Preemptive Analgesia by Intravenous Low-dose Ketamine and Epidural Morphine

To the Editor—Aida et al. present intriguing results regarding the intraoperative administration of epidural morphine combined with intravenous ketamine. However, I question their conclusion that these results provide definitive evidence for a preemptive analgesic effect. Because there was no control group to which similar doses of analgesics were administered nonpreemptively, the possibility must be considered that the results of this study were due to persistent effects of the analgesic regimen rather than a true preemptive effect.

The experimental design of this study included postoperative administration of a single intravenous dose of naloxone to the patients to whom preemptive epidural morphine had been administered. The authors postulate that this single dose of naloxone displaces the epidurally administered morphine from the spinal receptors and that the morphine present in the neuraxis is then distributed around the body. They further postulate that morphine will no longer be present in adequate concentrations to exert an analgesic effect once the naloxone has been eliminated. No evidence was provided to support this assertion.

The patients in this study to whom preemptive epidural morphine was administered without intravenous ketamine had significantly less postoperative pain than the patients to whom only postoperative epidural morphine was administered. This result is consistent with a prolonged effect of the preemptively administered morphine. (The average dose of intraoperative epidural morphine in the preemptive group was approximately 7.7 mg.) Because of its hydrophilic nature, clearance of morphine from the cerebrospinal fluid is slow.2 It seems likely that epidurally administered morphine is not rapidly redistributed after a dose of naloxone. Rather, a significant reservoir of neuraxial morphine may be expected to persist well beyond the duration of effect of the naloxone.

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Improved, but Not Preemptive, Analgesia

To the Editor—We read with much interest the study of Aida et al. regarding the "preemptive" analgesic effects of intrathecal ketamine and epidural morphine in gastrectomy patients. The improved postoperative analgesia, particularly in the group to which both medications were administered, is certainly a useful clinical effect. However, we disagree with the authors’ use of the term preemptive analgesia to describe their results.

As noted by McQuay, attributing improved pain control to a "preemptive analgesic" effect requires a comparison of the prestimulus ("preemptive") therapy with an identical therapy administered after the stimulus. Comparing groups to which a prestimulus analgesic was administered with a placebo group to which no poststimulus dose was administered merely examines the effects of increasing the total dose of analgesic. The study of Aida et al. is an example of this phenomenon. There were no groups to which equivalent poststimulus doses of either ketamine or morphine were administered.

In addition, the prolonged duration of epidural morphine (6–24 h) may have contributed to the postoperative analgesia in the epidural morphine groups. Although the authors attempted to compensate for this by administering a single dose of intravenous naloxone “after skin closure to block the continued effect of the preemptive morphine,” the validity of this is based on a series of assumptions: first, that the naloxone entered the spinal cord in sufficient quantities to release all the morphine from its receptors; then, that all the morphine diffused into the systemic circulation; and finally, that the morphine was completely eliminated from the body so that it could not reenter the spinal cord and bind to its receptors when the naloxone effects dissipated. Without evidence supporting these assumptions, the possibility remains that the "preemptive" epidural morphine was still present in sufficient quantities to produce postoperative analgesia.

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When Is Preemptive Analgesia Truly Preemptive?

To the Editor—We read with interest the article of Aida et al. and we wish to point out our concerns. First, the authors use the term preemptive analgesia even though they treated the three groups with analgesics both before and after the surgical incision. Such a study design is not appropriate to demonstrate a preemptive effect because no comparison is attempted between similar analgesic interventions
applied before or after the start of the surgical stimulus. Furthermore, before the start of the stimulus, nitrous oxide, which has a preemptive effect, was administered to all groups.

Second, the authors report that ‘for definitive preemptive analgesia, blockade of opioid and N-methyl-D-aspartate [NMDA] receptors is necessary,’ and that ‘This mechanism (dual blockade of opioid and NMDA receptors) may account for the current results.’ Apparently, there is a misconception because it is the activation of the opioid receptors by an agonist (and not their “blockade”) that exerts an antinociceptive effect.

Third, why did the authors need a control group when their assumption could have been tested by an enhanced analgesic effect in the combination group? For the same reason, the use of naloxone is not justifiable. On the contrary, it is hard to persuade for the precise dose of naloxone required to reverse the aftereffect of epidural morphine and at the same time to allow the postoperative morphine to produce analgesia. The authors report that the naloxone administered neither increased postsurgical pain nor interfered with the postoperative morphine, but this is based on a retrospective observation. At the time of the design and conduct of the study, it would not be possible to predict the response of the patients.

