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Sevoflurane-induced sensitivity of neuromuscular function in a patient with myasthenia gravis in true remission

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Introduction

The response of patients with myasthenia gravis in remission to anesthetics is poorly documented. The sensitivity of these patients to muscle relaxants is controversial [1–6]. The use of inhalational anesthesia for muscular relaxation has been recommended in patients with myasthenia gravis [7–9]. Although myasthenic patients have shown an increased sensitivity to inhalational halogenated anesthetics [8,10,11], the sensitivity of patients with myasthenia gravis in true remission to inhalational anesthetics has not been described in the literature. We monitored the response of neuromuscular function to sevoflurane anesthesia in the remission of myasthenia gravis.

Case report

A 52-year-old female patient, weighing 53 kg, who was in true remission from myasthenia gravis, was scheduled to undergo right hemithyroidectomy for treatment of right functional thyroid adenoma. She had suffered from myasthenia gravis (adult-onset, generalized severe type) characterized by generalized fatigue, bilateral ptosis, difficulty in swallowing, and weakness of the upper limbs at the age of 39. The diagnosis of myasthenia gravis had been confirmed by a positive tensilon test and an acetylcholine receptor antibody value of 743 nMol·l^{-1}. Pneumomediastinography and computed tomography had revealed a slightly enlarged thymus. Vital capacity and $FEV_{1.0\%}$ had been 2.371 and 79%, respectively. Treatment with 120 mg per day of oral pyridostigmine and 5 mg per day of distigmine had been started.

She had undergone transsternal thymectomy and partial resection of the left thyroid because of an enlarged thymus and left adenomatous goiter at the age of 47. Histology showed moderate involution of the thymus and adenomatous hyperplasia of the thyroid. After the operation, she continued to receive only pyridostigmine for about 5 years. Because her myasthenic state went into remission, the anticholinesterase was discontinued when she was 51. She did not show any myasthenic symptoms after the surgery.

Seven months after the pyridostigmine discontinuation, she complained of symptoms of thyroid enlargement. A thyroid function test showed hyperthyroidism (T_3, 332 ng·dl^{-1}; T_4, 16.4 μg·dl^{-1}; TSH, 0.1 μU·ml^{-1}). She was treated with 30 mg thiamazole and 40 mg metoprolol daily for 2.5 months to control her thyroid function. At the time of thyroidectomy, her myasthenic state was in true remission; she had not taken any medication for 7 months and had experienced no clinical symptoms of myasthenia gravis. Although she had palsy of the left recurrent nerve due to the previous surgical intervention, preoperative routine laboratory examinations showed no abnormalities. HLA typing showed that she was positive for A24(9), A31(W19), B29(16), BW61(40), and CW7.

The patient was premedicated with 100 mg of pentobarbital orally and 0.1 mg of buprenorphine and 0.5 mg of atropine intramuscularly. Anesthesia was induced through a mask with inhalation of nitrous oxide (4 l·min^{-1}), oxygen (2 l·mm^{-1}), and 5% sevoflurane at calibrated vaporizer settings. Endotracheal intubation without the use of a muscle relaxant was accom-

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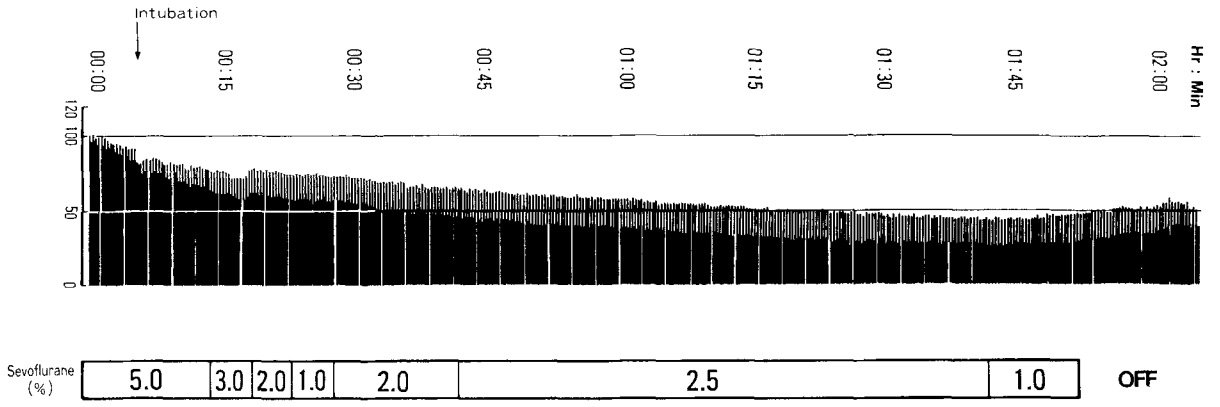

Fig. 1. Evoked electromyographic response after train-of-four (TOF) stimulation in a patient with myasthenia gravis in remission during sevoflurane anesthesia. Sevoflurane concentration is shown as the percentage. Sevoflurane induced a decrease in T_1 and fading of the TOF response

plished smoothly after application of topical anesthesia. Anesthesia was maintained by 1.0%–3% of sevoflurane with 66% nitrous oxide in oxygen. Body temperature was measured and maintained at 36°–37°C with a heating mat.

