Double standards in anesthesia

Key words: Anesthesiologist, negligence, standard of care.

Studies cannot distinguish between the quality of care provided by nurse anesthetists and the quality of care provided by anesthesiologists. In fact, the quality of anesthesia care in this country is remarkably high. Yet, malpractice attorneys, surgeons, and others sometimes recommend increased supervision of CRNAs or restrictions on CRNA practice. The AANA, of course, responds with facts showing that these actions will not make anesthesia any safer but will make it more expensive. One thread that many of these episodes have in common is that they begin with an anesthesia accident, sometimes one that involved a CRNA.

Although anesthesia today is very safe, it is not totally safe. Unfortunately, accidents happen, and given the nature of anesthesia, when they happen, they often have disastrous results. People read of an anesthetic disaster and ask, “How can we avoid that?” If the administrator is a nurse anesthetist (and since nurse anesthetists administer 65% of the anesthetics, then two out of three times it is), the uninformed will suggest that the nurse anesthetist be supervised by or replaced with an anesthesiologist. But this “solution” ignores the fact that studies show that anesthesia administered by an anesthesiologist is no safer than anesthesia administered by a CRNA. Nonetheless, the same arguments continue to be made and the same people, either out of ignorance or to promote their own purposes, continue to make the same arguments.

While I would hope to see an absence of error in anesthesia administered by CRNAs, I know that this cannot and will not happen. Anesthetists, both CRNAs and anestesiologists, are human. Anesthesia requires great effort, concentration, and organization, and occasionally there are lapses. That is the nature of anesthesia (and human life in general). What is upsetting is that when a CRNA makes an error, the automatic response is anesthesiologist supervision or replacement. When an anesthesiologist makes an error, there is no similar or corresponding outcry.

Anesthesiologists are human and make errors too. They suffer from the same problems as CRNAs. They lose concentration in the alternating boredom and terror of the operating room. They become confused. They do things they should know they should not, and they neglect to do things they should know they should. Does this make anesthesiologists, as a class, bad practitioners? Should anesthesiologists be forced to practice only with experienced CRNAs? Of course not, but surgeons, malpractice attorneys, administrators, and critics must recognize that while any anesthesia mishap is a tragedy and should have been avoided, mistakes are made by all anesthetists.

I have always known that I could easily find mistakes by anesthesiologists every bit as embar-
rassing as those committed by CRNAs. However, I did not look for them because I knew the irrelevance of finding an occasional error by an anesthesiologist. Even when the rate of anesthesia error is reduced to less than 1 in every 250,000 administrations, there are still millions and millions of anesthetics administered each year. Therefore, there will still be some sizable number of anesthetic incidents, no matter how safe anesthesia becomes.

Having seen restrictions imposed on nurse anesthetist practice because of a rare and unfortunate error by a CRNA, I feel it necessary to point out that anesthesiologists can also make anesthesia errors. The following mistakes were made by anesthesiologists. They are drawn from cases which have appeared in appellate decisions in the last year. Because I understand how irrelevant these errors are, I will not embarrass particular practitioners or institutions, and I will make these reports anonymous. The AANA, however, has the list of the actual cases from which these facts are taken. In none of the cases was a CRNA involved, in any way, with the patient's care. Yet, avoidable accidents happened. In some of these cases, surgeons and hospitals were sued along with the negligent anesthesiologist.

**Spinal cord injury caused by excessive attempts to intubate**

The patient was severely injured in a car accident. Paramedics administered first aid and immobilized the patient by placing him in a cervical collar and securing him to a rigid board. The paramedics then transported him to a trauma center. The patient had suffered, among other things, closed head trauma, a fractured scapula, a torn right brachial plexus, and a cervical spine injury. Although the patient could no longer move his right arm because of the torn brachial plexus, the patient had some voluntary movement of the left arm, pain reflexes in his legs, and rectal tone, an indication he was not paralyzed below the waist.

Because of the patient's closed head injury, the surgeon called for an anesthesiologist to establish an airway in order to reduce the swelling of the patient's brain by means of hyperventilation. The anesthesiologist responded and was informed of the patient's condition by the surgeon. Thereafter, the anesthesiologist made five attempts to establish an airway by inserting a tube through the patient's nasal passage. When these attempts failed, the anesthesiologist made five unsuccessful attempts at oral intubation using a laryngoscope. Following these attempts by the anesthesiologist and one further unsuccessful attempt by the surgeon, the surgeon established a surgical airway by making an incision in the patient's windpipe and inserting a tube. The following day, it was discovered that the patient had suffered a spinal cord injury rendering him a quadriplegic.

After a jury award in favor of the patient, the anesthesiologist appealed claiming he should have received a directed verdict because there was not sufficient evidence to establish the requisite causal connection between his acts and the patient's injuries.

