Anesthesiology 2006; 105:222

Is the Dose-related Reduction in Succinylcholine-induced Myalgia due to Cointervention?

To the Editor:—Schreiber *et al.*[1] noted an association between larger doses of succinylcholine and a reduced incidence of fasciculation and myalgia. However, pretreatment with a nondepolarizing neuromuscular blocker is also associated with a reduced risk of fasciculation and myalgia. It is a common practice for clinicians to use a larger dose of succinylcholine when they have provided pretreatment with a nondepolarizing neuromuscular blocker, making pretreatment a potential cointervention.[2] Consequently, pretreatment with a nondepolarizing neuromuscular blocker could be a confounder in the association between higher doses of succinylcholine and a reduced risk of fasciculation and myalgia: Pretreatment is a determinant of the outcome under investigation, it is not germane to the association under investigation, and it may not be equally distributed among study groups.[3]

Does the available data permit adjusting for this potential confounder, or is it better to consider the associations between the dose of succinylcholine and the risks of fasciculation and myalgia as hypotheses for future investigation?

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Dose Inflation When Using Precurarization

To the Editor:—I read with great interest the meta-analysis by Schreiber *et al.*[1] about the prevention of succinylcholine-induced fasciculation and myalgia. After reviewing carefully an abundant literature, the authors conclude that nondepolarizing neuromuscular blocking agents given before succinylcholine are effective in reducing fasciculations and myalgias. The meta-analysis also contains an analysis of the side effects that were reported in the studies, and the authors point out that the incidence of these side effects is not negligible. In particular, difficulty in breathing or swallowing is considered as potentially serious.

The incidence and magnitude of these neuromuscular side effects are most likely related to the dose given, and the meta-analysis by Schreiber *et al.*[1] provides evidence of this dose relation for pancuronium. The same is probably valid for all nondepolarizing agents. The authors recommend that ". . . the smallest dose of each agent that has shown efficacy in these randomized trials should be given. These doses are unlikely to be above 10% of the respective ED_{95}."[1] I agree. Most studies reporting adverse events involved doses that were clearly above 10% of the ED_{95}, and this applies especially to recent studies, using newer drugs. Of the six studies reporting difficulty in breathing or swallowing reported in Schreiber's table 2, two involved multiple doses of pancuronium.[2,3] In the other four, the dose of rocuronium ranged from 0.06 to 0.1 mg/kg (0.2–0.33 × ED_{95}),[4–6] whereas the doses of cisatracurium (0.01 mg/kg),[7] vecuronium (0.01 mg/kg),[5] atracurium (0.05 mg/kg),[5] and mivacurium (0.02 mg/kg)[5] all represented approximately 0.2 × ED_{95}. The occurrence of breathing or swallowing difficulties is therefore not surprising.

The initial studies on precurarization involved d-tubocurarine, and the dose was 3 mg for an adult. This represented 0.043 mg/kg for the 70-kg adult, or less than 0.1 × ED_{95}. The ED_{95} of d-tubocurarine is 0.45–0.5 mg/kg. When other neuromuscular blocking agents were introduced, the potency ratio between these drugs and d-tubocurarine was not respected. The precurarization doses used in the studies quoted by Schreiber *et al.*[1] were expressed as a fraction of their respective ED_{95}s and plotted against the year of their publication (fig. 1). The d-tubocurarine dose remained relatively constant throughout the last two decades of the 20th century, whereas the equivalent dose of other agents increased progressively. On average, the equivalent dose doubled between the late 1970s and the early 2000s (fig. 1).

Assuming that the studies were designed to reflect clinical practice, it follows that there has been a dangerous tendency to increase the precurarizing doses in the past 20–30 yr. Clinicians most likely administered the newer drugs in doses corresponding to the pub-

