**To the Editor—** The interesting article by Flaishon et al. included prospective data on the difficulties of performing anesthetic and critical care duties in mass casualty situations. An additional factor to consider is the challenge of continuing to perform one’s duties while wearing full antichemical protective gear.

As a member of the Air National Guard, I am obligated to perform chemical warfare training. Wearing the full MOPP 4 antichemical warfare ensemble is uncomfortable, especially in warm environments such as the Middle East. The clinician must contend with the intrinsic difficulties of wearing the suit and be mindful of preventing his own severe dehydration and the need to be resuscitated himself.

Most United States civilians do not appreciate the need to maintain adequate hydration. In the Middle East, constant hydration is a way of life. Military personnel have become familiar with disaster management concepts. In the future, such training will be mandatory for civilians as well. The Society of Critical Care Medicine (Des Plaines, IL) sponsored its first course on disaster medicine at its annual meeting this year to provide civilian clinicians with the basic concepts of disaster management. The course will heighten awareness of the challenges of airway management as well as the challenges and hazards of extended wear of chemical warfare gear.

*Eric L. Bloomfield, M.D., M.S., F.C.C.M.* Mayo Clinic, Jacksonville, Florida. bloomfield.eric@mayo.edu

**Reference**


*(Accepted for publication June 21, 2004.)*

**References**


*(Accepted for publication June 21, 2004.)*

**To the Editor—** We read with interest the well-written case report “Dexmedetomidine and Cardiac Arrest.” The inference of the authors seems to be simple, but a closer look reveals the omission of many implicating factors that would have contributed to the morbidity attributed to dexmedetomidine. Therefore, we dispute the conclusions. We believe that the patient received an excessive dose of dexmedetomidine after significant doses of other anesthetics and there was delay in treating the bradycardia. We believe that the progression to cardiac arrest could have been potentially prevented.

Dosing of 10 mg of midazolam during the placement of epidural catheter, 250 µg of fentanyl, and 200 mg of propofol for induction and maintenance at 0.9% isoflurane after a loading dose of dexmedetomidine at 1 µg/kg, followed by 0.2 µg·kg⁻¹·h⁻¹ by infusion, seems to be excessive. Even with normal dosing hypotension and bradycardia are the most common side effects of dexmedetomidine. The concomitant use of anesthetics, sedatives, hypnotics, and opioids has synergistic effects and may worsen bradycardia and hypotension. There may also have been increased vagal activity as a result of pyridostigmine and a
history of vigorous exercise. An unrecognized hypovolemic state was also present. The undiagnosed decrease in preload, even in the presence of acceptable vital signs, is at times overlooked. Excess dexmedetomidine, nonintervention of bradycardia at an appropriate time, and inadequate hydration sets the stage for unintentional cardiac arrest. Also, the episode seemed to have evolved at a faster pace against a background of what seemed to be benign. Later, cardiac arrest ensued. On hindsight, a stricter insight into potential and unintentional risks would have prevented the development of cardiac arrest.

In short, a close scrutiny of the case that resulted in bradycardia and cardiac arrest seems to stem from multiple factors rather than from dexmedetomidine alone. The authors direct implication of dexmedetomidine is questionable. Dexmedetomidine probably would have added to the sequence of events that followed but by itself it is an unlikely culprit in this particular case. In other words, dexmedetomidine can cause cardiac arrest if given in too great a dose after relatively large doses of other anesthetics. Bradycardia, if allowed unabated by nonintervention in the presence of other risk factors, can also progress to cardiac arrest. The episode would have been thwarted by a judicious insight into the complex series of events that one often recognizes only after the incident has occurred. In this particular case sternotomy with undiagnosed decrease in preload, even in the presence of what seemed to be benign. Later, cardiac arrest ensued. On hindsight, a stricter insight into potential and unintentional risks would have prevented the development of cardiac arrest.

Although we differ with the authors’ observations and the issue may be contentious because of its interwoven complexity, they must be complemented for their deft handling of a difficult case.

Muhammad Muntazar, M.D.,* Francis C. Kumar, M.D. * University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma. mohammad-muntazar@ouhsc.edu

References
1. Ingersoll-Weng E, Manecke GR, Thistlethwaite PA: Dexmedetomidine and cardiac arrest. ANESTHESIOLOGY 2004; 100:738–9

(Accepted for publication June 25, 2004.)

Dexmedetomidine and Asystole

To the Editor—We read with great interest the report of a cardiac arrest during dexmedetomidine use in a patient with myasthenia gravis. In this case the interaction of pyridostigmine and epidural anesthesia was cited as possible contributors to this complication. We would like to add our own experience with dexmedetomidine. We began to use it in 20–40-yr-old healthy patients scheduled for laparoscopic gynecological procedures under sevoflurane and fentanyl anesthesia plus cisatracurium for neuromuscular blockade. Dexmedetomidine was infused by the “sufentanil” program of an Anne® intravenous infusion pump (Abbott Laboratories, North Chicago, IL) with an initial infusion of 4 g·kg⁻¹·h⁻¹ for 15 min followed by 0.3 µg·kg⁻¹·h⁻¹. After 40 patients were anesthetized using this technique, there was one case of severe bradycardia (32 beats/min) and one case of asystole. No patient received pyridostigmine or had epidural anesthesia instituted.