The Appellate Court affirmed the award against the anesthesiologist. The plaintiff's expert had testified to the standard of care for physicians attempting to intubate a patient with a known or suspected cervical spine injury in a situation where establishing an airway was not "urgent." The patient's expert stated that, in his opinion, the anesthesiologist violated this standard of care by inappropriately and excessively attempting to intubate the patient orally. According to the patient's expert, one attempt at oral intubation without moving the patient would have been acceptable, but multiple attempts using a laryngoscope was a violation of the standard of care because such a procedure inevitably causes movement of the patient's head and neck.

As for causation, the patient's expert stated that his review of the medical records indicated the patient did not become a quadriplegic because of the motor vehicle accident. The patient's expert specifically testified that it was his opinion, to a reasonable degree of medical certainty, that the injury to the patient's spinal cord occurred during the oral intubation attempts, and that this injury resulted in quadriplegia and eventual death. Further, the patient's expert testified that, in his opinion, had the anesthesiologist not made multiple attempts at oral intubation, the patient would have walked out of the hospital within two or three weeks.

**Lack of anesthesiologist availability**

Plaintiff was experiencing labor symptoms and was admitted to a hospital in a suburb of a major East Coast city. Periodic examinations of the plaintiff suggested fetal distress. The attending nurse called the obstetrician. Within 5 minutes of receiving the nurse's call, the obstetrician appeared. By 8:56 p.m., the obstetrician had ordered the plaintiff to be moved to a "labor room." In the next 10 minutes, the obstetrician attempted to deliver the baby vaginally. By 9:07 p.m., the obstetrician called for cesarean section surgery and gave orders to call anesthesia and two additional surgeons, as well as to prepare the "delivery room" for surgery. The plaintiff was placed in the "delivery room" for preparation while the obstetrician pre-
pared for surgery. By the time the patient and doctor were prepared, no anesthesiologist had appeared.

Initially, the obstetrician decided to wait for the anesthesiologist, but after a while, he began the operation using local anesthesia. This decision required him to cut into the plaintiff while she was fully conscious, and required him to anesthetize each progressive layer of the abdomen before each incision. The baby was born at 9:34 p.m. Approximately 7 minutes later, an anesthesiologist arrived and administered an anesthetic to permit the doctors to complete the operation on the plaintiff.

The baby was born with complications. Testimony indicated that she had suffered from oxygen deprivation while in utero. As a consequence, she suffers from a seizure disorder and has a reduced mental capacity which borders on mental retardation.

The baby and her parents brought suit against the obstetrician, the anesthesiologist, the hospital, and the anesthesiologist corporation, asserting a number of claims including, but not limited to, negligence and negligent infliction of emotional distress. After a lengthy trial, the jury returned a verdict absolving the obstetrician and the anesthesiologist group of all liability. The jury awarded the plaintiff $2,500 on her claim against the hospital but failed to reach a final verdict on the baby's claim against the hospital. Upon consideration of post-trial motions, the trial court granted a new trial against the hospital only.

Plaintiffs appealed, and the Appellate Court ordered a new trial against the anesthesiologist group as well, because the trial court had not permitted the plaintiff to assert its claims fully. While this case does not involve an anesthesia mistake, the Appellate Court agreed with the plaintiff that it was negligence for the anesthesiologist group to fail to show up. Note that, in the view of the jury, the obstetrician was not responsible for the failure of the anesthesiologist group to show up but he was, nonetheless, sued.

**Negligent insertion of anesthesia needle into patient's eye**

The plaintiff instituted this action against an anesthesiologist and an ophthalmologist group (yet another case where surgeons were sued when working with anesthesiologists). The patient was having vision difficulties in his left eye and sought treatment from an ophthalmologist. It was agreed that the patient would have laser surgery. The anesthetic was supposed to be inserted into the tissue surrounding the eyeball, but in performing the anesthetic procedure the anesthesiologist inserted the needle directly into the eyeball itself and injected the anesthetic into the patient's eye. It caused extensive permanent damage including tearing and detachment of the retina and substantial impairment of the patient's vision.

The plaintiff's lawsuit was based on assault and battery for an alleged nonconsensual anesthetic procedure, negligence, res ipsa loquitur, and negligence based on medical malpractice.

**Negligently administered spinal**

During labor, the plaintiff received an epidural anesthetic administered by an anesthesiologist. The anesthesiologist first attempted to insert a catheter into the plaintiff's upper spinal cord near her neck but was unsuccessful. The anesthesiologist then administered the anesthetic by inserting the catheter into the plaintiff's spine in her lower back. Soon after delivering a healthy baby, the plaintiff began experiencing headaches, sensitivity to light and loud noises, and numbness in her back.

The plaintiff brought suit against the hospital which convinced the trial court that the anesthesiologist was an independent contractor for whom the hospital was not responsible and that the patient had failed to show that her injuries were caused by the spinal. The Court of Appeals sent the case back to the trial court for trial.