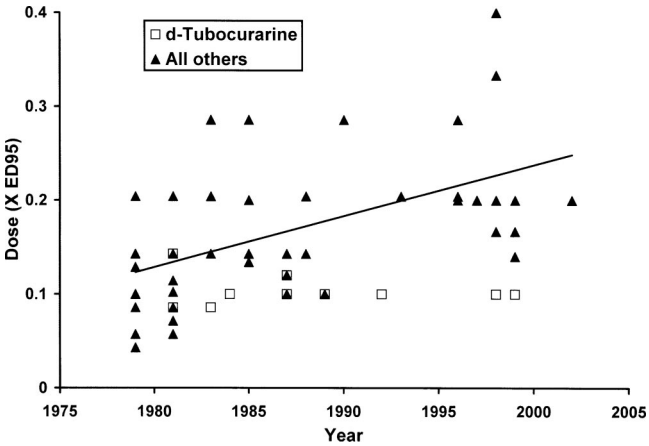

Fig. 1. Precurarization doses used in the studies quoted by Schreiber *et al.*,[1] expressed as a fraction of their ED_{95}, as a function of publication year. The dose of d-tubocurarine remains relatively constant during the period 1979–2002. The other drugs are pancuronium (7 studies), gallamine (4), fazadinium (1), metocurine (2), atracurium (8), mivacurium (2), vecuronium (5), rocuronium (6), cisatracurium (2), and alcuronium (1). The *line* shows the linear regression.

lished values. Some of them certainly observed side effects or heard of complications arising from such a practice. As a result, precurarization has been abandoned by many practitioners. However, the numbers to treat to avoid fasciculations (1.2–2.5) and myalgia (3–5)[1] are low, thus justifying the use of nondepolarizing blocking drugs. In comparison, even the most effective antiemetics have higher numbers to treat, and we feel justified to use them as prophylaxis. The concluding statement of Schreiber *et al.*[1] about nondepolarizing agents, which states that "[these drugs] should be used cautiously because the risk of potentially serious side effects is not negligible," should be more specific. I would suggest that precurarization with a nondepolarizing blocking agent is both safe and effective, provided that the dose does not exceed 10% of the ED_{95}. d-Tubocurarine, 3 mg, is equivalent to 2 mg rocuronium, 1.5 mg atracurium, 0.5 mg mivacurium, 0.3 mg vecuronium, or 0.4 mg pancuronium.

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In Reply:—We thank Drs. Kettler and Donati for their interest in our meta-analysis[1] and appreciate the opportunity to reply.

We agree with Dr. Kettler that pretreatment with a nondepolarizing neuromuscular blocker could be a confounder in the association between higher doses of succinylcholine and a reduced risk of fasciculation and myalgia. However, Dr. Kettler assumes that "It is a common practice for clinicians to use a larger dose of succinylcholine when they have provided pretreatment with a nondepolarizing neuromuscular blocker, making pretreatment a potential cointervention." Currently, the literature does not provide any evidence for this statement. Unfortunately, the available data do not permit adjusting for this potential confounder. As suggested by Dr. Kettler, the association between the dose of succinylcholine and the risk of fasciculation and myalgia may thus serve as a hypothesis for future research.

Dr. Donati analyzed the increase of precurarization doses during the past years using a linear regression analysis. His very interesting analysis shows that equivalent doses of most of the neuromuscular blocking agents that have been used in precurarization studies were doubled on average during the past 30 yr. Because of this dose inflation, the incidence of precurarization-related side effects increased in more recent studies. Dr. Donati suggests that pretreatment with a nondepolarizing neuromuscular blocker is effective to avoid myalgia and fasciculation and is also safe when the dose does not exceed 10% of ED_{95}. We agree with his comment that our conclusion on the risk of precurarization-related side effects should be more specific. However, there is some evidence in the literature that potentially serious side effects may occur even with the recommended dose of $0.1 \times ED_{95}$. Engbaek and Viby-Mogensen[2] reported the case of a healthy 32-yr-old man who received a dose of 0.3 mg (0.005 mg/kg) vecuronium for precurarization. In the minutes after administration of the agent, the patient developed serious signs of partial paralysis with respiratory impairment and was not able to swallow or to move. Engbaek and Viby-Mogensen suggested an extreme sensitivity for neuromuscular blocking agents in this patient without a preexisting neuromuscular disease. As a conclusion, they recommended to inform patients about possible side effects of precurarization preoperatively. In addition, clinicians should be alert to a possible hypersensitivity to neuromuscular blocking agents even after precurarization.

In a clinical trial on the effect of precurarization with atracurium on pulmonary function and neuromuscular transmission, Howardy-Hansen *et al.*[3] found a significant decrease in peak expiratory flow, vital capacity, and train-of-four-ratio after a dose of 0.02 mg/kg atracurium ($0.08 \times E_{95}$) compared with control. They concluded that careful observation of respiratory function should be mandatory after precurarization.

