particularly in the advanced stages of the disease. We would, therefore, recommend the individual titration of the dose of neuromuscular blocker with the aid of a nerve stimulator, even though the adductor pollicis muscle may not be fully accurate in
predicting the contractile force of the ventilatory muscles in the presence of muscle disease [7, 8].

Duchenne's muscular dystrophy confers a risk of delayed postoperative ventilatory failure which has occurred as long as 36 h after uneventful general anaesthesia [4]. Therefore, particular care should be taken to ensure complete restoration of muscle contractility before ventilatory support is discontinued. Despite normal sensitivity to vecuronium, the present patients showed a three- to almost six-fold prolongation of the recovery time (75–25% block) (normal children: 9 ± 1.6 min [6]). In myasthenia gravis, the evoked twitch tension has been found to be more sensitive in reflecting the delayed recovery of neuromuscular transmission than the EMG action potentials [8]. The data of patient 1 suggest that this applies also to Duchenne's muscular dystrophy.

The history of patient 2 should serve as a further warning as to the susceptibility of patients with muscular dystrophy to severe cardiac arrhythmia or cardiac arrest. Acute rhabdomyolysis has been observed to occur in connection with cardiac complications [9–11]. The scarcity of well documented cases does not allow a definite conclusion as to whether acute rhabdomyolysis with cardiac arrest should be regarded as a variant of malignant hyperthermia or as a syndrome in its own right [3, 12]. A triggering effect of suxamethonium is generally accepted [4]; however, the role of halothane remains to be defined. Richards [3] reported 37 uneventful halothane anaesthetics in patients with Duchenne's muscular dystrophy. Subsequent authors published three cases of rhabdomyolysis and cardiac arrest after halothane anaesthesia without the use of suxamethonium [9, 11]. Yet, one author questioned the significance of halothane while focusing attention on pre- or postoperative hypoxaemia which may have gone unnoticed [9]. Likewise, a recent textbook does not mention halothane as being contraindicated in Duchenne's muscular dystrophy [13]. Also, no adverse effects of halothane were noticed in patient 1, whereas cardiac arrest had previously occurred in patient 2 when, apart from halothane, suxamethonium was also involved.

Both the risk of delayed postoperative ventilatory failure unrelated to muscle paralysis [4] and the slow recovery from vecuronium-induced neuromuscular blockade should preclude the use of long-acting neuromuscular blocking drugs such as tubocurarine, pancuronium and alcuronium. In addition, pharmacological antagonism of persisting non-depolarizing neuromuscular blockade should not be attempted. It may be anticipated that, like suxamethonium, the accumulation of acetylcholine at the motor end-plate secondary to the administration of anticholinesterase agents may trigger rhabdomyolysis. Adverse neuromuscular reactions to neostigmine in dystrophia myotonica and progressive muscle dystrophy have been reported previously [14].

With reference to the management of anaesthesia in patients with Duchenne's muscular dystrophy, it can be concluded: (i) Vecuronium, and probably any non-depolarizing neuromuscular blocker of intermediate or short duration of action, may be used safely if, with the aid of a peripheral nerve stimulator, the dose is assessed on an individual basis. (ii) The duration of neuromuscular blockade may be prolonged although the patient's sensitivity to vecuronium, and probably any other non-depolarizing neuromuscular blocker, may be normal. (iii) The evoked compound EMG may be less reliable in reflecting the recovery of neuromuscular transmission than the evoked twitch tension.

REFERENCES