This event of asystole occurred while the patient was in Trendelenburg position with the peritoneal cavity insulated with carbon dioxide (12 cmH₂O), and it lasted less than 2 min, responding to abdominal deflation, horizontal positioning, intravenous atropine 1 mg, and a brief period of thoracic compressions. End-tidal carbon dioxide and capnographic curve were normal before and after the asystole. We wonder if the incidence of asystole with dexmedetomidine is different from that with other anesthetic drugs. A study to verify the safety and not only the efficacy of this new drug should be undertaken while more subtype-selective α₂ receptor agonists with decreased side effects are awaited for clinical practice.

Rogerio L. R. Videira, M.D.,* Roberto Manara V. Ferreira, M.D. * Hospital das Clinicas da Universidade de Sao Paulo and Univesidade Federal do Estado de Sao Paulo, Sao Paulo, Brazil. rovid@uol.com.br

References
1. Ingersoll-Weng E, Manecke GR, Thistlethwaite PA: Dexmedetomidine and cardiac arrest. ANESTHESIOLOGY 2004; 100:738–9

(Accepted for publication June 25, 2004.)

In Reply—we appreciate and agree, for the most part, with the comments of Drs. Muntazar and Kumar and those of Drs. Videira and Ferreira. Our purpose in presenting this case was to bring to light the potentially disastrous results from a particular combination of negative chronotropic influences. We have used an anesthetic combination similar to this many times for thymectomy (minus the dexmedetomidine) and never experienced a case of asystole. Thus, we believe it

(Accepted for publication June 25, 2004.)

Copyright © by the American Society of Anesthesiologists. Unauthorized reproduction of this article is prohibited.
To the Editor— I read with great interest the case report by Augoustides et al.1 published in the April issue of Anesthesiology. They highlight the important issue of rebound pulmonary hypertension after withdrawal of inhaled prostacyclin and make a case for the use of inhaled iloprost. They propose that inhaled iloprost may allow gradual controlled withdrawal of perioperative inhaled selective pulmonary vasodilation, probably as a result of its favorable pharmacokinetics. Hence, in their opinion it has great promise in the management of perioperative pulmonary hypertension after cardiac surgery. However, I think that if the authors had highlighted the advantages of using sildenafil, instead of iloprost, in this scenario their case report would have made a more lasting and useful contribution to the existing literature on the topic of management of rebound pulmonary hypertension.

Pulmonary hypertension remains a major complication after surgical correction of congenital and long-standing valvular heart disease. Inhaled nitric oxide has been shown to reduce, but not eliminate, potentially life-threatening episodic pulmonary hypertensive crises.2 Nitric oxide increases intracellular cyclic guanosine monophosphate, resulting in smooth muscle vasodilation. Phosphodiesterase type 5 is responsible for cyclic guanosine monophosphate breakdown in lung tissue. Abrupt discontinuation of nitric oxide may be complicated by life-threatening events, and phosphodiesterase activity may play a role in this phenomenon.3 Sildenafil (Viagra; Pfizer Laboratories, New York, NY), a selective and potent inhibitor of phosphodiesterase type 5, augments pulmonary vasodilation with nitric oxide and reduces the risk of pulmonary hypertensive crises in an at-risk postoperative patient.4 Furthermore, it ameliorates the rebound pulmonary hypertension caused by withdrawal of inhaled pulmonary vasodilators.5

Compared with the standard treatment, inhaled nitric oxide, sildenafil is superior in decreasing the mean pulmonary artery pressure and equally effective and selective in reducing pulmonary vascular resistance.6 It also causes a significant increase in the cardiac index.6 Its availability in oral, inhaled and intravenous forms, longer half-life of 4 h,7 and proven efficacy in randomized controlled trials8–10 are some of the distinguishing features which make sildenafil first-choice agent for managing rebound pulmonary hypertension. We appreciate Drs. Videira and Ferreira sharing their experiences and agree that a large-scale safety study of the drug should be considered. We believe that when used appropriately, dexmedetomidine is very safe and useful. Perhaps by performing such a study and sharing our experiences with the drug, we, as a community, can avoid future closed claims analyses and unnecessary “black box” Food and Drug Administration warnings.