The plaintiff's expert stated that, in his opinion, the anesthesiologist's care fell below the standard of care required by physicians administering an epidural. Another expert stated that “Plaintiff's symptoms of low back pain and headaches are consistent with the loss of spinal fluid which accompanied the insertion of the epidural in the cervical region of the plaintiff's back.” The Appellate Court held that this was sufficient testimony, if believed by a jury, to support a verdict of malpractice on the part of the anesthesiologist. Whether or not the hospital will be liable will depend on whether the jury believes the hospital allowed people to think that the anesthesiologist was its apparent agent.

**Permitting oxygen too close to a hot surgical instrument**

During the removal of a cyst, the plaintiff suffered burns on the face, left ear, and shoulders because an instrument being used during her surgery ignited the oxygen being administered to the anesthetized plaintiff. The patient sued the hospital and the surgeon. The case is primarily concerned with the effects of legal maneuvering as the patient dismissed the surgeon and then attempted to sue him again. While the plaintiff consistently
referred to the surgeon as a defendant, for some reason, the actual caption of the case omitted the surgeon. The court permitted the plaintiff to amend the complaint because it was clear that the surgeon was being sued and he could not have been unfairly surprised. It was the hospital that named the anesthesiologist as a defendant.

Drug abuse

A State Medical Board filed a petition for an order to enforce a subpoena issued to a hospital for peer review records concerning a physician who was the subject of an investigation regarding an apparent drug problem. The Superior Court granted the petition and ordered the hospital to comply with the subpoena. The Court of Appeals affirmed. The hospital sought further review. The State Supreme Court granted review and held that the investigative subpoena issued by the State Medical Board as part of its inquiry into the conduct of a physician with an apparent drug problem was not "discovery" within the meaning of a statute providing that records of a hospital peer review committee are not "subject to discovery."

In the spring of 1992, several nurses at a hospital observed an anesthesiologist on the medical staff behaving, while on duty, as if he were under the influence of narcotic drugs. The first incident took place one evening in March 1992. The anesthesiologist was on call when a patient required emergency surgery. As the anesthesiologist was interviewing the patient, a nurse observed that his speech was slurred. In discussing the case with him before surgery, she saw that his attention and comprehension were impaired. Nonetheless, the anesthesiologist administered a general anesthetic. Following the surgery, the nurse reported the anesthesiologist's abnormal behavior to her supervisor.

The second incident occurred in late May 1992. A patient was awaiting surgery, but the anesthesiologist could not be found. After being paged several times he arrived and began interviewing the patient. A nurse observed that his speech was even more slurred than during the first incident. She promptly called her supervisor and expressed her "grave concern" about his condition. Thereafter the patient was taken into the operating room and the anesthesiologist administered sedation intravenously.

On another day that month a nurse was trying to take a patient into a bathroom but found the door locked. A visitor told her that someone had been in the bathroom for a long time. She unlocked the door and found the anesthesiologist asleep in the room. He did not respond to his name, and the nurse had to shake him several times. When he awoke, he was disoriented and unsteady; in the nurse's opinion, he "did not behave like someone who had simply fallen asleep." She told him that he was needed in surgery; he responded "OK," and went off to the operating room. She then reported the incident to her supervisor. Later that day, another nurse remarked that the anesthesiologist's behavior in the recovery room had been "strange" and he had had to lay his head on a desk.

Approximately 6 weeks thereafter, a nurse noticed that the anesthesiologist's handwriting was shaky on several occasions and again reported it. She also saw that the anesthesiologist had made an entry in a record—possibly a patient's chart—stating that he had broken an ampule of fentanyl during a procedure.

At some point during this period, the Medical Executive Committee—a peer review committee—began to investigate the matter. The anesthesiologist appeared before the committee and admitted he had been injecting himself with fentanyl, which he had taken from the hospital's narcotics supplies.

Based on these facts, the State Supreme Court ruled that the State Medical Board was entitled to enforce its subpoena to examine the hospital's peer review records.

Conclusion

The episodes described above are not particularly shocking or outrageous. They do not imply that anesthesiologists are bad practitioners and in fact, for the most part, they do not even suggest that the anesthesiologists mentioned in these cases are even bad practitioners. What they do make clear is that anesthesia is a difficult process. While education and dedication have made it very safe, practitioners cannot lose concentration. When they make an occasional human error, it can have disastrous consequences.

Of course, the most important thing it shows is that anesthesiologists are human. While nurse anesthetists cannot and should not deny that anesthesia can have disastrous consequences, anesthesiologists are also human and suffer the same consequences with the same frequency.

Both anesthesia providers, CRNAs and anesthesiologists, must recognize that despite their best efforts, they are human and accidents will happen. We should resolve to dedicate ourselves to identify and eliminate those errors which can be avoided. But using an occasional and isolated error as an excuse to change the way anesthesia care is delivered is a cynical game which only the foolish will play.
Rapid onset and short duration make Nesacaine-MPF the logical epidural anesthetic for outpatient procedures.