Fourth, whether the vagus nerve conveys visceral true nociceptive information and to what degree remain controversial. Vagal afferent pathways may have a modulatory antinociceptive and analgesic effect, and dorsal horns and spinothalamic tracts receive vagal inhibitory influences. It seems more likely that the primary nociceptive input from the stomach comes from the afferent fibers following the sympathetic route to the dorsal horns. With regard to the effects of the gastrectomy in particular, it seems more likely that nociception and pain originate mostly from the injury to the somatic structures of the area, rather than the viscera themselves. This nociception is predominantly conveyed by somatic afferent fibers to spinal segments, where nociceptive signals from sympathetic afferents also converge. It has been previously shown that systemically administered analgesics may potentiate the effect of other antinociceptive or analgesic agents administrated neuraxially. Therefore, in this context, the findings could be consistent with an interactive potentiation of the epidurally administered morphine by the systemically administered ketamine.

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gesia with morphine or fentanyl, or epidural block, is usually required to avoid intrasurgical reaction to nociception. Thus, central sensitization is established during anesthesia with nitrous oxide.

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To the Editor—The Draeger Narkomed 6000 anesthesia delivery system (Telford, Pennsylvania) incorporates self-testing features that are designed to automate the checkout process. However, while evaluating the system (S/N 10038, software version M1/7.0) for use in our hospital, I discovered three significant deficiencies, which pose a risk to patient safety.

First, in an emergency situation, with the machine turned off, the flush valve delivers high-flow oxygen, provided there is a source of oxygen (pipeline or tank) available. However, in contrast to other machines, positive-pressure ventilation cannot be administered via the breathing circuit because the ventilator’s built-in pressure relief valve is “on” under these circumstances.

Second, immediately after the system is turned on, it remains impossible to deliver positive-pressure ventilation. After filling the circuit from the flush valve or flow meters, the circuit does not hold pressure, even if the pop-off valve is completely closed. Positive-pressure ventilation can only be accomplished after the self-test procedure is completed (requiring 4 min), the self-test procedure is interrupted by pressing the standby button (requires about 35 s), or the red, emergency ventilator bypass button is pressed (requires about 15 s). In the third instance, although manual ventilation is possible, the machine must be completely reset and tested before the ventilator can be used.

Third, if the machine is turned off briefly while running on battery power (which might occur accidentally, or perhaps intentionally if it is necessary to reset the computer) and then restarted, the computerized electronics may fail. The display first indicates “Please wait while system writes unsaved data to disk.” This is followed by the message “It is now safe to turn off your computer.” accompanied by a small box on the screen indicating “Restart.” Touching this box causes the computer to restart, but shortly thereafter, the machine electronics abruptly power down: The screen goes dark, the fans go silent, and even the flowmeter lights switch off. Furthermore, during the abortive start-up process, there is no indication of the AC power failure. Despite this electronic failure, the flowmeters continue to operate properly because the pneumatic switch remains in the “on” position. However, manual positive-pressure ventilation may not be possible, depending on the internal state of the ventilator pressure relief valve.

I believe that these characteristics pose a significant risk to patient safety. If an electrical or electronic failure occurs, the ventilator’s internal pop-off mechanism cannot be bypassed, and it is impossible to deliver positive-pressure ventilation manually with the rebreathing bag. Although internal battery backup power provides a measure of protection, a failure in the internal power supply circuitry could result in inability to provide positive-pressure ventilation. A mechanical switch-over device, similar to those used in previous anesthesia delivery systems, would reduce or eliminate the risk of these problems.

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Ventilator Failure during Use of a New Anesthesia Machine

To the Editor—Our department recently installed new North American Draeger Narkomed 6000 anesthesia machines (Telford, PA). These are microprocessor controlled and software driven and use an internal flow-dependent, piston-driven ventilator instead of a bellows. Thorough in-service education was done before use. Within a month, we experienced an unusual but significant problem with the ventilator. Neither the cause nor the solution was obvious or intuitive, thus prompting this letter.

In a patient requiring bronchial blockade for one-lung ventilation, we planned bronchoscopy using an Olympus LF-2 fiberoptic bronchoscope (Olympus, Lake Success, NY) and a Portex swivel adapter (Concord/Portex, Keene, NH). While maintaining mechanical ventilation, secretions were suctioned from the trachea using a 14-French Kendall-Curity suction catheter (Kendall-Curity, Mansfield, MA). After bronchoscope insertion, the Apnea-Low Pressure alarm sounded in response to the deliberate leak. However, it became apparent by observation of the patient and machine that there was no effective ventilation occurring. The reservoir bag was grossly displaced and would not empty, the display panel read “resetting piston,” the control switches were unresponsive, and we were unable to convert to manual ventilation. We disconnected the circuit and finished the procedure while maintaining ventilation with an Ambu bag. We then opened the locking lever under the ventilator cover, pulled up the ventilator and piston components, and reseated them. The piston reset itself, and the ventilator function resumed according to the original settings. The procedure continued uneventfully.

North American Draeger technical support was consulted, the problem was successfully recreated, and the cause was defined: The use of

‘on’ position, the ventilator executes a self-test process. This is another safety feature that ensures that the ventilator is functioning properly and informs the user about any leaks or internal sensor problems. Evidence that clinicians often fail to detect machine faults, despite a recommended anesthesia machine checklist, supports the value of the automated self-test as a means to enhance detection of ventilator problems.