Gerard R. Manecke Jr., M.D.,* Esperanza Ingersoll-Weng, M.D., and Patricia A. Thistlethwaite, M.D., Ph.D. *Thornton Hospital, La Jolla, California. gmanecke@ucsd.edu

Reference

1. Ingersoll-Weng E, Manecke GR, Thistlethwaite PA: Dexmedetomidine and cardiac arrest. Anesthesiology 2004; 100:738–9

(Accepted for publication June 25, 2004.)

To the Editor:—I read with great interest the case report by Augoustides et al.1 published in the April issue of Anesthesiology. They highlight the important issue of rebound pulmonary hypertension after withdrawal of inhaled prostacyclin and make a case for the use of inhaled iloprost. They propose that inhaled iloprost may allow gradual controlled withdrawal of perioperative inhaled selective pulmonary vasodilation, probably as a result of its favorable pharmacokinetics. Hence, in their opinion it has great promise in the management of perioperative pulmonary hypertension after cardiac surgery. However, I think that if the authors had highlighted the advantages of using sildenafil, instead of iloprost, in this scenario their case report would have made a more lasting and useful contribution to the existing literature on the topic of management of rebound pulmonary hypertension.

Pulmonary hypertension remains a major complication after surgical correction of congenital and long-standing valvular heart disease. Inhaled nitric oxide has been shown to reduce, but not eliminate, potentially life-threatening episodic pulmonary hypertensive crises.2 Nitric oxide increases intracellular cyclic guanosine monophosphate, resulting in smooth muscle vasodilation. Phosphodiesterase type 5 is responsible for cyclic guanosine monophosphate breakdown in lung tissue. Abrupt discontinuation of nitric oxide may be complicated by life-threatening events, and phosphodiesterase activity may play a role in this phenomenon.3 Sildenafil (Viagra; Pfizer Laboratories, New York, NY), a selective and potent inhibitor of phosphodiesterase type 5, augments pulmonary vasodilation with nitric oxide and reduces the risk of pulmonary hypertensive crises in an at-risk postoperative patient.4 Furthermore, it ameliorates the rebound pulmonary hypertension caused by withdrawal of inhaled pulmonary vasodilators.5

Compared with the standard treatment, inhaled nitric oxide, sildenafil is superior in decreasing the mean pulmonary artery pressure and equally effective and selective in reducing pulmonary vascular resistance.6 It also causes a significant increase in the cardiac index.6 Its availability in oral, inhaled and intravenous forms, longer half-life of 4 h,7 and proven efficacy in randomized controlled trials8–10 are some of the distinguishing features which make sildenafil first-choice agent for managing rebound pulmonary hypertension. We appreciate Drs. Videira and Ferreira sharing their experiences and agree that a large-scale safety study of the drug should be considered. We believe that when used appropriately, dexmedetomidine is very safe and useful. Perhaps by performing such a study and sharing our experiences with the drug, we, as a community, can avoid future closed claims analyses and unnecessary “black box” Food and Drug Administration warnings.

Gerard R. Manecke Jr., M.D.,* Esperanza Ingersoll-Weng, M.D., and Patricia A. Thistlethwaite, M.D., Ph.D. *Thornton Hospital, La Jolla, California. gmanecke@ucsd.edu

Reference

1. Ingersoll-Weng E, Manecke GR, Thistlethwaite PA: Dexmedetomidine and cardiac arrest. Anesthesiology 2004; 100:738–9

(Accepted for publication June 25, 2004.)

To the Editor:—I read with great interest the case report by Augoustides et al. published in the April issue of Anesthesiology. They highlight the important issue of rebound pulmonary hypertension after withdrawal of inhaled prostacyclin and make a case for the use of inhaled iloprost. They propose that inhaled iloprost may allow gradual controlled withdrawal of perioperative inhaled selective pulmonary vasodilation, probably as a result of its favorable pharmacokinetics. Hence, in their opinion it has great promise in the management of perioperative pulmonary hypertension after cardiac surgery. However, I think that if the authors had highlighted the advantages of using sildenafil, instead of iloprost, in this scenario their case report would have made a more lasting and useful contribution to the existing literature on the topic of management of rebound pulmonary hypertension.

Pulmonary hypertension remains a major complication after surgical correction of congenital and long-standing valvular heart disease. Inhaled nitric oxide has been shown to reduce, but not eliminate, potentially life-threatening episodic pulmonary hypertensive crises. Nitric oxide increases intracellular cyclic guanosine monophosphate, resulting in smooth muscle vasodilation. Phosphodiesterase type 5 is responsible for cyclic guanosine monophosphate breakdown in lung tissue. Abrupt discontinuation of nitric oxide may be complicated by life-threatening events, and phosphodiesterase activity may play a role in this phenomenon. Sildenafil (Viagra; Pfizer Laboratories, New York, NY), a selective and potent inhibitor of phosphodiesterase type 5, augments pulmonary vasodilation with nitric oxide and reduces the risk of pulmonary hypertensive crises in an at-risk postoperative patient. Furthermore, it ameliorates the rebound pulmonary hypertension caused by withdrawal of inhaled pulmonary vasodilators.

