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RESEARCH PAPER

Twitch potentiation: a potential source of error during neuromuscular monitoring with acceleromyography in anesthetized dogs

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Abstract

Objective To measure twitch potentiation (the staircase phenomenon) in anesthetized dogs, and assess its relevance during neuromuscular monitoring with acceleromyography (AMG).

Study design Randomized, prospective clinical trial.

Animals Sixteen dogs undergoing ovariohysterectomy.

Methods Under isoflurane anesthesia, neuromuscular function was monitored with train-of-four (TOF) stimuli every 15 seconds and quantified by AMG. Neuromuscular blockade (NMB) was produced with 0.15 mg kg^{-1} atracurium IV. Dogs were randomly divided into two groups; a potentiation group (PG) in which TOF stimulation was applied for 20 minutes before atracurium was administered; and a control group (CG) where no such time was allowed. In both groups, the AMG was calibrated (at tCAL) just before atracurium was administered. TOF stimulation continued throughout the experiment in all dogs. The height of the first twitch (T_1) (expressed as a fraction of T_1 at tCAL) and train-of-four ratio (TOFR) were recorded until TOFR returned to ≥90%.

Results In PG, T_1 increased significantly (p = 0.0078) from a median of 102% (range, 95, 109) at baseline to 118% (100, 142) at 20 minutes. In PG, no difference was found between T_1 at tCAL (immediately before atracurium administration) and T_1 when neuromuscular transmission returned (p = 0.42). In the CG, T_1 increased significantly between tCAL and the time neuromuscular transmission returned (p = 0.027). TOFR did not increase during twitch potentiation (all p = 0.32).

Conclusions and clinical relevance T_1 increased significantly during 20 minutes of uninterrupted TOF stimulation in the absence of NMB, establishing that twitch potentiation occurs in anesthetized dogs. With no time for potentiation, T_1 increased during the course of recovery from NMB; this phenomenon introduces a bias in T_1 measurements and could affect studies reporting potency and duration of NMB based on T_1 or single twitches. TOFR was unaltered by potentiation emphasizing its clinical usefulness for excluding post-operative residual NMB.

Keywords acceleromyography, anesthesia, atracurium, neuromuscular blockade.

Introduction

Accurate quantification of neuromuscular blockade (NMB) is necessary for safe redosing of

neuromuscular blocking agents (NMBAs) and to exclude post-operative residual curarization (Murphy et al. 2005; Martin-Flores et al. 2008). It is also necessary for studies in which the duration and potency of an NMBA is the subject of investigation.

Neuromuscular transmission is usually assessed by measuring the magnitude of muscle contractions (twitches) evoked by stimulation of a peripheral motor nerve. Single twitch (ST) and train-of-four (TOF) are the most commonly used stimulating patterns for this purpose. ST stimuli are usually given every second or every 10 seconds (1 Hz or 0.1 Hz respectively) (Ali et al. 1970). TOF stimulation usually consists of groups of four twitches at 2 Hz with at least 10-second intervals between groups (Ali et al. 1970). Using ST to measure neuromuscular transmission requires a baseline value to be obtained (control twitch or *Tc*) before any NMBA is administered; the magnitude of subsequent twitches is then expressed as a percentage of that baseline value. After NMBA administration, the decrease in the amplitude of elicited response (ST) is largely attributable to post-synaptic effects of the drug (Bowman 1980). The extent of maximal ST depression and time to 25% and 75% recovery are conventionally reported when describing potency and duration of NMBAs (Auer et al. 2007; Claudius et al. 2009).

Twitch potentiation (or the staircase phenomenon) describes a process whereby repetitive stimulation of a motor nerve in the absence of NMB causes the magnitude of the muscle response to increase over time and then stabilize at a greater value (Krarup 1981; Kopman et al. 2001). Higher frequencies of stimulation result in larger increases in the magnitude of evoked twitches, and although the staircase phenomenon has been documented during neuromuscular monitoring, the underlying mechanism is not yet clearly understood (Eleveld et al. 2004). As noted earlier, when ST depression is used to assess NMB, *Tc* must be obtained before any neuromuscular blocking agent is administered. However, if calibration is carried out before potentiation is complete, *Tc* might be smaller than it would be had potentiation run its course, and under these circumstances subsequent twitches appear larger than they should be thus underestimating the extent of NMB. This could lead to premature extubation and post-anesthetic residual NMB. For research studies it is recommended that potentiation be accommodated by allowing twitch magnitude to stabilize for at least 2–5 minutes before NMBAs are administered (Fuchs-Buder et al. 2007).

During clinical anesthesia TOF offers an important advantage over ST depression; it does not require a baseline value (i.e., *Tc*) to be measured before NMBAs are administered. During each TOF, the ratio of the magnitude of the fourth twitch to that of the first twitch can be calculated (T_4/T_1; train-of-four ratio or TOFR). The presence of fade during each TOF (i.e., a TOFR < 1) represents incomplete neuromuscular transmission; under these circumstances the first twitch of each TOF behaves as the control for that TOF. Fade during TOF reflects a pre-synaptic effect of NMBAs (Bowman 1980). When recording TOF, the magnitude of T_1 can be used as a surrogate for ST; hence ST and TOFR can be measured simultaneously.

The effects of potentiation on the usual measures of neuromuscular function have yet to be measured in anesthetized dogs. Hence, the present study tests the hypotheses that: 1) twitch potentiation occurs in anesthetized dogs during repetitive nerve stimulation; and that 2), if ST depression is measured using a value for *Tc* obtained without baseline stabilization (potentiation), T_1 will eventually return to values >100% and the degree of NMB will be underestimated.

Materials and methods

After approval by the Institutional Animal Care and Use Committee at Cornell University (protocol number 2008-0152), and obtaining owner consent, 16 adult female dogs classified as ASA 1 and scheduled for elective ovariohysterectomy were included in this prospective, randomized study. Patients were randomly assigned (selection of one closed opaque envelope of 16 containing equal assignments to each group) to one of two treatment groups; the potentiation group (PG) had 20 minutes allowed for twitch potentiation, and the control group (CG) which had no time allowed for potentiation to occur before the NMBA was administered.

Each dog received a combination of hydromorphone and either dexmedetomidine or acepromazine prior to anesthesia. General anesthesia was induced with propofol (1.5–3.6 mg kg^{-1}) or thiopental (5.7–12 mg kg^{-1}). After the trachea was intubated with a cuffed tube, general anesthesia was maintained with isoflurane in oxygen and the lungs were mechanically ventilated. The electrocardiogram, SpO_2, and end-tidal carbon dioxide were