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suction in the airway during mechanical ventilation generates negative-pressure flows of approximately 30 l/min, causing the piston to empty and lock, shutting down the ventilator. In addition to deliberate airway suctioning, unintentional placement of a nasogastric tube in the trachea or negative pressure from chest tubes put to suction with the chest closed in the presence of a large bronchopleural communication may also produce this problem. The flow rate through the bronchoscope suction port was measured at only 4.6 l/min (at −575 mmHg wall suction)—a flow inadequate to cause the malfunction. Flow rates in larger bronchoscopes were not tested. The solution to this situation requires the maneuver described. By breaking the vacuum seal, the piston is allowed to reset. The mechanical ventilation override control present on this machine does not work in this situation.

In this case, the patient was unharmed. In review, we make the following recommendations: (1) awareness of the causes and avoidance where possible; (2) switching to manual ventilation and filling the reservoir bag before airway suctioning; (3) availability of an Ambu bag to simplify the circuit if a ventilator problem occurs; and (4) machine function and problem-solving education. Routine procedures may trigger new problems when performed with new equipment. We recognize that the benefits of new technology can be tempered by their complexities and our limited ability to achieve intuitive solutions when those problems occur.

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In Reply:—In their letter, Drs. Barahal and Sims describe a situation in which suction to the patient’s airway before bronchoscopy caused a problem with the Narkomed 6000 ventilator (Draeger Medical Inc., Telford, PA). Draeger Medical Inc. investigated this problem and would like to describe the findings and the results of the investigation.

When the clinical circumstances of this event were recreated, it was determined that a negative pressure of −375 mmHg was applied to the airway through a 14-French suction catheter drawing a flow of 30 l/min through the catheter. When the same suction level was applied through the bronchoscope suction port, only 4.6 l/min of flow was drawn through the port, and the problem could not be recreated. Therefore, it seems that the initial airway suctioning was the inciting event, not the suction through the bronchoscope.

The problem described by Drs. Barahal and Sims occurred when a relatively high negative pressure, resulting in a high degree of suction flow, was applied to the patient’s airway during ventilation. If the suction flow is high enough, it will exceed the capacity of the ventilator’s negative-pressure relief system. The resulting negative pressure in the breathing system holds the diaphragm control valves closed in such a way that gas cannot enter the breathing system and relieve the negative pressure. A similar situation was reported to Draeger Medical Inc. by another institution where a high degree of negative pressure flows of approximately 30 l/min, causing the piston to empty and lock, shutting down the ventilator. In addition to deliberate airway suctioning, unintentional placement of a nasogastric tube in the trachea or negative pressure from chest tubes put to suction with the chest closed in the presence of a large bronchopleural communication may also produce this problem. The flow rate through the bronchoscope suction port was measured at only 4.6 l/min (at −575 mmHg wall suction)—a flow inadequate to cause the malfunction. Flow rates in larger bronchoscopes were not tested. The solution to this situation requires the maneuver described. By breaking the vacuum seal, the piston is allowed to reset. The mechanical ventilation override control present on this machine does not work in this situation.

In this case, the patient was unharmed. In review, we make the following recommendations: (1) awareness of the causes and avoidance where possible; (2) switching to manual ventilation and filling the reservoir bag before airway suctioning; (3) availability of an Ambu bag to simplify the circuit if a ventilator problem occurs; and (4) machine function and problem-solving education. Routine procedures may trigger new problems when performed with new equipment. We recognize that the benefits of new technology can be tempered by their complexities and our limited ability to achieve intuitive solutions when those problems occur.

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To the Editor:—We wish to report a useful technique for positioning infants requiring surgery in the prone position, using a commonly available adult Schiec headrest (fig. 1; Sunrise Medical, part No. 8815, Baldwyn, MS). After anesthetic induction etc., the infant’s torso is placed prone in the concave cavity of the headrest, and the head is supported on a soft foam, gel, or surgical headrest (fig. 2). Because the base of the device is flat, it provides a stable support that will not slip or move as occurs if cloth or foam rolls are used. The polyurethane foam is rigid enough to support the infant, but pliable enough not to compress the tissues. The T-shaped cutout allows free movement of the abdomen, avoiding compression and secondary venous congestion.

This technique is useful for procedures on both the lower and the upper back, as well as the posterior fossa of the skull. For cervical spine or posterior fossa operations, the neck can easily be flexed by

Positioning of Infants in the Prone Position: A Useful Technique

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elevating the support. The arms may be positioned at the infant’s side or along the head, depending on the site of the operation. Padding should be used for the extremities as needed.

Monitor cables are directed away from the site of surgery. A forced-air heater may be placed above or below the device to facilitate temperature control. The technique is useful for any infant who fits comfortably in the cradle.


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Fig. 1. Scheie Headrest (Sunrise Medical, Baldwyn, MS).

Fig. 2. Infant positioned on headrest.