- 6–12 minute onset.
- 60-minute or less duration.

- No methyparaben.
- No disodium EDTA dihydrate.
- No preservatives, period.
- Available in 2% and 3% 20-mL single-dose vials.
Cardiovascular System Reactions: High doses, or unintended intravascular injection, may lead to high plasma levels and related depression of the myocardium, hypotension, bradycardia, ventricular arrhythmias, and, possibly, cardiac arrest. Allergic: Allergic type reactions are rare and may occur as a result of sensitivity to the local anesthetic or to other formulation ingredients, such as the antimicrobial preservative methylparaben, contained in multiple dose vials. These reactions are characterized by signs such as urticaria, pruritis, erythema, angioneurotic edema (including laryngeal edema), tachycardia, sneezing, nausea, vomiting, diarrhea, syncope, excessive sweating, elevated temperature, and possibly aerial edema type symptomaticity (including severe hypertension). Cross sensitivity among members of the ester-type local anesthetic group has not been reported. The usefulness of screening for sensitivity has not been definitely established.

Neurologic: In the practice of caudal or lumbar epidural block, occasional unintentional penetration of the subarachnoid space by the catheter may occur (see PRECAUTIONS). Subsequent adverse observations may depend partially on the amount of drug administered intrathecally. These observations may include spinal block of varying magnitude (including total spinal block), hypotension secondary to spinal block, loss of bladder and bowel control, and loss of perineal sensation and sexual function. Anaphylactoid, persistent motor, sensory and/or autonomic (spinal cord) block of some lower spinal segments with slow recovery (several months) or incomplete recovery have been reported in rare instances. (See DOSAGE AND ADMINISTRATION discussion of Caudal and Lumbar Epidural Block.) Backache and headache have also been noted following lumbar epidural or caudal block.

4. The role of drug factors and non-drug factors associated with fetal bradycardia occurring following paracervical block are unexplained at this time.

Nursing Mothers

If it is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when chloroprocaine is administered to a nursing woman.

Pediatric Use

Guidelines for the administration of Nesacaine and Nesacaine-MPF Injections to children are presented in DOSAGE AND ADMINISTRATION.

ADVERSE REACTIONS

Systemic: The most commonly encountered acute adverse experiences that demand immediate countermeasures are related to the central nervous system and the cardiovascular system. These adverse experiences are generally dose related and may result from rapid absorption from the injection site, diminished tolerance, or from unintentional intravascular injection of the local anesthetic solution. In addition to systemic dose-related toxicity, unintentional subarachnoid injection of drug during the intended performance of caudal or lumbar epidural block or nerve blocks near the vertebral column (especially in the head and neck region) may result in vertebroarterial or arterial (“Total Spinal”) factors influencing plasma protein binding, such as acidosis, systemic diseases that alter protein production, or competition of other drugs for protein binding sites, may diminish individual tolerance. Plasma cholinesterase deficiency may also account for diminished tolerance to ester-type local anesthetics.

Central Nervous System Reactions: These are characterized by excitation and/or depression. Restlessness, anxiety, dizziness, tremors, blurred vision or tremors may occur, possibly progressing to convulsions. However, excitement may be transient or absent, with depression being the first manifestation of an adverse reaction. This may quickly be followed by drowsiness merging into unconsciousness and respiratory arrest. The incidence of convulsions associated with the use of local anesthetics varies with reactions. This may quickly be followed by drowsiness merging into unconsciousness and respiratory arrest. The incidence of convulsions associated with the use of local anesthetics varies with

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Letters
(continued from page 104)

ing Center in Chicago. After speaking with CRNAs from all over the country, I realized that many of them were seeing problems of hypotension on induction of general anesthesia in patients taking Redux® or fenfluramine/phentermine (fen/phen) combination. I stated that very little information regarding these medications appears in the literature and after reviewing the drug pharmacology noted that a relationship may exist between the drug's potential catecholamine-depleting effects and persistent hypotension on induction of anesthesia.

I have a background in trauma anesthesia providing coverage in a level I trauma center. I began to question myself and others about the potential effects of Redux or fen/phen on the trauma victim. If an individual taking Redux or fen/phen is involved in an accident and is potentially catecholamine depleted, what effect will that have on patient outcome or survival from the time of the traumatic event to the arrival of the first medical responder capable of treating the patient with appropriate vasopressors? I have not cared for a trauma patient on any of the antiobesity medications, but I think the question is important.

It is reported that the number of prescriptions for Redux has increased dramatically in just a short period of time. As a concerned anesthetist, I encourage all healthcare providers to remain vigilant and informed regarding these medications.*

LYNETTE A. JEFFERS, CRNA, MSN
Clinical Faculty Instructor of Nurse Anesthesia
Mt. Sinai School of Nurse Anesthesia
Cleveland, Ohio

*Note: In March 1997, the Food and Drug Administration Medical Products Reporting Program (MedWatch) issued an alert concerning Pondimin® C-IV (fenfluramine tablets) indicating that its use with phentermine (fen/phen) is not approved. It was also noted that potent anesthetic agents should be administered with caution in patients taking Pondimin. For more information, contact MedWatch at 1-880-934-5556.
FROM
GLAXO WELLCOME INC.