Based on the data of our meta-analysis, we agree with Dr. Donati that pretreatment with neuromuscular blocking agents is an effective method to avoid postoperative myalgia and fasciculation. Moreover, side effects from precurarization may occur less frequently when using a dose of $0.1 \times ED_{95}$. However, in context of the cited reports, there is a finite risk of side effects related to the use of neuromuscular blocking agents even with a dose of $0.1 \times ED_{95}$. Clinicians should be aware of this risk when using precurarization. To maximize patients' safety, a close monitoring for precurarization-related side effects is strongly recommended.

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David C. Warltier, M.D., Ph.D., acted as Handling Editor for this exchange.

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Effects of an Anesthesia Preoperative Medicine Clinic

To the Editor—Ferschl *et al.*[1] recently reported that preoperative preparation at an anesthesia preoperative medicine clinic (APMC) can reduce both case cancellations and case delays. Their study showed that the median time to start a case in the operating room decreased significantly (by 2–3 min) in patients who were evaluated at the APMC. This time gain as a result of the APMC has not been shown previously. Furthermore, the authors demonstrated a significant decrease in day-of-surgery cancellations (64% for same-day cases and 63% for admitted surgical patients). Although this latter benefit of an APMC has been reported previously,[2,3] the authors still can be commended for their contribution to the increasing evidence of the positive effects of an APMC on the cost effectiveness of the perioperative process.

However, we do have some important questions regarding this study. First, it is not clear who was responsible for the ultimate decision to cancel a case: the anesthesiologist or the surgeon? Second, the authors report a very high rate of cancellations compared with the rates reported in previous studies (11% in the current study *vs.* 2% cancellations for medical reasons in previous studies).[2,3] In the article, no explanation is given for this high cancellation rate. Therefore, although this was a retrospective study, it would have been interesting to have at a minimum some indication of the reasons for these cancellations. For example, if cancellations were caused by incomplete laboratory test results, a similar reduction in cancellations would possibly have been obtained by reeducation using a protocol for preoperative additional testing. Furthermore, cancellations for nonmedical reasons (*e.g.*, surgery no longer indicated, patient "bumped" from the room, emergency patient instead of the planned surgery) can hardly be influenced by an APMC. In a large cohort study (n = 21,553), we described the effects of a gradual introduction of an APMC for all surgical patients in a university hospital.[3] This study also documented the reasons for cancellations within 24 h before the planned surgery. After adjustment for age and sex, we found a significant decrease with 30% for cancellations due to medical reasons (*e.g.*, unstable cardiovascular disease or insufficient diagnostic workup) but a decrease of only 10% for cancellations for nonmedical reasons. Third, at the authors' institution, the decision as to whether a patient is seen in the APMC is made by the referring surgeon. This resulted in a referral to the APMC of only 43% of the 6,524 surgical patients included in the study. However, as the authors acknowledge, the effect of the APMC on the rate of day-of-surgery case cancellations would likely have been greater when the decision to refer patients to the APMC was not made by the surgeons. We therefore wonder why the authors do not recommend an APMC visit for every patient scheduled for surgery. Do they believe that it will not further enhance patient safety and the utilization of hospital resources?[3,4] Of course, it may be difficult to compel surgeons to refer all of their patients to the APMC. However, by using the accumulating evidence demonstrating that an APMC yields fewer cancellations on the day of surgery, precious operation room time can be saved. The APMC also guarantees that truly necessary preoperative tests will be ordered timely.[2,3] Finally, an APMC for all surgical patients reduces the responsibilities and workloads of the surgeons.

Therefore, combining the available evidence, we may conclude that when the APMC is used as an integral component of perioperative care for all surgical patients, the number of unnecessary cancellations due to medical reasons will decrease considerably. Furthermore, patient safety can be expected to increase by a more timely preoperative evaluation and the possibility to discover and treat clinically relevant comorbidity (*e.g.*, starting a β blocker in patients at high risk for perioperative myocardial ischemia).