Compared with the standard treatment, inhaled nitric oxide, sildenafil is superior in decreasing the mean pulmonary artery pressure and equally effective and selective in reducing pulmonary vascular resistance. It also causes a significant increase in the cardiac index. Its availability in oral, inhaled and intravenous forms, longer half-life of 4 h, and proven efficacy in randomized controlled trials are some of the distinguishing features which make sildenafil first-choice agent for managing rebound pulmonary hypertension. We appreciate Drs. Videira and Ferreira sharing their experiences and agree that a large-scale safety study of the drug should be considered. We believe that when used appropriately, dexmedetomidine is very safe and useful. Perhaps by performing such a study and sharing our experiences with the drug, we, as a community, can avoid future closed claims analyses and unnecessary “black box” Food and Drug Administration warnings.

Gerard R. Manecke Jr., M.D.,* Esperanza Ingersoll-Weng, M.D., and Patricia A. Thistlethwaite, M.D., Ph.D. *Thornton Hospital, La Jolla, California. gmanecke@ucsd.edu

Reference

1. Ingersoll-Weng E, Manecke GR, Thistlethwaite PA: Dexmedetomidine and cardiac arrest. Anesthesiology 2004; 100:738–9

(Accepted for publication June 25, 2004.)

To the Editor:—I read with great interest the case report by Augoustides et al. published in the April issue of Anesthesiology. They highlight the important issue of rebound pulmonary hypertension after withdrawal of inhaled prostacyclin and make a case for the use of inhaled iloprost. They propose that inhaled iloprost may allow gradual controlled withdrawal of perioperative inhaled selective pulmonary vasodilation, probably as a result of its favorable pharmacokinetics. Hence, in their opinion it has great promise in the management of perioperative pulmonary hypertension after cardiac surgery. However, I think that if the authors had highlighted the advantages of using sildenafil, instead of iloprost, in this scenario their case report would have made a more lasting and useful contribution to the existing literature on the topic of management of rebound pulmonary hypertension.

Pulmonary hypertension remains a major complication after surgical correction of congenital and long-standing valvular heart disease. Inhaled nitric oxide has been shown to reduce, but not eliminate, potentially life-threatening episodic pulmonary hypertensive crises. Nitric oxide increases intracellular cyclic guanosine monophosphate, resulting in smooth muscle vasodilation. Phosphodiesterase type 5 is responsible for cyclic guanosine monophosphate breakdown in lung tissue. Abrupt discontinuation of nitric oxide may be complicated by life-threatening events, and phosphodiesterase activity may play a role in this phenomenon. Sildenafil (Viagra; Pfizer Laboratories, New York, NY), a selective and potent inhibitor of phosphodiesterase type 5, augments pulmonary vasodilation with nitric oxide and reduces the risk of pulmonary hypertensive crises in an at-risk postoperative patient. Furthermore, it ameliorates the rebound pulmonary hypertension caused by withdrawal of inhaled pulmonary vasodilators.

Compared with the standard treatment, inhaled nitric oxide, sildenafil is superior in decreasing the mean pulmonary artery pressure and equally effective and selective in reducing pulmonary vascular resistance. It also causes a significant increase in the cardiac index. Its availability in oral, inhaled and intravenous forms, longer half-life of 4 h, and proven efficacy in randomized controlled trials are some of the distinguishing features which make sildenafil first-choice agent for managing rebound pulmonary hypertension. We appreciate Drs. Videira and Ferreira sharing their experiences and agree that a large-scale safety study of the drug should be considered. We believe that when used appropriately, dexmedetomidine is very safe and useful. Perhaps by performing such a study and sharing our experiences with the drug, we, as a community, can avoid future closed claims analyses and unnecessary “black box” Food and Drug Administration warnings.

Gerard R. Manecke Jr., M.D.,* Esperanza Ingersoll-Weng, M.D., and Patricia A. Thistlethwaite, M.D., Ph.D. *Thornton Hospital, La Jolla, California. gmanecke@ucsd.edu

Reference

1. Ingersoll-Weng E, Manecke GR, Thistlethwaite PA: Dexmedetomidine and cardiac arrest. Anesthesiology 2004; 100:738–9

(Accepted for publication June 25, 2004.)
In Reply.—I thank Dr. Raja for an excellent appraisal of the role of sildenafil (Viagra; Pfizer Laboratories, New York, NY) in the management of rebound pulmonary hypertension after withdrawal of inhaled prostacyclin, as highlighted in our recent case report.1 Dr. Raja has correctly highlighted that sildenafil is an alternative to iloprost in this setting.2-7 Our discussion of iloprost in the case report focused on its advantages over inhaled prostacyclin in the withdrawal of inhaled pulmonary vasodilator therapy. The pharmacokinetics of iloprost highlight a limitation of inhaled prostacyclin, namely its short half-life, that may facilitate serious rebound pulmonary hypertension.

