MUSCLE RELAXATION RATES IN INDIVIDUALS SUSCEPTIBLE TO MALIGNANT HYPERTERMIA

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SUMMARY

Muscle relaxation rate following a tetanic stimulus of adductor pollicis muscle was measured prospectively in 26 patients potentially susceptible to malignant hyperthermia (MH) the day before a muscle biopsy was obtained for MH in vitro screening. Eleven subjects were found to be MH susceptible (MHS) and 15 subjects MH-negative (MHN). In all patients, relaxation rate was recorded at three different temperatures of the skin overlying adductor pollicis (30, 34 and 38 °C) achieved by a small surface heating unit placed over the thenar eminence. The MHS group exhibited slightly higher relaxation rate at 34 and 38 °C compared with the MHN group and this difference was accentuated with increasing temperature, but was not statistically different. The results of the present study suggest that relaxation rates are normal in MHS individuals under physiological conditions and cannot be used diagnostically for MH screening.

KEY WORDS

Malignant hyperthermia: muscle relaxation, skin temperature.

Malignant hyperthermia (MH) is an uncommon but serious pharmacogenetic disorder, triggered by volatile anaesthetics and suxamethonium. The only widely accepted diagnostic method for screening MH-susceptible (MHS) individuals at present involves a muscle biopsy followed by both halothane and caffeine in vitro contracture tests. This procedure is invasive, time consuming, expensive, and requires special expertise, but none of the alternative diagnostic tests which have been described has been shown to be as reliable [1].

In 1987 Lennmarken, Rutberg and Henriksson reported significantly greater rates of muscle relaxation in MHS subjects compared with controls [2]. Although the population overlap rendered the use of relaxation rate unsuitable as a diagnostic screening test, their findings suggested that MHS subjects differed from MH-negative (MHN) subjects in the way in which they mobilized substrate in the muscle.

Previous work has shown that relaxation rate is both reproducible and independent of sex and age. However, muscle temperature is important, as it correlates linearly with relaxation rate [3]. Fortunately, an acceptable correlation between skin and muscle temperature has been shown which allows for the use of a non-invasive temperature control [4] rather than direct measurement of muscle temperature.

The aim of the present study was to repeat that by Lennmarken and colleagues while attempting to reduce variability by better control of muscle temperature, and to investigate directly the effect of temperature on relaxation rate.

METHODS AND RESULTS

We studied 26 ASA I patients (13 female) aged 20–63 yr. They were admitted for diagnostic muscle biopsy followed by both halothane and caffeine in vitro contracture tests. They were either probands or were related to an MHS proband. All patients gave written informed consent to take part in the study, which was approved by the Leeds Eastern Health Authority Ethics Committee. There were 11 patients (six females) in the MHS group and 15 patients (seven females) in the MHN group. Mean ages were 33
(sd 9) yr and 36 (16) yr, in the MHS and MHN groups, respectively.

Relaxation rate was measured the day before the muscle biopsy on the adductor pollicis muscle of the non-dominant hand after a supramaximal electrical stimulation of the ulnar nerve at the wrist for 1.6 s at 20 Hz, as described previously [4]. The negative electrode was placed distally. Muscle contraction force was recorded using a force transducer (Grass FT 10) connected to a preamplifier (Gould 13-4615-50). Electromyography was recorded using a universal amplifier with an isolated preamplifier (Gould 13-4615-58) to demonstrate supramaximal stimulation. Signals were recorded on a digital storage oscilloscope (Gould 1602) using an automatic trigger, stored in a memory module (Gould 105) and analysed later with a waveform processor (Gould 260).

Skin temperatures over adductor pollicis were measured using an infra-red thermometer (Thermopoint, Agema Sweden). If the initial skin temperature was greater than 30 °C, the lowest temperature at which relaxation rate was measured, the hand was immersed in running cold water for 2-3 min. Warm water which was controlled thermostatically and circulating in a special plastic enclosure, was used to warm the skin overlying adductor pollicis. The time needed to warm up this area from 30 to 34 °C and from 34 to 38 °C was found in preliminary tests to vary between 10 and 20 min. The heating system was removed regularly for measurements of skin temperature and relaxation rate to be made.

Relaxation rate is expressed as % force loss/10 ms calculated from the time to decrease from 90% to 50% of the maximal plateau force (fig. 1). Values increased linearly with increasing skin temperatures (correlation coefficient = 0.999 for both groups). This increase was greater in the MHS than the MHN group, but the difference was not significant (Student's t test). The increase in relaxation rate between 30 and 38 °C (MHS group: t = 2.698; MHN group: t = 2.453) was significant in both groups (P < 0.02), whereas the differences between 30 and 34 °C (MHS group: t = 1.100; MHN group: t = 1.088) and 34 and 38 °C (MHS group: t = 1.180; MHN group: t = 1.410) were not (Student's t test, P > 0.05).

**COMMENT**

As we were unable to confirm the previous finding that muscle relaxation rate was abnormally high in MHS individuals [2], this method may not be used as an MH screening test.

Published data of "normal values" for relaxation rate are unreliable, because the technique is not standardized. Different electrical stimulation and recording equipment were used. There was no temperature standardization, and different warming-up techniques were used. In addition, relaxation rate was calculated in a variety of

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**Fig. 1.** Electromyography (EMG) and force curve of adductor pollicis muscle developed after supramaximal electrical stimulation for 1.6 s at 20 Hz. Muscle relaxation rate (RR) is calculated from the time to decrease from 90% to 50% of the maximal plateau force. Group means (SEM) and individual results are presented for MHS subjects (n = 11) and MHN subjects (n = 15) at 30, 34 and 38 °C.
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different ways. Although normal values in muscle relaxation rate studies are expected to vary from ours, we cannot explain why Lennmarken’s group found differences between MHN and MHS groups, whereas we did not (mean relaxation rate was 12.0% in the MHS group compared with 8.8% in the control group, each expressed as percentage decrease during a 10-ms period [2]).

We have been able to confirm that muscle temperature alters the relaxation rate linearly [3]. In the present study the temperature was controlled rigorously using a surface heating unit over a 10–20 min period, whereas Lennmarken and colleagues used immersion of the hand in warm water at 40 °C for 5 min, followed by an undefined time interval before the investigation of relaxation rate [2]. The temperature of the muscle may not have been at a steady state. However, it seems unlikely that the significantly greater rate of relaxation in MHS individuals in the study by Lennmarken and colleagues was caused by greater muscle temperatures because their mean skin temperatures were 31.1 °C in the MHS and 30.6 °C in the MHN groups, compared with 30, 34 and 38 °C in the present study.

Muscle relaxation is associated with calcium reuptake into the sarcoplasmic reticulum. This process requires ATP, as calcium is pumped actively into sarcoplasmic reticulum. Relaxation rate is related to the rate of energy turnover in the contracting muscle [3]. As increased concentrations of adenylate cyclase were found in MHS subjects, Lennmarken and colleagues speculate that this causes calcium to rebind to sarcoplasmic reticulum faster in MHS muscle, thus increasing the relaxation rate [2]. It could be postulated, however, that in the former retrospective study [2] MHS subjects had been more stressed than the controls and therefore were exhibiting faster substrate cycling and therefore increased relaxation rate. In the present study, however, stress at the moment of the investigation was similar for all patients, as they were all investigated before their MH status was known (all had the muscle relaxation rate investigation on the day before the muscle biopsy). It could be that relaxation rate under physiological conditions should be normal in MHS muscle, because studies using graded physical exercise showed no differences in metabolic muscle response between MHS and MHN individuals [5].

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REFERENCES