J Anesth (2008) 22:167–169
DOI 10.1007/s00540-007-0591-1

Journal of
Anesthesia

Repeated sudden falls in heart rate in a diabetic patient during sevoflurane anesthesia

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Abstract
Repeated sudden falls in heart rate were experienced in a diabetic patient during general anesthesia. During each fall in heart rate, analysis of heart rate variability showed a rapid increase in entropy and normalized power of high frequency. Simultaneously, a decrease was also shown in the power of the low–high frequency ratio, preceded by a trivial transient increase. These data indicated the excitation of vagal activity and the inhibition of sympathetic activity just after trivial sympathetic activation.

Key words Heart rate variability · Diabetic neuropathy · General anesthesia

Introduction

Neuropathy is a well-known complication in patients with long-standing diabetes, along with retinopathy and nephropathy. Especially, autonomic neuropathy, which is characterized by early and widespread neuronal degeneration of small nerve fibers of both the sympathetic and parasympathetic tracts, potentially modifies normal cardiovascular responses [1]. Therefore, autonomic neuropathy could cause unexpected abnormal cardiovascular responses to surgical intervention and anesthesia.

We report a diabetic patient who had repeated sudden falls in heart rate (HR) during general anesthesia. During each such event HR variability (HRV) data were continuously monitored. These data were then analyzed.

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Received: April 3, 2007 / Accepted: November 2, 2007

Case report

The patient was a 78-year-old woman, 141 cm in height and 39 kg in weight. She was scheduled for the open reduction and internal fixation of a left femoral fracture. She was first diagnosed as having severe diabetes mellitus during preoperative examination. Although the glycosylated hemoglobin blood level was 8.6%, her blood sugar level was reduced from 405 to 221 $mg \cdot dl^{-1}$ by insulin injected subcutaneously. She also demonstrated uncontrolled hypertension and resting tachycardia.

On the day of surgery, premedication was not administered. On her enterance to the operating room, electrocardiography, invasive blood pressure monitoring, and pulse oximetry were performed with a conventional anesthesia monitor. Heart rate (HR) was 100 $beats \cdot min^{-1}$, blood pressure was 181/92 mmHg, and percutaneous oxygen saturation (Sp_{O_2}) was 97%. The electrocardiography signal was obtained from the monitor to calculate the following components of HRV, done with MemCalc/Tarawa (Suwa Trust, Tokyo, Japan): the entropy of four RR intervals, and the power of low-frequency (LF; 0.04–0.15 Hz) and high-frequency (HF; 0.15–0.4 Hz) components for 30 s. Anesthesia was induced with intravenous injections of 80 mg propofol and 0.05 mg fentanyl. Then, 6 mg vecuronium was administered for muscle relaxation and subsequent tracheal intubation. Subsequently, anesthesia was maintained with 1%–3% sevoflurane with fentanyl (total amount, 0.2 mg) as needed. Under volume-controlled ventilation, fixed throughout the operation (tidal volume, 380 ml; frequency, 10 min^{-1}, i.e., 0.17 Hz; airway pressure, approximately 15 mmHg) with 40% oxygen in air, endotidal carbon dioxide (Et_{CO_2}; 35 mmHg) and Sp_{O_2} (100%) were stable.

Around 10 min after tracheal intubation, a sudden and brief fall of HR occurred, without warning. The sinus rhythm was retained. Simultaneously, blood pres-