However, this discussion was by no means intended to minimize the role of alternative approaches to the management of rebound pulmonary hypertension. As emphasized, a tiered multimodal therapeutic approach to pulmonary hypertension is essential for successful management.1,8,9 Indeed, this multimodal therapeutic approach to this clinical scenario not only includes sildenafil but also extends beyond this agent. The withdrawal of inhaled pulmonary vasodilators with a short half-life (nitric oxide, prostacyclin) should be managed in the setting of optimized ventilation, and where required, sufficient supplemental pulmonary vasodilator, whether inhaled, intravenous, or oral. There is a wide selection of possible agents that may be administered alone or in synergistic combination.8,10 The choice of regimen should also take into account drug availability, drug familiarity, and patient idiosyncrasies.

In summary, rebound pulmonary hypertension with withdrawal of nitric oxide or prostacyclin should be approached in a tiered multimodal fashion. Although sildenafil is eminently suitable, it is but one of a possible menu of pharmacologic choices.

John G. Augoustides, M.D. Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania. yiandoc@hotmail.com

References


(Accepted for publication July 27, 2004.)

To the Editor.—I read with interest the article recently published by Haspeslagh et al.1 concerning an inadvertent lumbar disc injection which occurred during unilateral diagnostic infiltration of lumbar L3 nerve root.

Although the authors did mention the importance of fluoroscopy, they did not extensively discuss the reasons for the complication. This event must have the caused by a failure to note the depth of needle insertion during the procedure. The needle tip on the lateral view should be in the posterior aspect of the foramen when the transforaminal epidural injection is performed.2 The authors’ figure suggests that the needle had been inserted too far; the tip of the needle was beyond the dura, therefore no epidurogram was demonstrated in the fluoroscopic images.

As the authors indicated, “meticulous care should be taken when a transforaminal epidural injection . . . is performed.” In addition, frequent utilization of fluoroscopy in different planes during the needle insertion (not just at the time of dye injection) is essential for precise needle placement.

Jeffrey Huang, M.D. Anesthesiologists of Greater Orlando, Orlando, Florida. jeffrey_j_huang@hotmail.com

References


(Accepted for publication July 28, 2004.)
In Reply.—We thank Dr. Huang for his interesting comments. We agree that frequent control of the correct needle position by the use of fluoroscopy is important during interventional pain procedures.1

The depth of the needle position on a lateral view is important because antiinflammatory agents must be injected as close as possible to the site of pathology; i.e., in the anterior plane of the epidural space.2 With respect to the presented anteroposterior view (Fig 2a in our article)1 and in accordance with another review,3 the insertion of the needle no further medial than the six o’clock position in the anteroposterior view reduces the risk of dural puncture.3 Moreover, when our needle had been positioned intradurally at this level, a discogram could not have been explained.

Finally, low back pain and sciatica resulting from migrated disc herniations are an indication for transformaminal epidural infiltrations.4 By placing the needle in a correct fluoroscopic position, the needle can accidentally encounter a rostrally displaced disc herniation, which possibly explains this unexpected event. Our finding emphasizes the use of fluoroscopy in interventional pain procedures.

References


(accepted for publication July 28, 2004.)
Cholinesterase Inhibitors, Neuromuscular Blocking Drugs and Perioperative Memory Enhancement

To the Editor:—I read the fascinating review by Dr. Ghoneim with great interest, especially the section on memory-enhancing or memory-improving drugs. Anesthetics impair memory function in perisurgical periods, whereas cholinesterase inhibitors enhance memory and act at central muscarinic cholinergic receptors involved in the process of memory consolidation. These rhythms constitute background activity that is associated with a reduction of gamma or 40 Hz oscillations in the neocortex. Physostigmine that results from potentiation of 40 Hz oscillations via increased muscarinic tone, whereas anesthetic-induced unconsciousness is associated with a reduction of gamma or 40 Hz oscillations in thalamocortical systems. These rhythms constitute background activity reflecting depolarization of thalamic and cortical neurons, a physiologic condition required for consciousness. The first line of treatment in Alzheimer disease and the only drugs of proven benefit are under clinical evaluation.