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Anesthesia Preoperative Medicine Clinic: Beyond Surgery Cancellations

To The Editor:—We read with great interest the article of Dr. Ferschl *et al.*[1] titled "Preoperative Clinic Visits Reduce Operating Room Cancellations and Delays," in which the authors reported a decrease in same-day surgery cancellation rate from 16.2% to 8.4% using an anesthesia preoperative medicine clinic (APMC). The value of an APMC, besides the physical and psychological preparation for surgery, was clearly demonstrated by their study. We applaud their excellent work and would like to present our own data to support their conclusion: An evaluation in the APMC can significantly reduce case cancellations and delays on the day of surgery.

In 1998, Kaiser Permanente Baldwin Park Medical Center (Baldwin Park, California) was built to provide a full spectrum of medical and surgical service to a large and diversified population 225,000. We set up an AMPC lead by board-certified anesthesiologists from the beginning, in which all patients were evaluated 1–30 days before their scheduled surgery. Our objectives were (1) to complete preoperative anesthesia evaluation at one time in one hospital visit, (2) to reduce same day surgery cancellations, (3) to minimize operative room delays, and (4) to improve patient's safety and patient's satisfaction. As of the end of September 2005, we had a total of 66,424 scheduled surgical procedures (46,959 ambulatory surgeries and 19,465 inpatient surgeries). With respect to the 66,424 scheduled surgeries, we had a total of 1462 same-day case cancellations due to various reasons, with a surgery cancellation rate of 2.2% (medically related, administrative related, and patient related), the lowest same-day cancellation rate reported so far in the literature. We attribute our low same-day surgery cancellation to our successful implementation of APMC.

Despite the various benefits of APMC, such as decreased perioperative morbidity and mortality,[2–4] the value of a full-service APMC for all preoperative patients is increasingly under scrutiny because of the cost of APMCs.[5] There are growing number of facilities and ambulatory surgical centers replacing APMCs with "cost-effective" alternatives such as phone preanesthesia evaluations, reviews of health surveys, and computer-assisted information gathering.[6] It is also increasingly common that preoperative anesthesia evaluation is conducted in preoperative holding hours even minutes before scheduled surgery and anesthesia. The study of Dr. Ferschl *et al.* clearly raises questions about the practice and calls for more studies to evaluate the safety, efficiency, cost, and patient and staff satisfaction of this practice.

Operating room efficiency is a major determinant of hospital cost. Reengineering the perioperative process, rather than focusing on operating room turnover time, has recently shown promising result for improving overall operating room productivity.[7] It was estimated that the cost of operating room time was between $1,430 and $1,700/h plus the variable setup cost of the individual case.[8–10] However, the negative impact of case cancellations goes far beyond its financial consequence to the hospital; it also impacts patients, family members, and society.[10] Furthermore, frequent case cancellations can decrease both patient and staff satisfaction. In a health industry that is more frequently pay-for-performance oriented, quality, efficiency, and patient satisfaction are increasingly used as indicators for consumers as well as insurers for selecting healthcare providers. In the cost-driven environment, only hospitals that deliver high-quality care and high patient satisfaction at an affordable price can maintain their financial viability. The study of Dr. Ferschl *et al.*, along with others, clearly demonstrates that streamlining the perioperative practice, including APMCs, can be more rewarding.

We will share our full APMC experience, in addition to our decreased surgery cancellation rate, in our following report.

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The authors thank Rosie Rivera, R.H.I.T. (System Administrator, Kaiser Permanente Baldwin Park Medical Center, Baldwin Park, California), for her effort in collecting perioperative data.

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In Reply:—We thank Drs. van Klei *et al.* and Qiu *et al.* for their kind comments about our report[1] and for insights into the potential benefits that preoperative visits to an anesthesia-directed clinic can have on operating room efficiency, patient safety, and hospital-wide cost savings. We strongly agree with their position that the use of these clinics should be expanded in efforts to extend these benefits.