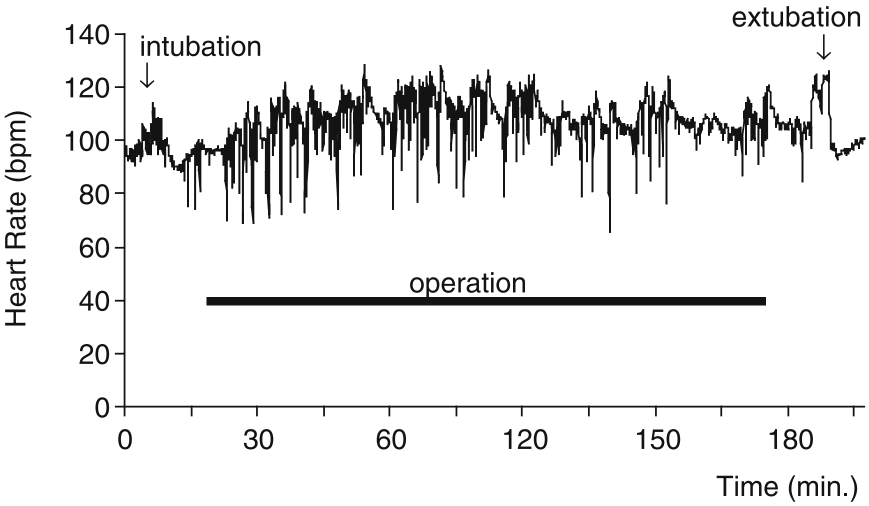

Fig. 1. Heart rate during general anesthesia

sure fell slightly. Subsequently, such falls were repeated frequently until the end of anesthesia (Fig. 1), and they showed no relation to any surgical procedures. Also, entropy and normalized unit power of HF (nuHF; nuHF(%) = HF/(LF + HF) × 100) at the time of the falls in HR rapidly increased, whereas LF/HF decreased after a trivial transient increase. Representative trends in HR, entropy, nuHF, and LF/HF are shown in Fig. 2. Changes like those shown in Fig. 2 were observed in all episodes.

The duration of surgery was 157 min. The fluid balance during anesthesia was as follows: blood loss, 880 g; urination, 200 ml; blood transfusion, 260 ml; fluid administration, 1500 ml crystalloid and 500 ml colloid. Repeated falls in HR were no longer seen after extubation or when she was in the intensive care unit (ICU). She was discharged uneventfully from the ICU to the ward the next morning.

Discussion

We encountered a diabetic patient who demonstrated repeated sudden and brief falls in heart rate (HR) under general anesthesia during orthopedic surgery. Although the reason for these falls in HR remained unknown, we were monitoring HRV continuously during the event and we analyzed the recording postoperatively.

HRV is a well-established, noninvasive probe to assess autonomic nervous activity [2]; it allows assessment of the balance between the sympathetic and parasympathetic nervous systems. Recently, the "MemCalc" method, which is a combination of the maximum entropy method for spectral analysis and the nonlinear least squares method for fitting analysis, has been developed [3], and its use for determining HRV under general anesthesia has been reported [4]. This method facilitates reliable estimations of HRV and entropy from a series of RR intervals for 30 s. Efferent vagal activity is a major contributor to the HF component, as seen in clinical and experimental observations of autonomic maneuvers such as electrical vagal stimulation, muscarinic receptor blockade, and vagotomy [5]. If HF does not correlate with vagal activity under conditions such as general anesthesia when total power is reduced, normalization is needed [6]. With respect to the LF component, disagreement exists. Some studies suggest that LF is a quantitative marker of sympathetic modulations when expressed in normalized units [7,8]. Other studies view LF as a reflection of both sympathetic activity and vagal activity [2,9]. The LF/HF ratio is considered to mirror sympatho-vagal balance or to reflect sympathetic modulation [10]. Entropy is a concept that addresses system randomness and predictability, with greater entropy often being associated with greater randomness and less predictability [11]. Also, changes in entropy measures of HRV seem to be similar to changes in HF [12]. In our patient, nuHF and entropy rapidly increased while the sudden and brief fall in HR occurred, and, in contrast, the LF/HF ratio decreased. These data apparently indicate excitation of vagal activity and inhibition of sympathetic activity. Moreover, it is a noteworthy phenomenon that these changes occurred just after a trivial transient increase in the LF/HF, i.e., sympathetic activation. This HRV phenomenon shows us the therapeutic possibility that adequate sympathetic inactivation may prevent repeated episodes of bradycardia.