Drugs affecting central cholinergic activity also influence the anesthetic effect. Increasing central cholinergic tone with physostigmine antagonizes the hypnotic effect of propofol, shown by the return of consciousness defined as responsiveness to commands or wakefulness (appearance of being awake with open eyes but without cognitive content). Plourde et al. measuring the action of physostigmine on the hypnotic effect of inhaled volatile anesthetics, conclude that physostigmine can, at least partially, antagonize the hypnotic effect of sevoflurane (subanesthetic concentrations) and that the resulting arousal is reflected by an increase in the amplitude of auditory steady-state response and, to a lesser extent, of the bispectral index. An interesting possibility is the antagonism of the anesthetic effect with physostigmine that results from potentiation of 40 Hz oscillations via increased muscarinic tone, whereas anesthetic-induced unconsciousness is associated with a reduction of gamma or 40 Hz oscillations in thalamocortical systems. These rhythms constitute background activity reflecting depolarization of thalamic and cortical neurons, a physiologic condition required for consciousness. In addition, Hill et al. demonstrated that physostigmine decreased the time for return of consciousness after halothane anesthesia. These data, taken together, suggest not only that if reversal of the neuromuscular blockade occurs during anesthesia using cholinesterase inhibitors patients could be at risk of intraoperative awareness, as we recently underlined, but also that these drugs may promote an enhancement of implicit memory for any awareness event that occurs. It may occur above all during light levels of anesthesia, common during the final period of anesthesia. During this period, cholinesterase inhibitors are given by anesthesiologists to reverse neuromuscular block. In other words, patients may better recall memories of the awareness experienced intraoperatively. It was also reported that inhibition of central nicotinic acetylcholine receptors contributes to secondary effects attributed to anesthesia such as impairment in memory and cognitive performance, whereas nicotinic acetylcholine receptors agonists improve memory. Other drugs used in anesthesia, as well as the neuromuscular blocking drugs atracurium and the atracurium and cisatracurium metabolite laudanosine, activate nicotinic acetylcholine receptors at concentrations comparable to those measured in the central nervous system during, and for several hours after, general anesthesia. Administration of these neuromuscular blocking drugs, resulting in laudanosine production, has been suggested to improve postoperative cognitive functions, with the clinical relevance that they could have a potentially therapeutic effect in patients with Parkinson’s disease. We ask if atracurium, cisatracurium, and their metabolite laudanosine should be included in the list of drugs acting at the cholinergic receptors and therefore potentially enhancing memory, with advantages and disadvantages mentioned above, and if these data merit, as do the anticholinergic agents, more detailed exploration by laboratory and clinical studies.

Vincenzo Fodale, M.D.,* Marco Tescone, M.D., Caterina Praticò, M.D. * University of Messina, Messina, Italy. vfodale@unime.it

References

8. Andoh T: Effects of general anesthetics on neuronal nicotinic acetylcholine receptors and their roles in the mechanism of anesthesia. Masui 2001; 50:1072–84
To the Editor.—The authors must be congratulated for undertaking the study attempting to answer the question of protocol-based airway management in the event of unanticipated difficult intubation. However, this raises some serious questions about the content and conclusions of the study.

First, we are unclear as to how the investigators have concluded that their local protocol-based approach to airway management in the event of unanticipated difficult intubation after induction is efficacious. In an 18-month interval, 100 patients who were anticipated to be easy to intubate on preoperative work-up were subsequently found to be difficult to intubate. Sixteen percent of these patients suffered severe hypoxemia. Although the authors have not provided any data regarding the incidence of hypoxemia at induction among the true positive participants, it is unlikely that the incidence in that population could be as high as 16%. One patient suffered significant dental trauma and one ended up aspirating gastric contents. In addition, 89 patients were subjected to multiple attempts at direct laryngoscopy. The authors fail to acknowledge that these adverse events could very well have been the result of the sticking with the proposed airway algorithm. It appears that most of the patients suffered hypoxemia as a result of multiple attempts at laryngoscopy. Hypoxemia, as we understand, is a clear sign of ventilatory failure under these situations unless it is attributable to other causes. Failure to keep a substantial number of patients oxygenated highlights the inefficiency of the proposed algorithm. Unless the study was designed to evaluate the efficacy of the Intubating Laryngeal Mask Airway™ (LMA North America, Inc., San Diego, CA) as a tool for rescue ventilation, the conclusion that 100 percent of the patients were successfully ventilated underestimates the significant problems at ventilation encountered by the anesthesiologists while following the algorithm.

We are also unclear on what basis the authors claim that the study has validated the local protocol-based approach to airway management. The study has neither the design nor the power to answer this question, as we do not know what would happen if the anesthesiologist were not restricted by the protocol to the use of direct laryngoscopy, gum elastic bougie, Intubating Laryngeal Mask Airway™, or the transtracheal jet ventilation. Whether anticipated or unanticipated, the approach to airway management in the event of failed intubation at induction depends on multiple factors. The result of preliminary laryngoscopy, the view of the glottis, the primary reason for intubation failure (is it the poor laryngoscopic view or the failure to pass the tube?), ease of ventilation with the mask, the muscle relaxant used, emergency or elective surgery, state of oxygenation of the patient, presence or absence of risk factors for aspiration, the condition of upper dentition, and, above all, the skill and expertise of the anesthesiologist all must be taken into account before defining the next step. A protocol-based approach like the one proposed by the investigators may limit anesthesia providers from applying individual problem-based solutions in the event of inadvertent difficult intubation. The end result: the patient with the poor dentition suffers dental trauma, the patient with full stomach may wind up aspirating gastric contents; failure of the Intubating Laryngeal Mask Airway™ regardless of the cause (morbid obesity/limited mouth opening) commits the anesthesia provider to expose the patient to the risk of transtracheal jet ventilation although switching to simple a laryngeal mask airway or laryngeal tube might have solved that problem. A broad-based protocol that incorporates all the fundamental goals and objectives of airway management, e.g., the American Society of Anesthesiologists airway protocol, allowing for stepwise evaluation based interventions while taking into account factors specific to operator skill and experience, available resources, and patient continues to be the most prudent approach to management of inadvertent difficult intubation.