Dr. van Klei *et al.* noted that the impact of preoperative clinics on day-of-surgery case cancellations has already been reported. We suggest, however, that the data they cite do not represent contemporary practice as accurately as the data presented in our study. Specifically, their data[2] were gathered in a setting where almost all patients (92% even after the creation of their evaluation center) were still being admitted ahead of surgery. Furthermore, their average clinic visit occurred 3 weeks ahead of the scheduled operation. In contrast, none of the patients in our study were admitted ahead of surgery, and nearly all were seen within 2 weeks of their operation. Goals of a preoperative clinic and factors linking clinic efforts to cancellation rates may be different when the clinic visit is so removed in time. The other referenced study was Fisher's landmark article describing the creation of a preoperative anesthesia clinic at Stanford.[3] The data on the impact of clinic visits on day-of-surgery cancellations in this study also differ from ours in that "an 'informal assurance' existed that, if a patient was evaluated . . . in the [clinic], the case would proceed to surgery without cancellation or delay." This "informal assurance" made it very likely that the number of cancelled cases in that study had to decline. No such agreement existed in our report.

Van Klei *et al.* also noted that our report did not identify the reasons why cases were cancelled, and that our cancellation rates were high. We agree that identifying the reasons for cancellation can significantly affect the interpretation and implementation of our results. Although these data were not available to us at the time of publication, we are currently pursuing this issue. With respect to why our cancellation rate was so high, we note that other studies[4] have shown cancellation rates identical to our overall 11% incidence. The lower results in the studies cited by van Klei *et al.* may reflect a focus on only "medical reasons" for cancellation and the concerns mentioned above (preadmission of patients and tacit guarantees of no cancellations). Finally, we agree with van Klei *et al.* that in a perfect world, all patients would be seen in an anesthesia preoperative medical clinic (APMC). This would almost certainly improve patient satisfaction and safety and improve operating room morale and efficiency. One important implication of our data was proof of the assertion that an APMC can improve operating room efficiency. We hope that these data will increase hospitals' willingness to provide financial support for these endeavors. Nevertheless, until this financial support materializes, APMCs must make decisions about how best to use the available resources. To this point, our data argue that if we do not have the resources to see all patients in the APMC, emphasis should be placed on seeing the elderly and patients with significant comorbidities because the greatest impact of a clinic visit was seen in these groups.

The data of Dr. Qiu *et al.* certainly validate our findings and demonstrate the usefulness of the APMC concept in nonuniversity settings as

well. Furthermore, the discussion by Qiu *et al.* of the financial pressures and scrutiny that an APMC must overcome directly addresses the final question of van Klei *et al.*: Why can't everyone be seen in an APMC? We believe it likely that in the United States, a compelling demonstration of societal cost savings must be demonstrated before any organization will help pay for the clinic. It was our purpose to document that an APMC can produce financial savings to the hospital and that the costs of the clinic should rationally be borne by all of the institutional members who benefit.

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An Error Associated with an Epidural Drug Infusion Pump

To the Editor:—A 32-yr-old gravida 2, para 1 woman underwent uneventful placement of an epidural catheter at L3–L4. A bolus of 10 ml bupivacaine, 0.25%, was given incrementally, without adverse effect. A member of the anesthesia care team primed the epidural tubing (primary IV Plumset; Hospira Inc., Lake Forest, IL; Convertible Pin 107 inch with option lock) with 0.0625% bupivacaine containing 2 μg/ml fentanyl (250 ml bag total). The epidural tubing was inserted into an Abbott Labs Micro/Macro PlumXL infusion pump (Abbott Park, IL). No filter was used between the epidural catheter and tubing. Approximately 2 h after epidural insertion and pump hookup, the patient called the nurse and reported difficulty with breathing and numbness of the chest. On physical examination, the patient was observed to have good grip strength, a T4 sensory level to cold test, and blood pressure within normal limits. There were no fetal heart rate abnormalities.

It was observed that the epidural infusion bag was empty and that both the flow regulator and the door on the infusion pump were in the open position. Epidural infusion was temporarily suspended, and the mother delivered a healthy baby, with no adverse sequelae.

Support was provided solely from institutional and/or departmental sources.

The situation noted seems to be due to an interaction between a human error and the design of the infusion pump—an error that might be avoided by changes in the design of the device. Specifically, human error might be avoided if the cassette device were designed so that the flow regulator must be in the closed position when it is inserted into the pump. Also, the flow regulator might be designed with a spring that automatically retracts inward after priming. In lieu of a design change, we attached a notice regarding proper use on each pump, and all members of the care team were reeducated regarding safe and proper use of an infusion pump.