THE FIRST NONSPECIFIC ESTERASE-METABOLIZED OPIOID

NOW,
OPIOID CONTROL
GOES EXACTLY
AS FAR AS
YOU NEED IT
The benefits of esterase metabolism result in a unique opioid

Rapid, nonspecific esterase metabolism
- Non-organ-dependent elimination
- Consistent offset of action regardless of gender, age, weight, or renal/hepatic status
- Metabolism unaffected in patients with pseudocholinesterase deficiency

No accumulation means predictable offset of action within 5 to 10 minutes
- No opioid accumulation regardless of dose or duration of infusion
- Rapid clearance
- No change in context-sensitive half-time, even with prolonged administration
- Clinically inactive metabolite

No accumulation, unlike other opioids.

Time Required for a 50% Decrease in the Effect-Site Opioid Concentration of Fentanyl Analogs

Minutes Required for a 50% Decrease in Effect-Site Concentration

Adapted from Egan et al.
Esterase metabolism provides an opioid with rapid onset and offset.

<table>
<thead>
<tr>
<th>Pharmacokinetics</th>
<th>ULTIVA</th>
<th>Alfentanil</th>
<th>Fentanyl</th>
<th>Sufentanil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset—blood-brain equilibration (mean)</td>
<td>1 min²</td>
<td>1 min²</td>
<td>6.6 min³</td>
<td>6.2 min³</td>
</tr>
<tr>
<td>Offset—context-sensitive half-time * (mean)</td>
<td>3 min¹</td>
<td>50–55 min¹¹</td>
<td>&gt;100 min¹⁰</td>
<td>30 min¹⁰</td>
</tr>
<tr>
<td>Non-organ-dependent metabolism</td>
<td>Yes</td>
<td>No⁴</td>
<td>No⁵</td>
<td>No⁵</td>
</tr>
<tr>
<td>Nonspecific esterase metabolism</td>
<td>Yes</td>
<td>No⁴</td>
<td>No⁵</td>
<td>No⁵</td>
</tr>
</tbody>
</table>

*The time required for drug concentrations in blood or at effect-site to decrease by 50%. Based on 3-hour infusion duration.

Rapid clearance and lack of accumulation result in rapid offset of analgesic effects (5 to 10 minutes) following discontinuation of ULTIVA; therefore, when postoperative pain is anticipated, adequate postoperative analgesia should be established before discontinuation.
ULTIVA™
(REMIFENTANIL HCl)
FOR INJECTION

Optimizes intraoperative analgesia without delaying recovery

Rapid onset for profound analgesia during intubation

- Onset of action achieved in approximately 1 minute
- Fewer responses to intubation versus other opioids

The flexibility to administer higher opioid doses—for superior control of intraoperative stress responses

- Ability to use higher relative doses (ED$_{90}$) of ULTIVA permits optimal analgesia without prolonging recovery*
- Rapidly titratable to desired depth of anesthesia/analgesia for precise control of intraoperative stress
- Can be titrated to preempt occurrence of major stressful events
- Allows decreased use of propofol, isoflurane, and thiopental by up to 75%†

*The higher relative doses of ULTIVA (ED$_{90}$) resulted in a higher frequency of hypotension (16%) compared to ED$_{50}$ doses of other opioids (5%).
†Subhypnotic doses should be avoided.

Consistently reduces responses to skin incision, signs of light anesthesia, and responses to skin closure in various anesthetic techniques.

<table>
<thead>
<tr>
<th>Output Laparoscopic Surgery</th>
<th>Inpatient Major Abdominal Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response to Skin Incision</td>
<td>Response to Skin Incision</td>
</tr>
<tr>
<td>9%</td>
<td>4%</td>
</tr>
<tr>
<td>P&lt;0.05</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>Signs of Light Anesthesia</td>
<td>Signs of Light Anesthesia</td>
</tr>
<tr>
<td>34%</td>
<td>33%</td>
</tr>
<tr>
<td>P&lt;0.05</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>Response to Skin Closure</td>
<td>Response to Skin Closure</td>
</tr>
<tr>
<td>6%</td>
<td>3%</td>
</tr>
<tr>
<td>P&lt;0.05</td>
<td>P&lt;0.05</td>
</tr>
</tbody>
</table>

ULTIVA 0.4 mcg/kg/min (n=35) Alfentanil 1 mcg/kg/min (n=35) ULTIVA 0.4 mcg/kg/min (n=91) Fentanyl 1.5-3 mcg/kg bolus (n=97)

---

WHILE NOT ALL DOSES OF ULTIVA WERE EQUIPOTENT TO THE COMPARATOR OPIOID (ED$_{90}$ VERSUS ED$_{50}$), ALL COMPARATOR AGENTS WERE ADMINISTERED IN ACCORDANCE WITH THEIR RECOMMENDED DOSING GUIDELINES.
Fast recovery, well-suited for outpatient procedures

- Recovery from opioid effects within 5 to 10 minutes
- No cases of recurrent respiratory depression*

- Recovery rate limited by concurrent longer-acting anesthetics, not ULTIVA
- Consistent offset may help speed PACU discharge

*Occurring >30 minutes following discontinuation.