Neuromuscular function was monitored by electromyography (Relaxograph, Datex, Helsinki, Finland) during anesthesia. The ulnar nerve was stimulated every 20 s with the train-of-four (TOF) impulse, and the compound action potential was recorded from the adductor pollicis muscle. Inhalation of sevoflurane decreased both the height of the first twitch (T_1) and the ratio of the fourth to the first response (T_4/T_1) to TOF stimulation (Fig. 1). After the patient had inhaled sevoflurane and nitrous oxide for 100 min, T_1 and T_4/T_1 were 44% and 59%, respectively.

When the surgery was completed, she regained consciousness. The tidal volume was 450 ml and respiratory rate was $12 \cdot min^{-1}$. Blood gas analysis showed pH 7.34, partial pressure of arterial carbon dioxide ($Paco_2$) 55.9 mmHg, and partial pressure of arterial oxygen (Pao_2) 461 mmHg during spontaneous breathing with 100% oxygen. As she became restless due to irritation of the endotracheal tube during blood gas analysis, the trachea was extubated. The patient's postoperative course was uneventful. She was discharged on the 11th postoperative day. Histological examination of her thyroid revealed adenomatous hyperplasia.

One year later, the patient was scheduled to undergo laser uterocervical conization to treat carcinoma in situ. She had not received any medicine for myasthenia gravis after the thyroidectomy. Spinal anesthesia at L3–4 was performed with injection of 2.5 ml dibucaine. Anesthesia was induced and maintained with nitrous oxide, oxygen, and light sevoflurane anesthesia by mask. After 30 min inhalation of 0.75% sevoflurane, T_1 decreased to 56% and T_4/T_1 to 84% of those of before the induction. She emerged from anesthesia smoothly at the end of procedure. She was discharged after an uneventful postoperative course.

Discussion

Sevoflurane has potentiated nondepolarizing muscle relaxants to a greater degree than halothane and enflurane in anesthetized normal subjects [12]. Sevoflurane is rapidly eliminated from the blood after discontinuation of anesthesia and is less likely to cause postoperative respiratory depression because it has a lower blood/gas partition coefficient than other halogenated anesthetics. These characteristics suggest that sevoflurane may be suitable in patients with myasthenia gravis.

The few reports in the literature on the effects of anesthesia in myasthenic patients in remission describe conflicting results [1–6]. Brown and Charlton [1] reported that one patient showed excessive sensitivity to a regional curare test. Lumb and Calder [3] and Eisenkraft et al. [4] also reported that asymptomatic myasthenic patients who had discontinued all therapy showed increased sensitivity to neuromuscular blocking agents. Fillmore et al. [5] reported that an asymptomatic myasthenic patient receiving steroid therapy had a normal neuromuscular response to curare, and Abel et al. [6] found a normal response to suxamethonium in a myasthenic patient in remission.

When halothane [10] and isoflurane [11,13] were used without muscle relaxants in normal subjects, T_1 decreased in a dose-related fashion but T_4/T_1 did not change. Sevoflurane has produced similar effects in normal individuals [12]. Patients with myasthenia gravis have been found to show increased neuromuscular sensitivity to halogenated anesthetics [10,11] and nondepolarizing muscle relaxants [1]. Because

administration of halothane [10], isoflurane [8,11], or sevoflurane [14] alone were associated with decreases in T_1 and T_4/T_1 in patients with myasthenia gravis, the decrease of T_1 and T_4/T_1 in myasthenic patients in remission may indicate a sensitivity to inhalational anesthetics.

We observed a significant decrease in T_1 and a fading of the TOF response in association with an average sevoflurane concentration of 2.5%. This concentration, which is used clinically and showed T_1 and T_4/T_1 depression in myasthenic patients [14], did not demonstrate any cardiovascular depression in the present case. The patients also demonstrated a decrease of T_1 and T_4/T_1 during light sevoflurane anesthesia with spinal anesthesia for laser uterocervical conization. These electromyographical findings indicated that the patient still had a myasthenic response to anesthetics.

Pirskanen et al. [15] described an association between the HLA-B8 antigen and myasthenia gravis. Nilsson et al. [10,11] suggested that HLA-B8-positivity with a high acetylcholine receptor antibody value was associated with fading of T_4/T_1 when anesthesia was maintained with halothane or isoflurane. Our patient was not HLA-B8-positive, but showed a high acetylcholine receptor antibody value and a TR-fade.

Our patient with myasthenia gravis in true remission, who had discontinued all medications for myasthenia gravis, showed a marked sensitivity to sevoflurane, as demonstrated by electrostimulation responses. Although the patient exhibited no clinical signs of myasthenia gravis, she had a myasthenic response to sevoflurane. Sevoflurane provided adequate muscle relaxation in this patient, who had not been given any muscle relaxants.

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