This case underscores the inherent safety of using low-dose local anesthetic for continuous epidural infusion. If a more concentrated solution had been used, a potentially more adverse outcome might have occurred. With a free drip system, gravity determines how fast an infusion occurs. The height of the epidural bag thus determines the rapidity of infusion.

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A New Method for Detecting the Proximal Aortic Arch and Innominate Artery by Transesophageal Echocardiography

To the Editor:—Because of the interposition of the trachea between the esophagus and the great vessels, transesophageal echocardiography (TEE) visualization of the proximal aortic arch and innominate artery (INA) is usually fraught with difficulty.[1–5] After institutional research ethics board approval (West China Hospital, Sichuan University, Sichuan, PR China), we studied a new acoustic window for TEE imaging of large vessels anterior to the trachea by using a saline-filled endotracheal balloon during cardiopulmonary bypass (CPB). The methods are as follows.

The endotracheal balloon was made with the shaft of a No. 37 Univent® (Fuji Systems Corporation, Tokyo, Japan) blocker and part of a surgical glove. First, the blocker balloon of a Univent® blocker was removed, and the segment over the middle digit of a size 8 latex surgical glove was cut to a total length of 8 cm. The glove segment was attached to the distal part of the Univent® shaft using a No. 4 silk suture. The balloon was made to possess a diameter of 1.8 cm and a length of 6 cm while fully inflated.

In cardiac surgery patients, general anesthesia was induced with intravenous midazolam, muscle relaxant, fentanyl, and propofol. The endotracheal tube was initially inserted into either the left or the right main stem bronchus as evident by unilateral air entry with auscultation. The endotracheal tube was subsequently withdrawn until breath sounds were first heard over both lungs. At this point, the tip of the tube was considered to be located immediately proximal to the carina. The depth of the endotracheal tube between the teeth was recorded. The endotracheal tube was withdrawn 3–4 cm from the carina and fixated using tape. This recorded depth of the endotracheal tube with the tip at the carina would be used for positioning of the endotracheal tube after the initiation of CPB.

Transesophageal echocardiography was performed after anesthesia induction with a 4- to 7-MHz phased array probe (model 21396A; Hewlett-Packard, Andover, MA) and an ultrasound system (Hewlett-Packard Sonos 4500). Before tracheal intubation, the endotracheal balloon was passed

Support was provided solely from institutional and/or departmental sources.

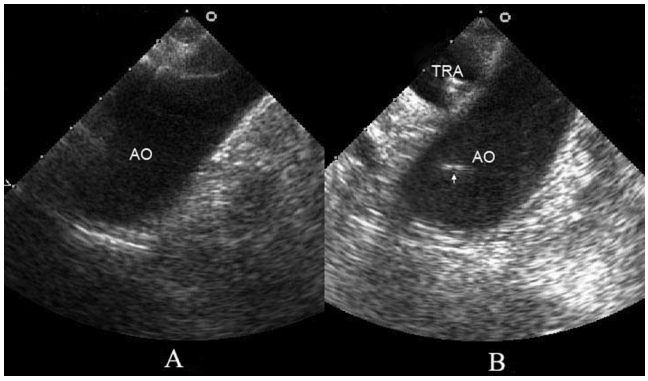

Fig. 1. Transesophageal echocardiographic images of upper esophageal aortic arch long axis with and without the saline-filled endotracheal balloon. (*A*) Without the endotracheal balloon, approximately two thirds of the posterior wall of the aortic arch was not seen. (*B*) With the presence of a saline-filled endotracheal balloon, the trachea was seen as a round echo-free space, and the proximal aortic arch was visualized anterior to the trachea. The entire posterior wall of the aortic arch was seen clearly in this view. There is a reverberation artifact resulting from the tracheal balloon shaft in the aorta (*arrow*). AO = aortic arch; TRA = trachea.

