

# Clinical reports

# Halothane enhances the negative chronotropic and dromotropic effects of calcium channel antagonists

Masanobu Manabe<sup>1</sup>, Iwao Ookawa<sup>2</sup>, Takashi Matsukawa<sup>2</sup>, Teruo Kumazawa<sup>2</sup>, Yukiko Kataoka<sup>1</sup>, Eri Takimoto<sup>1</sup>, and Wasa Ueda<sup>1</sup>

<sup>1</sup> Department of Anesthesiology and Resuscitology, Kochi Medical School, Kochi 783, Japan

**Key words:** Halothane, Calcium channel antagonist, Cardiac interaction, Inhalation anesthetics

#### Introduction

There are many reports describing cardiac interactions between inhalation anesthetics and calcium channel antagonists in animals [1–2]; however, only a few clinical cases with impaired myocardial conduction have been reported [3]. We describe the interaction between verapamil, diltiazem, and halothane in a patient.

# Case report

A 74-year-old woman with a history of chest pain, tachycardia, hypertension, ventricular arrhythmias, and bronchial asthma was scheduled for resection of a brain tumor. She had been medicated with oral verapamil during past several years for cardiac problems. Preoperative assessment demonstrated sinus rhythm with first-degree AV block (Fig. 1a) and decreased vital capacity (67%).

She received no premedication and no oral verapamil on the day of surgery. On arrival in the operating room, she was found to have a heart rate of 176 bpm, blood pressure of 102/64 mmHg, and supraventricular tachycardia on ECG (Fig. 1b). Intravenous diltiazem (5 mg) corrected the tachycardia (Fig. 1c). Anesthesia was induced with halothane and 66% nitrous oxide in oxygen since she had a history of asthma. Halothane concentration was gradually increased to 1.5% in 3 min,

when ventricular escape beats appeared on ECG (Fig. 1d,e). She was ventilated with 100% oxygen. In 1 min, sinus arrest occurred (Fig. 1f). In 5 min, she was awake and ECG returned to a sinus rhythm (Fig. 1g). The surgery was canceled, and she was referred to cardiologists.

## Discussion

Hantler et al. [3] reported an additive depressive effect of enflurane and diltiazem on atrioventricular nodal conduction and sinus node function in humans, but they did not show the ECG. In the present study, the additive negative chronotropic and dromotropic effects of verapamil, diltiazem, and halothane are presented on a patient together with the ECG changes. We examined the interaction between diltiazem and halothane in canine blood-perfused papillary muscle preparations [1]. Blood flow to these preparations was supplied by dogs which were either conscious or anesthetized with 0.8% halothane. After infusion of diltiazem 20 μg·kg<sup>-1</sup>·min<sup>-1</sup> for 60 min, contractility of papillary muscle, heart rate, and sinoatrial rate were significantly decreased, while PQ interval was significantly prolonged. Sinus arrest was induced in four of seven sinoatrial node preparations and second-degree AV block was induced in one of seven halothane-anesthetized dogs. The mechanisms of the interaction between inhalation anesthetics and calcium channel antagonists are still unknown. Possible causes are inhibition of the Ca++ entry through the plasma membrane and interference with cytoplasmic Ca++ flux by reducing the release of Ca++ from the sarcoplasmic reticulum [4].

In conclusion, whatever the mechanisms, calcium channel antagonists must be used carefully together with inhalation anesthetics since AV-block and sinus arrest can result.

Address correspondence to: M. Manabe Received for publication on May 29; accepted on April 14

<sup>&</sup>lt;sup>2</sup> Department of Anesthesiology, Yamanashi Medical College, Yamanashi 409–38, Japan

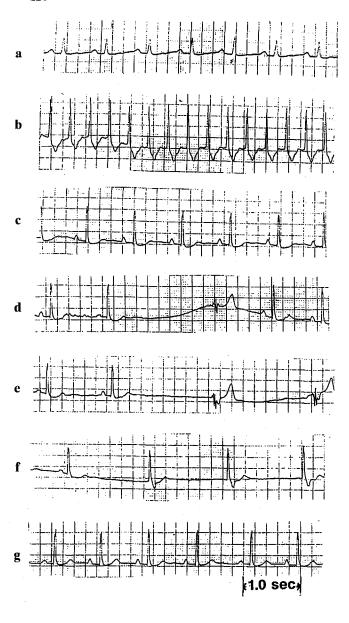


Fig. 1a-g. ECG pattern. a Preoperative: Sinus rhythm with first-degree AV block. b On arrival in the operating room: Paroxysmal supraventricular tachycardia. c Following the administration of diltiazem (5 mg): First-degree AV block. d, e Three min after induction of anesthesia with halothane: Ventricular escape beats. f One min after e: Sinus arrest. g Patient conscious: Sinus rhythm with first-degree AV block

### References

- Manabe M, Motomura S, Hashimoto K (1988) Interaction between diltiazem and halothane or enflurane in the canine bloodperfused papillary muscle and sinoatrial node preparations crosscirculated by chronically instrumented conscious donor dog. J Anesth 2:50-62
- Chelly JE, Hysing ES, Abernethy DR, et al. (1986) Effects of inhalational anesthetics on verapamil pharmacokinetics in dogs. Anesthesiology 65:266–271
- Hantler CB, Wilton N, Learned DM, et al. (1987) Impaired myocardial conduction in patients receiving diltiazem therapy during enflurane anesthesia. Anesthesiology 67:94–96
- Tosone SR, Reves JG, Kissin I, et al. (1983) Hemodynamic responses to nifedipine in dogs anesthetized with halothane. Anesth Analg 62:903–908