The following abnormalities on HRV analysis are associated with diabetic autonomic neuropathy [5]: (1) reduced power in all spectral bands (the most common finding), (2) failure to increase LF on standing (a reflec-

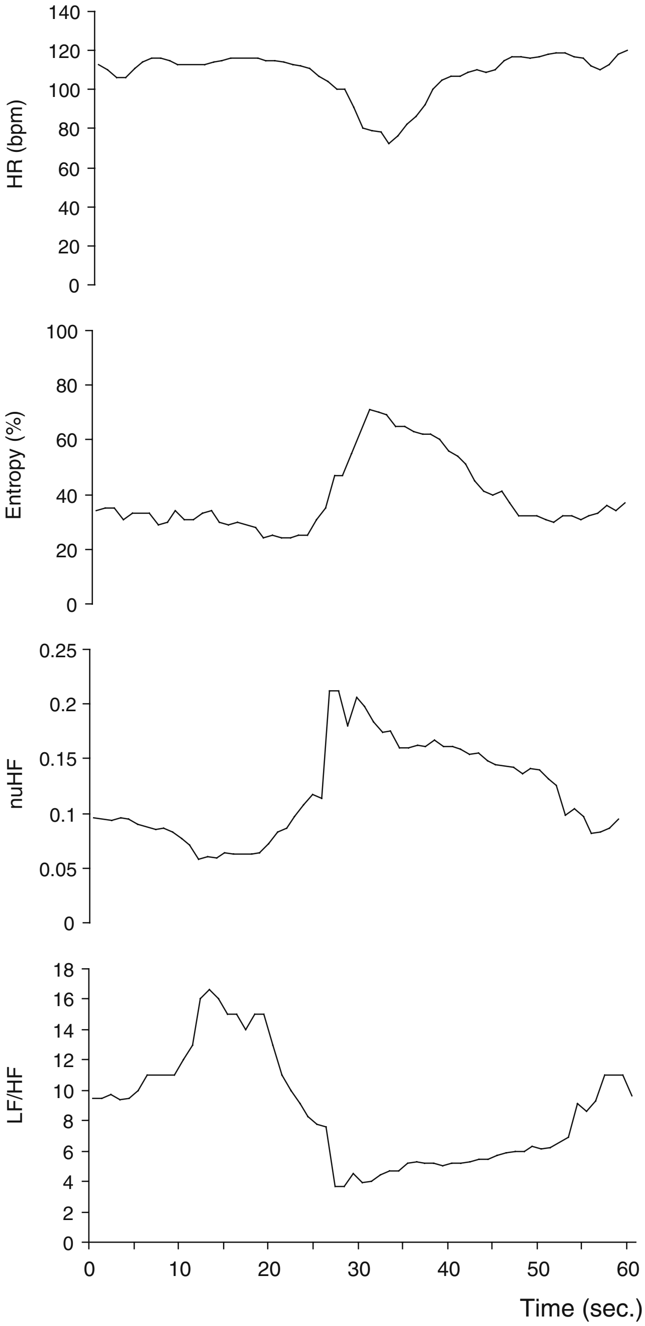

Fig. 2. Representative traces of heart rate (*HR*), entropy, normalized unit power of high frequency (*nuHF*), and the power of the low–high frequency ratio (*LH/HF*) during a sudden fall in heart rate

tion of impaired sympathetic response or depressed baroreceptor sensitivity), (3) abnormally reduced total power with an unchanged LF/HF ratio, and (4) a leftward shift in the LF central frequency. Even in diabetic patients without evidence of autonomic neuropathy, a reduction of the absolute power of LF and HF was reported [13]. Thus, the initial manifestation of this neuropathy is likely to involve widespread neuronal degeneration of small nerve fibers of both sympathetic and parasympathetic limbs. Although it is not known how diabetic neuronal degeneration affects HRV under general anesthesia, this degeneration may have been at least one of the causes of the repeated sudden episodes of bradycardia in our patient.

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