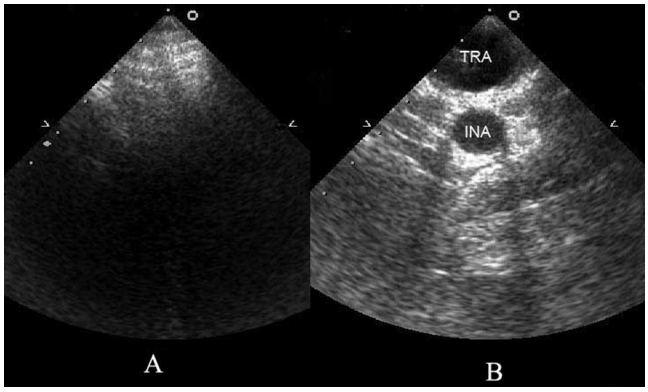

Fig. 2. Transverse views 2 cm above the aortic arch with and without the saline-filled endotracheal balloon at multiplane angle of 40°. (*A*) Without the endotracheal balloon, the innominate artery cannot be visualized. (*B*) With the presence of a saline-filled endotracheal balloon, the upper esophageal innominate short axis can be clearly visualized. It is located directly anterior to the trachea. INA = the innominate artery; TRA = trachea.

through the endotracheal tube until the balloon tip was located exactly at the endotracheal tube tip. A mark was made on the balloon shaft for identification. After initiation of CPB, the endotracheal tube was withdrawn so that its tip was located 6 cm above carina as previously described. The balloon was inserted 6 cm beyond the above-noted marking on the balloon shaft. At this point, the distal end of the balloon was considered to be located immediately above the carina. The process of filling the balloon was monitored by TEE, and saline was injected until the outline of trachea was seen or the balloon pressure reached 30 mmHg.

The transverse view of the trachea with the saline filled balloon was detected as a round echo-free space that was located at the tip of the fan-shaped view. When the probe was placed at a depth of approximately 18–25 cm from the incisor, the sausage-shaped aortic arch, with its proximal part anterior to the trachea, was viewed at a multiplane angle of 0°. Using the upper esophageal (UE) aortic arch long axis, the TEE probe was adjusted until the image with the maximal major diameter was obtained. Figure 1 is a sample image of UE aortic arch long axis with and without the endotracheal balloon.

To image the INA, using the UE aortic arch long axis, the probe was withdrawn gradually while visualization of the endotracheal balloon was maintained. As the aortic arch disappeared from the view, the transverse view of the INA was seen anterior to the trachea at multiplane angle of approximately 40° (20°–65°). The TEE probe was adjusted until the transverse INA image, which was most circular in form at 2 cm above the aortic arch, was obtained. This plane was named UE innominate short axis. The UE innominate long axis was detected at a multiplane angle of approximately 130° (110°–160°). In this view, the INA was seen to be arising from and connected directly to the proximal aortic arch. Figure 2 is a sample image of UE innominate short axis with and without the endotracheal balloon.

The main reason for the "blind zone" in TEE is the tracheal air column, which lies right and ventral to the esophagus. Echo waves are scattered completely by air. In patients undergoing cardiovascular surgery involving CPB, ventilation is terminated, and endotracheal balloon insertion is feasible. The insertion of a saline-filled endotracheal balloon eliminates the tracheal air column, thereby making possible the TEE imaging of the proximal aortic arch and INA anterior to the trachea. This new acoustic window is named "TEE transtracheal acoustic window."

This TEE transtracheal acoustic window seems to provide improved visualization of the proximal aortic arch and INA. The major limitation of this window is that it can only be used when the ventilator is disconnected or during CPB. Before and after CPB, routine TEE must be used. Further studies are required to compare quantitatively the image quality of the proximal aorta and INA, with and without the presence of an endotracheal saline-filled balloon.

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Methylene Blue Treatment for Methemoglobinemia and Subsequent Dramatic Bispectral Index Reduction

To the Editor:—We report a clinical case in which a patient was recognized to have methemoglobinemia from dapsone therapy and was treated intraoperatively with intravenous methylene blue. Each time methylene blue was administered, there was a concurrent dramatic reduction in Bispectral Index (BIS) to burst suppression values.