Rapid clearance even after prolonged administration.

Rapid recovery of respiratory drive.

Within 5 to 10 minutes after the discontinuation of ULTIVA, no residual analgesic activity will be present; therefore, when postoperative pain is anticipated, adequate postoperative analgesia should be established before discontinuation.

Failure to adequately clear the IV tubing to remove residual ULTIVA has been associated with the appearance of respiratory depression, apnea, and muscle rigidity upon the administration of additional fluids or medications through the same IV tubing.

Please consult Brief Summary of complete Prescribing Information for ULTIVA following this advertisement.
Rapid response to titration that meets specific monitored anesthesia care needs

Unique esterase metabolism means precision and titratability during monitored anesthesia care procedures

- Provides patient comfort and analgesia during placement of local or regional anesthetic block
- Optimizes analgesia without oversedation
- Highly titratable to maintain adequate respiration
- Optimal administration with midazolam at 2 mg for comfort, analgesia, and adequate respiration
- Rapid and precise analgesic control of discomfort and pain

Single dose of ULTIVA effective in control of pain.

<table>
<thead>
<tr>
<th>% Patients With No or Mild Pain to an Ophthalmic Block*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ophthalmic regional block</td>
</tr>
<tr>
<td>No Pain 77%</td>
</tr>
<tr>
<td>Mild Pain 19%</td>
</tr>
<tr>
<td>ULTIVA 1 mcg/kg over 30 seconds (n=26)</td>
</tr>
<tr>
<td>96%</td>
</tr>
</tbody>
</table>

*Ophthalmic block was placed 90 seconds after administration of ULTIVA. The incidence of nausea, respiratory depression, and muscle rigidity was 12%, 4%, and 7%, respectively.

ULTIVA effectively provides patient comfort.

<table>
<thead>
<tr>
<th>% Patients With No Treated Discomfort Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orthopedic, urological, gynecological, lower abdominal procedures requiring subarachnoid, epidural, or peripheral block</td>
</tr>
<tr>
<td>ULTIVA 0.5 mcg/kg bolus; 0.1 mcg/kg/min (n=61)</td>
</tr>
<tr>
<td>97%</td>
</tr>
</tbody>
</table>

The incidence of nausea was 26%.

In monitored anesthesia care, when patients are breathing spontaneously rather than on a ventilator, it is not recommended that bolus doses of ULTIVA be administered simultaneously with a continuous infusion of ULTIVA because of a high incidence of apnea and muscle rigidity.

It is strongly recommended that supplemental oxygen be supplied whenever ULTIVA is administered.

Please consult Brief Summary of complete Prescribing Information for ULTIVA following this advertisement.
Adverse events typical of μ-opioids

Well tolerated without the effects of opioid accumulation during general anesthesia or monitored anesthesia care

- Widespread use with experience in over 2,800 surgical patients
- Opioid-related adverse events may occur rapidly, however, dissipation occurs within minutes of rate reduction or discontinuation of ULTIVA
- No cases of recurrent respiratory depression
- Less need for naloxone postoperatively compared to fentanyl or alfentanil (respiratory depression after discontinuation: 2% ULTIVA, 4% fentanyl/alfentanil; P<0.05)

Well tolerated in a wide range of patient populations, including children (2-12 yr), hepatic/renally impaired patients, elderly and obese patients

Muscle rigidity is related to the dose and speed of administration of ULTIVA

Muscle rigidity incidence reduced to <1% when ULTIVA is administered concurrently or after a hypnotic induction agent or neuromuscular blocker

*Occurring >30 minutes following discontinuation.

General anesthesia: Adverse Events ≥5%

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>ULTIVA (n=921)</th>
<th>Alfentanil/Fentanyl (n=466)</th>
<th>ULTIVA (n=929)</th>
<th>Alfentanil/Fentanyl (n=466)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>&lt;1%</td>
<td>0%</td>
<td>36%</td>
<td>43%</td>
</tr>
<tr>
<td>Hypotension</td>
<td>19%</td>
<td>6%</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>&lt;1%</td>
<td>&lt;1%</td>
<td>16%</td>
<td>20%</td>
</tr>
<tr>
<td>Muscle rigidity</td>
<td>11%</td>
<td>8%</td>
<td>&lt;1%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>7%</td>
<td>5%</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Shivering</td>
<td>&lt;1%</td>
<td>0%</td>
<td>5%</td>
<td>2%</td>
</tr>
<tr>
<td>Fever</td>
<td>&lt;1%</td>
<td>0%</td>
<td>5%</td>
<td>2%</td>
</tr>
</tbody>
</table>

WHILE NOT ALL DOSES OF ULTIVA WERE EQUIPOTENT TO THE COMPARATOR OPIOID, ALL COMPARATOR AGENTS WERE ADMINISTERED IN ACCORDANCE WITH THEIR RECOMMENDED DOSING GUIDELINES.