Govind R. Rajan, M.D.
Veterans Affairs Medical Center and Saint Louis University, St. Louis, Missouri. govind_r@hotmail.com

References

To the Editor.—We read with great interest the recent report on unanticipated difficult airway in anesthetized patients by Combes et al. The article confirms that by strictly adhering to a simple predefined algorithm most problems occurring during management of an unexpected airway can be solved. This has already been proven in two other large prospective studies. Using the gum elastic bougie as the first choice in a “can ventilate” but “cannot intubate” situation is a well-established technique, especially in Great Britain, and, of course, is much cheaper than, for example, a fiberoptic bronchoscope.
However, the study raises several questions. The algorithm was only applied in elective cases. It would be very informative whether this airway algorithm was also used in emergency situations (out of the study) and how they succeeded.

The authors did not mention the distribution of intubations across surgical disciplines in detail although it is well known that many difficulties occur in Ear, Nose and Throat departments.

The authors correctly pointed out that the results are not transposable to patients with an anticipated difficult airway. Nevertheless, it would be very interesting how they managed these scenarios and how they decided what is an anticipated difficult airway and consequently excluded them from the study.

Thomas Heidegger, M.D.,* Hans J. Gerig, M.D. * Cantonal Hospital St. Gallen, St. Gallen, Switzerland. thomas.heidegger@kssg.ch

Anesthesiology 2004; 101:1485– 6 © 2004 American Society of Anesthesiologists, Inc. Lippincott Williams & Wilkins, Inc.

In Reply—We read with interest the letters of Drs. Rajan and Heidegger. Dr. Rajan asks if our study was a validation or an invalidation of the Airway Management Algorithm. Clearly, our study was designed to assess a difficult Airway Management Algorithm and not The Airway Management Algorithm because we do not think that there is only one way to manage the unanticipated airway.1

We do not agree with Dr. Rajan that the 16 patients who experienced transient hypoxemia prove the inefficiency of the algorithm assessed. Indeed, most of these patients experienced arterial desaturation at the end of gum elastic bougie challenge only a few seconds before effective tracheal intubation. On the other hand, the Intubating Laryngeal Mask Airway™ (LMA North America, Inc., San Diego, CA) was used as a first step alternative technique in patients demonstrating a difficult ventilation scenario whenever arterial desaturation occurred. We agree with Dr. Rajan that several factors must be taken into account before defining the different steps of the algorithm. Obviously, in our algorithm, difficulties with face mask ventilation and oxygenation have been taken into account. Last, our study was not a comparative study assessing different management strategies of unanticipated difficult airway, but we are convinced of the great interest of such a study.

In our study, we have considered that difficult airway was unanticipated when occurring in a patient who was considered to have normal preanesthesic evaluation of the airway (thyromental distance ≥60 mm, mouth opening ≥50 mm, Mallampati classification less than III, free from any history of difficult airway management in the past, unknown of ear, nose, and throat pathology, and a body mass index <35 kg/m²).

During the study period, 253 patients with anticipated difficult airway were managed in our institution. Ninety-nine underwent primary fiberoptic intubation under topical and locoregional anesthesia. For the other patients, general anesthesia was induced using short-acting anesthetic agents and succinylcholine. With difficult face mask ventilation or class III–IV Cormack laryngeal view, gum elastic bougie was used as first alternative technique (n = 42) and Intubating Laryngeal Mask Airway™ as a second step in case of gum elastic bougie failure (n = 3).

Xavier Combes, M.D.,* Gilles Dhonneur, M.D. * Hôpital Henri Mondor, Creteil, France. xavier.combes@hmn.aphp.fr

References


Xavier Combes, M.D.,* Gilles Dhonneur, M.D. * Hôpital Henri Mondor, Creteil, France. xavier.combes@hmn.aphp.fr

Reference


Use of a Fogarty Catheter Sheath as an Endotracheal Tube Changer

To the Editor—We recently encountered a case that required extubation strategy for difficult airway as recommended by American Society of Anesthesiologists task force.1 A 50-year-old lady underwent segmental mandibulectomy and radical neck dissection with deltopectoral flap for carcinoma parotid gland. At the end of surgery the oral endotracheal tube was left in place and she was shifted to the intensive care unit.

