Antagonism of suxamethonium-induced jaw muscle contracture in rats

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Summary
Masseter muscle rigidity (MMR) induced during general anaesthesia by suxamethonium is a clinical problem that may interfere with tracheal intubation. We have investigated the relation between twitch tension and contracture response to suxamethonium in rats. Rats were anaesthetized with 1% halothane (1.35 MAC). Jaw muscle temperature was maintained at either 37 or 41°C while rectal temperature was kept at 37°C by radiant heat. Twitch tension was produced by nerve stimulation at 0.2 Hz. Rats were pretreated with either a low dose of vecuronium (0.03 mg kg⁻¹) or dantrolene (0.8 mg kg⁻¹). Thereafter suxamethonium 750 µg kg⁻¹ was administrated i.v. Low-dose vecuronium pretreatment significantly (90%) decreased suxamethonium-induced jaw muscle contracture (JMC) with minimal (3%) twitch block during local hyperthermia. Low-dose vecuronium decreases suxamethonium-induced JMC clinically. (Br. J. Anaesth. 1997; 78: 332–333).

Key words

Suxamethonium may produce masseter muscle rigidity (MMR) during induction of anaesthesia and cause difficulty in tracheal intubation.¹ Previous laboratory studies showed that suxamethonium can induce jaw muscle contracture (JMC) during halothane anaesthesia in rats. The interaction between local hyperthermia of the jaw muscle and halothane can greatly increase suxamethonium-induced JMC.²³ Vecuronium is a non-depolarizing neuromuscular blocking agent while dantrolene is used in the prevention and treatment of malignant hyperthermia (MH). The purpose of the study was to examine if low doses of vecuronium and dantrolene, which have minimal effects on twitch, can block JMC in the rat.

Methods and results
The study was approved by the University Animal Welfare Committee. We designed two sets of experiments using similar methods. Male Wistar–Furth rats (278–440 g) were anaesthetized with 1% halothane (1.35 MAC). After tracheotomy and establishing mechanical ventilation, the right femoral vein was cannulated for drug administration. Isometric jaw muscle tension was recorded via a tension transducer connected to the lower incisors. Twitch tension was produced by bilateral supramaximal mandibular nerve stimulation (0.2 Hz). Jaw muscle temperature was maintained at 37°C (normothermic) or 41°C (hyperthermic) by radiant heat and monitored by a temperature probe (Mon-a-Therm 6501) which was secured into the left jaw muscle while rectal temperature was maintained at 37°C by a heat lamp.

In preliminary experiments, the dose effects of vecuronium and dantrolene on twitch tension and suxamethonium-induced JMC were examined to obtain the correct doses which could maximally block JMC with minimal inhibition of twitch tension. In the first set of experiments vecuronium was tested. Rats were allocated randomly to one of two groups (n=6 each): vecuronium and control groups. Vecuronium 0.03 mg kg⁻¹ was administered i.v. 40 s before administration of suxamethonium 750 µg kg⁻¹. Saline was injected i.v. before suxamethonium injection in the control group. Jaw muscle temperature was maintained at 41°C with rectal temperature kept at 37°C. In the second set of experiments, dantrolene was tested. Rats were allocated randomly to one of four groups (n=6 each): control hyperthermic, control normothermic, dantrolene hyperthermic and dantrolene normothermic groups. Dantrolene 0.8 mg kg⁻¹ or saline was administered i.v. 5 min before administration of suxamethonium 750 µg kg⁻¹ i.v. The percentage of twitch tension block by vecuronium or dantrolene and peak contracture after suxamethonium were measured. Data

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are presented as mean (SEM). Student’s t test and two-factor ANOVA were used. P<0.05 was considered significant.

In the absence of pretreatment, suxamethonium produced JMC. Low-dose vecuronium (0.03 mg kg⁻¹) had a significant effect on JMC but little effect on twitch. Compared with control, suxamethonium-induced JMC was reduced by approximately 90% (48 (7.3) vs 4.7 (1.0) g; P<0.01, t test). In contrast, twitch tension was blocked minimally (3 (1.5)% by vecuronium.

Low-dose dantrolene (0.8 mg kg⁻¹) also had a significant effect on JMC but modest effect on twitch (fig. 1). Compared with the control groups, dantrolene pretreatment reduced suxamethonium-induced contracture by 81% (1.3 (0.1) vs 7.0 (1.1) g) under normothermic conditions and by 82% (13 (4.4) vs 72 (6.3) g) under hyperthermic conditions (P<0.01, ANOVA). Twitch tension block by dantrolene was also similar in both hyperthermic and normothermic groups (31 (2.6) vs 30 (1.7)%).

As elevation in jaw muscle temperature increased suxamethonium-induced JMC by approximately 10-fold in both the control (7.0 (1.1) vs 72 (6.3) g) and dantrolene (1.3 (0.1) vs 13 (4.4) g) groups, dantrolene 0.8 mg kg⁻¹ did not alter the temperature dependent effect of suxamethonium-induced JMC.

Vecuronium is often used in low doses to reduce the cholinergic agonist action of suxamethonium (i.e. fasciculations). We found that low-dose vecuronium (0.03 mg kg⁻¹) pretreatment, which only minimally affected twitch, almost completely blocked suxamethonium-induced JMC. The explanation for the greater sensitivity of suxamethonium-induced contracture than twitch to vecuronium may be that JMC is caused by a halothane-suxamethonium interaction at extrajunctional receptors, as contracture is more sensitive to non-depolarizing block than twitch because the latter has a “margin of safety”.⁴

Smith and colleagues⁵ reported that increases in muscle tension of approximately 50% are a normal response to suxamethonium in children and suggested that MMR may be considered as an exaggerated form of the normal pharmacological effect of suxamethonium. Smith and colleagues found that a sub-paralysing dose of tubocurarine (0.05 mg kg⁻¹) was ineffective in preventing the increase in suxamethonium-induced masseter muscle tension in children. If we consider that the contracture at normal jaw muscle temperature is a “normal response” to suxamethonium, it is reasonable to propose that the contracture at elevated jaw muscle temperature (which is 10-fold the contracture at normal temperature) is an “exaggerated response” to suxamethonium. Therefore, we believe that our findings are more relevant to generation of MMR.

We conclude that both dantrolene and vecuronium, at doses that minimally depressed twitch response, antagonized suxamethonium-induced JMC. JMC may be mediated by extrajunctional acetylcholine receptors in rats. We also speculate that pretreatment with small doses of vecuronium decreases suxamethonium-induced MMR clinically.

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References