* Included in the muscle rigidity, incidence is chest wall rigidity (5%).

Monitored anesthesia care: Adverse Events ≥5%

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>ULTIVA (n=159)</th>
<th>ULTIVA + 2 mg midazolam (n=103)</th>
<th>Propofol (n=63)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>44%</td>
<td>18%</td>
<td>32%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>22%</td>
<td>5%</td>
<td>21%</td>
</tr>
<tr>
<td>Pruritus</td>
<td>18%</td>
<td>16%</td>
<td>0%</td>
</tr>
<tr>
<td>Headache</td>
<td>18%</td>
<td>12%</td>
<td>10%</td>
</tr>
<tr>
<td>Shivering</td>
<td>5%</td>
<td>&lt;1%</td>
<td>2%</td>
</tr>
<tr>
<td>Sweating</td>
<td>6%</td>
<td>0%</td>
<td>2%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>5%</td>
<td>5%</td>
<td>2%</td>
</tr>
</tbody>
</table>

In monitored anesthesia care, it is not recommended that bolus doses of ULTIVA be used simultaneously with a continuous infusion because of a high incidence of apnea and muscle rigidity.
OPIOID POWER
WITHOUT OPIOID ACCUMULATION

FROM HERE TO RECOVERY

- The first nonspecific esterase-metabolized opioid
- Rapid onset of action (approximately 1 minute)
- Superior control of intraoperative stress responses*
- Rapid response to titration
- Rapid, predictable recovery from opioid effects within 5 to 10 minutes
- Consistent offset regardless of gender, age, weight, or renal/hepatic status

A comprehensive educational program is available. Contact your Glaxo Wellcome Representative for more information.

- For additional information call:
  1-888-4-ULTIVA (1-888-485-8482) for automated information;
  1-800-334-0089 for a Glaxo Wellcome Drug Information Specialist
  (8:30 AM to 5:00 PM Mon-Fri; emergency access 24 hours a day)

ULTIVA™ (REMIFENTANIL HCl)
FOR INJECTION

PRECISE CONTROL, PREDICTABLE RECOVERY

*The higher relative doses (ED90) of ULTIVA administered resulted in fewer responses to intraoperative stress compared to fentanyl and alfentanil (approximately ED50). The doses of ULTIVA used to achieve this profile resulted in a higher frequency of hypotension (16%) versus the other opioids (5%).

Rapid clearance and lack of accumulation result in rapid offset of analgesic effects (5 to 10 minutes) following discontinuation of ULTIVA; therefore, when postoperative pain is anticipated, adequate postoperative analgesia should be established before discontinuation.

References:
7. Data on file, Glaxo Wellcome Inc.

Please consult Brief Summary of complete Prescribing Information for ULTIVA following this advertisement.
For IV Use Only

Approximately 2,492 patients were exposed to

Irrigation of IVTIVA should be made into IV tubing at a rate of 50 mL/min. Failure to adequately clear IV tubing to remove residual IVTIVA has been associated with the appearance of respiratory depression, apnea, and rigidity with the administration of additional fluids or medications through the same IV tubing.

USE OF IVTIVA IS ASSOCIATED WITH APNEA AND RESPIRATORY DEPRESSION. IVTIVA SHOULD BE ADMINISTERED ONLY BY PERSONS SPECIFICALLY TRAINED IN THE USE OF ANESTHETIC DRUGS AND THE MANAGEMENT OF THE RESPIRATORY EFFECTS OF POTENT IOPIOIDS, INCLUDING RESPIRATORY AND CARDIAC RESPIRATIONS IN PATIENTS IN THE AGED GROUP BEING TREATED. SUCH TRAINING MUST INCLUDE THE ESSAYAND AND MAINTENANCE OF A PATIENT AIRWAY AND ASSISTED VENTILATION.

IVTIVA SHOULD NOT BE USED IN DIAGNOSTIC, OR THERAPEUTIC PROTOCOLS OUTSIDE THE MONITORED ANESTHESIA CARE SETTING. PATIENTS RECEIVING MONITORED ANESTHESIA CARE SHOULD BE CONTINUOUSLY MONITORED BY PERSONS NOT INVOLVED IN THE CONDUCT OF THE SURGICAL OR DIAGNOSTIC PROCEDURE. COXICIAN SATURATION SHOULD BE MONITORED ON A CONTINUOUS BASIS.