In the absence of either a jet stylet or commercially available tube changer2 that is "rigid to facilitate intubation and/or hollow to facilitate ventilation,"1 we thought of using a readily available tube changer. We were wary of using the previously described tube changers because of their lack of lumen to provide oxygen,3 lack of stiffness,3–5 or small

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

Anesthesiology 2004; 101:1485– 6 © 2004 American Society of Anesthesiologists, Inc. Lippincott Williams & Wilkins, Inc.
Support was provided solely from institutional and/or departmental sources.
To the Editor—Linezolid is a valuable drug that is finding increased use in the hospitalized surgical patient for the treatment of infections resulting from resistant, gram-positive organisms. Along with its known efficacy as an antibacterial agent, linezolid is a mild, reversible monoamine oxidase inhibitor. Reviews on the subject of its monoamine oxidase inhibitor-like profile have expressed caution about the use of linezolid in the clinical setting, specifically when combined with sympathomimetic agents, but there have been few, if any, reported clinical examples of a significant interaction. Recently, however, we observed unexpected intraoperative hemodynamic lability, as well as severe intermittent hypertension, in a psychiatric patient maintained on bupropion who was subsequently placed on linezolid for treatment of an infected vascular graft. We raise the concern that we have seen one of the first examples in the perioperative setting of a potentially dangerous interaction between linezolid and bupropion.

The patient was a 57-yr-old male status post axillary-femoral bypass graft who presented to the emergency room with evidence of a graft infection and was admitted for antibiotics. After a trial of several antibiotics, he was placed on linezolid for treatment of resistant, gram-positive organisms. As an outpatient, he had been stably maintained on bupropion for long-standing depression; this drug was continued throughout his hospital course. After about 24 h of linezolid therapy, the patient was taken to the operating room for graft removal, where he underwent a propofol/succinylcholine induction with standard doses and a maintenance anesthetic of 1.5% isoflurane and fentanyl 250 µg. His intraoperative course was notable for several episodes of severe hypertension (as high as 260/145 mmHg), despite an otherwise stable anesthetic. The unexpected hemodynamic lability was severe enough to result in an unplanned admission to the intensive care unit, where the patient had an unremarkable postoperative course.

The possibility of a significant drug interaction between linezolid and bupropion was suspected immediately and is supported by a careful analysis of the underlying pharmacologic mechanisms. Bupropion is an antidepressant that, in concert with its primary metabolite hydroxybupropion, acts as a norepinephrine reuptake inhibitor as well as a mild dopamine reuptake inhibitor. Both norepinephrine and dopamine are monoamine compounds metabolized by monoamine oxidase. The use of bupropion with older, more traditional monoamine oxidase inhibitor drugs (such as phenelzine and tranylcypromine) has long been contraindicated in standard psychiatric practice because of the risk of a hypertensive crisis. The older monoamine oxidase inhibitors do differ from linezolid in that they are strong, irreversible inhibitors of monoamine oxidase. As linezolid is a weak, reversible monoamine oxidase inhibitor, it had not been appreciated that coadministration with bupropion might cause a similar hypertensive state.

However, linezolid clearly resembles the stronger monoamine oxidase inhibitors in its capacity to interact adversely with certain drugs. Combining the older monoamine oxidase inhibitors with serotoninergically active drugs, such as selective serotonin inhibitors, meperidine, and dextromethorphan, may lead to a severe central serotonin syndrome. Similarly, linezolid has been implicated in producing a central serotonin syndrome when combined with either paroxetine or citalopram (both selective serotonin reuptake inhibitors). Furthermore, it is known that sympathomimetic agents, when administered in combination with the traditional monoamine oxidase inhibitors, may produce severe hypertensive events. Again, linezolid mimics the interaction profile of the stronger monoamine oxidase inhibitors by producing statistically significant increases in blood pressure when
combined with pseudoephedrine and phenylpropanolamine. Based on this information, it is not surprising that linezolid acts like a more traditional monoamine oxidase inhibitor when combined with buproprion, especially in the context of the well-known physiologic stimulation and adrenergic stress of surgery.

It is hoped that this letter will alert clinicians to the monoamine oxidase inhibitor-like profile of linezolid and prevent the combination of linezolid with agents that enhance the function of any of the monamines (serotonin, norepinephrine, epinephrine, and dopamine).

Catherine Marcucci, M.D.,* Neil B. Sandson, M.D., Joyce A. Dunlap, C.R.N.A. * University of Maryland Medical System and Baltimore Veterans Administration Hospital. sandson.marcucci@comcast.net

References


(Accepted for publication July 14, 2004.)