Short Report

**Enflurane Induces Contracture of in Vitro Muscle
from a Patient with Malignant Hyperthermia**

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IWATSUKI, N., KOGA, Y. and AMAHA, K. *Enflurane Induces Contracture of in Vitro Muscle from a Patient with Malignant Hyperthermia*. Tohoku J. exp. Med., 1983, **140** (2), 221-222 — The possibility of enflurane being an inducer of malignant hyperthermia (MH) was examined by using the contracture test in in vitro muscle from a patient with MH. An administration of 2% enflurane elicited contracture in MH muscle and an elimination of enflurane relaxed this contracture. This result, therefore, strongly suggested that enflurane is the one of the trigger-agents for MH.

Potent inhalation anesthetics may be capable of inducing malignant hyperthermia (MH). It has been widely accepted that halothane induces MH. However, whether enflurane would induce MH has not been confirmed. Caropreso et al. (1975) and Pan et al. (1975) reported cases suggesting the possibility of enflurane as a trigger-agent of MH.

At present an induction of muscle contracture in vitro muscle is the most reliable test of screening whether some drug induces MH or not (Gronert 1980). Although the enhancement of caffeine-mediated muscle contracture by the administration of enflurane in vitro was demonstrated in frog skeletal muscle (Reed and Strobel 1978) and in human skeletal muscle susceptible to MH (Britt et al. 1980) direct evidence of contracture response to a single administration of enflurane has not been reported. We encountered a patient with MH, thus examined the contracture response of in vitro muscle from this patient to enflurane.

METHODS AND MATERIALS

A 14-year-old boy had a severe hyperthermic episode with muscle rigidity under halothane anesthesia. Five months later of this episode muscle biopsy was performed from tensor fasciae latae for the differential diagnosis of MH. The obtained muscle specimen was dissected to several strips (20 mm in length and 5 mm in width). Three of these strips were used for this study. Along this study, the caffeine-contracture test using other muscle strips from the same specimen confirmed the susceptibility of this patient to MH. The muscle strips were suspended in an organ bath which contained 40 ml of Krebs-Henseleit's solution oxygenated with 95% O₂-5% CO₂ gas mixture and kept at 36°C by surrounding thermo-bath. The experimental setup was similar to that used for an isolated heart muscle study (Iwatsuki et al. 1980), except electrical stimulation which in this study was of supramaximal intensity and 20-msec duration at a frequency of 0.1 Hz. Isometric twitch tensions and resting tensions were measured continuously under the preload of 0.5 g. Enflurane vapor obtained by passing O₂-CO₂ gas mixture through an "Enflurotec" vaporizer was bubbled in the organ bath.

Fig. 1. Response of human MH muscle to enflurane (Ethrane®) in vitro. Note clearly increased basal tension (contracture) by the administration of 2 % enflurane. Position of the trace was moved downwards at the maximal contracture response.

RESULTS AND DISCUSSION

All three muscle strips used for this study showed the contracture response (increase in resting tension) by the administration of 2 % enflurane. By the elimination of enflurane these contractures were relaxed to the pre-administration level. Fig. 1 illustrates the typical response of MH muscle to enflurane.

This is the first report illustrated a direct contracture response of in vitro MH human muscle to enflurane. It has been widely accepted that a drug elicited contracture on in vitro MH muscle or enhanced the caffeine-mediated contracture may induce MH (Gronert 1980). In normal muscle an administration of enflurane did not produce any muscle contracture in our preliminary study. This result, therefore, strongly suggested that enflurane is the one of the trigger-agents for MH.

References

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