The case we report is of a 71-yr-old woman with a medical history remarkable for ophthalmic pemphigoid, which was treated with dapsone therapy. She presented for pelvic exenteration surgery for endometrial cancer. A thoracic epidural (T9–T10) was placed preoperatively for postoperative analgesia, and a test dose only of 3 ml lidocaine, 1.5%, with epinephrine (15 μg) was given in the preoperative area, without event. During induction of general anesthesia with intravenous propofol (180 mg) and fentanyl (100 μg), the patient underwent intubation with succinylcholine (90 mg). After intubation, despite her breathing 100% oxygen, the patient's oxygen saturation did not improve to greater than 94%. The patient had no known pulmonary disease. After an otherwise uneventful induction of general anesthesia and placement of radial artery and central venous catheters, arterial blood gas analysis revealed a pH of 7.37, a partial pressure of carbon dioxide (P_{CO_2}) of 34 mmHg, and a partial pressure of oxygen (P_{O_2}) of 169 mmHg with an oxygen saturation of 92.3%. It was also shown that the methemoglobin value was 6.5%. A diagnosis of methemoglobinemia was made and attributed to the patient's long-term use of the medication dapsone. Given the extent of the surgery and the age of the patient, methylene blue was given to treat the methemoglobinemia and optimize oxygen-carrying capacity. After administration of 5 ml methylene blue, 1%, the BIS was noted to decrease immediately from a stable value of mid 40s to the low teens, while the patient's oxygen saturation improved to 97%. There also followed some hypertension (peak systolic value of 179 mmHg) necessitating labetalol (20 mg) therapy a few minutes later. The BIS value remained low for 5–6 min before returning to the 40s again. On the next blood gas analysis, the methemoglobin had decreased to 4.3%, and the oxygen saturation improved to 94.7%, with no significant change in pH or P_{CO_2}. More methylene blue was titrated into the patient, with 5-ml (1%) increments up to 20 ml total (1% solution), which resulted in improvement of the oxygen saturation to 100% and a decrease in the methemoglobin to 1.9%. On each occasion of administering methylene blue, the BIS decreased from the 40s to the low teens (lowest value 13) almost immediately. The end-tidal isoflurane concentration remained constant at 1.1% throughout these episodes, and no intravenous analgesia was given during or just before the reduction in the BIS values. The case proceeded uneventfully, except for significant blood loss, which required a transfusion of 5 units of packed erythrocytes and 2 units of fresh frozen plasma. The patient did well postoperatively, with no relocation of any operative events, and was discharged home on postoperative day 5.

There are a number of drugs that have been implicated in causing methemoglobinemia, with dapsone being on the list.[1] Treatment of methemoglobinemia involves removal of the causative agent and administration of methylene blue, which was done in this case. Methylene blue is an α-receptor agonist and works as a nitric oxide scavenger, both of which can result in hypertension. This patient received up to 20 ml methylene blue (1%), and her baseline arterial oxygen saturation on inspired oxygen of 1.0 improved to 100%. In addition, her methemoglobin decreased to a nadir of 1.9%.

In this case, upon administration of methylene blue, the BIS decreased from the 40s to the low teens (burst suppression range), and this precipitous decrease in the BIS seemed to occur with each administration of methylene blue. There are a number of nonanesthetic factors that can influence the BIS value.[2] Muscle relaxants have been shown to reduce the BIS value.[3] There are no clinical reports of methylene blue's effect on muscle relaxation, save a couple of laboratory interactions with smooth muscle, both of which suggest an action to increase rather than decrease smooth muscle tone, so this is an unlikely explanation of this effect.[4,5] Other conditions shown to reduce the BIS value are related to central nervous system perfusion, *e.g.*, hypoglycemia, hypovolemia, and cerebral ischemia. In this case, methylene blue administration not only led to a reduction in the BIS value but increased the blood pressure, necessitating labetalol therapy, with all the other anesthetic variables being unchanged, so it difficult to explain this effect with cerebral perfusion changes. There are no clinical reports of methylene blue having a direct central nervous system effect, save its use to treat and prevent ifosfamide-induced encephalopathy[6]; however, laboratory studies have shown that the nitric oxide neurotogenic activity of nitric oxide donors can be inhibited by methylene blue and other inhibitors of guanylyl cyclase.[7] This longer-term neuronal action would be unlikely to impact such a rapid change in BIS value; however, it cannot be ruled out that methylene blue has a direct neuronal effect or displaces a centrally active drug.

Although there certainly could have been an artifactual reduction in the BIS, there are no reports to date that have shown that methylene blue interferes with the BIS monitor or other electroencephalographic recording. The fact that it occurred immediately after methylene blue dosing and on each subsequent occasion suggests a potential link between the two. Whatever the mechanism of this reduction, we suggest that anesthesiologists be vigilant for methemoglobinemia in patients receiving dapsone therapy and for BIS interference with methylene blue administration.

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