RESPIRATORY AND INTRAVENOUS EQUIPMENT, OXYGEN, AND AN OPIUM ANTIAGENS MUST BE READILY AVAILABLE.

Respiratory depression in spontaneously breathing patients is generally managed by decreasing the rate of the infusion by 50% or by temporarily discontinuing the infusion. Slurred muscle rigidity can be caused by IVTIVA and is related to the dose and speed of administration. IVTIVA may cause chest wall rigidity following an initial dose of 0.05 mg/kg or an infusion rate of 0.1 mg/kg/min. Single doses <1 mg/kg may cause chest wall rigidity when given concomitantly with a continuous infusion of IVTIVA. Muscle rigidity induced by IVTIVA should be managed in the context of the patient’s clinical condition. Muscle rigidity occurring during the infusion of IVTIVA should be managed by reducing the rate of administration of a neuromuscular blocking agent and the concomitant infusion rate; neuromuscular blockade or rigidity may be avoided.

Muscle rigidity seen during the use of IVTIVA in spontaneously breathing patients may be treated by stopping or decreasing the rates of administration of IVTIVA. Resolution of muscle rigidity after discontinuing the infusion of IVTIVA occurs within minutes. In the case of thromboembolic disease, rapid reversal of coagulopathy or nodule may be achieved. IVTIVA should not be administered in the same IV tubing with blood due to potential interaction with nonbiodegradable blood products.

PRECAUTIONS: Vitals signs and oxygenation must be continuously monitored during the administration of IVTIVA.

Gastrointestinal bleeding has been reported with IVTIVA and is responsive to aspirin or antiplatelet drugs, such as aspirin and glycoprotein IIb/IIIa inhibitors. Hypotension has been reported with IVTIVA and is responsive to decreases in the administration of IVTIVA to IV fluids or calcium (eg, calcium gluconate). Rapid Offset of Action: WITHIN 5 TO 10 MINUTES AFTER DISCONTINUATION OF THE INFUSION, IVTIVA, NO RESPIRATORY ACTIVITY WILL BE PRESENT. However, respiratory depression may occur as soon as 20 minutes after termination of infusion due to residual effects of anesthetized anesthetics. For patients undergoing surgical procedures where postoperative pain is generally anticipated, other analgesics should be administered prior to the discontinuation of IVTIVA.

Pediatric Use: IVTIVA has not been studied in pediatric patients under 2 years of age. See CLINICAL PHARMACOLOGY section for full prescribing information and DOSAGE AND ADMINISTRATION for clinical experience and recommendations for use in pediatric patients 2 to 12 years of age. Use in Elderly Patients: While the effects of IVTIVA in elderly patients were evaluated, elderly patients have been shown to be twice as sensitive to the effects of IVTIVA in comparison with younger patients. The recommended starting dose of IVTIVA should be decreased by 50% in patients over 65 years of age (see CLINICAL PHARMACOLOGY section for full prescribing information and DOSAGE AND ADMINISTRATION). Use in Moribund IVs: For all of these patients, caution is required with use in moribund IVs because of alterations in inotropic and respiratory function. See DOSAGE AND ADMINISTRATION.

Long-term Use in the ICU: Do not use IVTIVA in the long-term (longer than 16 hours) use of IVTIVA or as an ICU in patients. Concomitant Use: Concomitant use of IVTIVA should not be performed with other IVTIVA. Doses of IVTIVA administered by multiple routes may precipitate apnea or the onset of hypotension. IVTIVA may not be administered in the same IV tubing with blood due to potential interaction with nonbiodegradable blood products.

Rapid infusion has been shown to reduce fibrin in major sites when tested after 70+ days of daily administration of 0.5 mg/kg or 0.5 mg/kg with 80% by syringe infusion. Approximately 45% of patients have 30 mg/kg or 0.5 mg/kg. Drug distribution is approximately 400 to 1200 times the maximum recommended dose (MRD) in terms of mg/kg or mg/L of body surface area. The half-life of fentanyl is not affected by fentanyl in doses of 5 mg/kg, in the patient for whom administration is 15 minutes before giving another IVTIVA, 12 to 15 minutes before removing.

Penicillin Group C: The effects of fentanyl were not observed following administration of fentanyl at doses up to 5 mg/kg or 0.5 mg/kg. In the patient for whom administration is 15 minutes before giving another IVTIVA, 12 to 15 minutes before removing.

Animal Toxicity: Intracerebral administration of the glycyrrhizin formulation without neuraxial delivery caused agitation, pain, and hyperthermia. Intracerebral administration of the glycyrrhizin formulation without neuraxial delivery caused agitation, pain, and hyperthermia.

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Changes in the health care industry have brought many new challenges to CRNAs and we want to make sure you have the right insurance products to meet those challenges. **Anesthesia Professional Liability Services, (A+) now has policies for virtually every practice setting including:**

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