More unique applications for nalbuphine

To the Editor:

This letter is written in regard to the excellent case report "Reversal of narcotic-induced biliary spasm with nalbuphine hydrochloride" by Thomas McHugh, CRNA (December, 1985 AANA Journal). This case report clearly demonstrates one of several new and unique applications of nalbuphine (Nubain®). In addition, a previous study entitled "Outpatient anesthesia with nalbuphine hydrochloride" by Joseph Yanulevich, CRNA (August, 1983 AANA Journal) gave other applications of nalbuphine. The review article "Enkephalins and endorphins: the endogenous opiates" by Daniel Milloy, CRNA (December, 1982 AANA Journal) provides additional insight for the understanding of the relationship of various narcotic analogues and man's own production of opiate-like substances.

Having used nalbuphine extensively in our institution, we would like to offer other unique applications of nalbuphine that we have used or are investigating for possible use.

Despite the presence of several commonly known drugs being classified in the agonist-antagonist category, nalbuphine appears to be unique in its cardiovascular profile. In a randomized double blind study in patients with acute myocardial infarction, Lee and co-workers compared the hemodynamic effects of nalbuphine and morphine. Neither drug altered systolic arterial pressure, pulmonary artery pressure, pulmonar capillary wedge pressure, stroke index, stroke work index or pulmonary vascular resistance. These stable cardiovascular effects of nalbuphine are in contrast to the effects of other narcotic agonists-antagonists. Pentazocine (Talwin®) significantly increases mean aortic pressure, left ventricular diastolic pressure and mean pulmonary pressure in patients with coronary artery disease proven by catheterization.2

In a similar manner, butorphanol (Stadol®) produced increased cardiac index and mean pulmonary artery pressure in patients undergoing cardiac catheterization for the diagnosis of coronary artery disease.3 The medical letter concludes that the cardiovascular effects of nalbuphine are more like those of morphine than like those of pentazocine or butorphanol; some experts consider pentazocine and butorphanol to be contraindicated for patients with angina pectoris and myocardial infarction because they may aggravate myocardial ischemia by increasing the workload of the heart.4 In patients with acute myocardial infarction, nalbuphine has an advantage over morphine, pentazocine and butorphanol of not producing hypotension.

Since nalbuphine is characterized by good cardiovascular stability,5 we have used it extensively as an analgesic for local sedation techniques. In high risk patients undergoing procedures such as insertion of cardiac pacemakers and cataract extractions we titrate nalbuphine intravenously in doses of 0.1 – 0.2 mg/kg. Since nalbuphine has a documented respiratory ceiling effect,7 respiratory changes are generally minimal in those patients that are frequently susceptible to respiratory depression. Additionally, we have found nalbuphine to provide good analgesia with a moderate degree of sedation in patients receiving regional anesthesia techniques. The analgesia provided by nalbuphine tends to make patients comfortable in regards to the tourniquet pain that is frequently experienced during intravenous regional (Bier Block) anesthesia techniques. During spinal or epidural anesthesia, nalbuphine provides good sedation without potentiating hypotension or causing significant respiratory depression that is often seen with pure agonist narcotics.

For general anesthesia techniques, nalbuphine provides good analgesia when used as a narcotic base in balanced anesthesia or as a MAC reduction adjunct to potent inhalation anesthetic techniques. Clinical observation suggests that there is approximately a 0.3 MAC reduction when nalbuphine is used in balanced anesthesia techniques.8 As alluded to by McHugh in his case report, nalbuphine has several advantages over naloxone (Narcan®) as an antagonist of the respiratory depression produced by pure agonist narcotic in balanced anesthetic techniques. Consistent with the multiple opiate receptors concept pioneered by Martin, nalbuphine appears to be able to antagonize the respiratory depression caused by agonist narcotics while preserving and possibly potentiating the analgesia.9,10 Hug and co-workers have recently reported on the use of nalbuphine as a respiratory depression antagonist following high-dose fentanyl techniques used for open-heart procedures.11,12 In more conventional balanced anesthesia techniques utilizing fentanyl or oxymorphone (Narvan®) as analgesics, we have used nalbuphine in a 0.1 mg/kg range to antagonize any residual respiratory depression. We have generally seen a dramatic improvement in the respiratory rate and tidal volume that lasts 2 to 3 times as long as that seen with naloxone. Hence, the possibility of reanesthetization is highly unlikely.13

In contrast to naloxone, the patients receiving nalbuphine for antagonism of respiratory depression tend to remain comfortable without signs of reduction of analgesia.14,15 It appears that nalbuphine may be the analgesic of choice in the anesthetic management of patients undergoing surgical intervention who are in a hypovolemic low flow state. Hunt and co-investigators observed anesthetized dogs that were bled to a mean arterial pressure (MAP) of 45 mm Hg. The animals were treated with 0.9% NaCl as a control or nalbuphine at various doses. When compared to the control, nalbuphine at 1 – 4 mg/kg bolus plus 1 – 4 mg/hr infusion intravenously for 3.5 hours increased MAP, cardiac output, left ventricular contractility, heart rate and survival. The investigators concluded that the effects were dose-dependent and support the hypothesis that endorphins acting on opiate receptors contribute to the cardiovascular pathophysiology of canine hemorrhagic shock. They further concluded that nalbuphine may be a logical alternative to naloxone, since its analgesic properties obviate the theoretical objection of enhanced pain perception with the use of naloxone in shock.

Dr. John Stene, Director of Anesthesia at the Maryland Institute for Emergency Medical Services Systems (Baltimore Shock-Trauma Center) has shown nalbuphine to be of benefit in the management of trauma patients.16 Nalbuphine in dose ranges of 0.5 mg/kg helped to restore the hemodynamic status of these patients while providing analgesia. An additional advantage of nalbuphine is its low abuse potential. Nalbuphine is not classified as a controlled substance. Due to the high cost of controlling scheduled drugs in hospitals, the agonists-antagonists drugs like nalbuphine merit special therapeutic evaluation.16 Widespread use of these drugs can simplify medication systems and lower drug distribution and control costs.

The final area we would like to point out as a promising indication for nalbuphine is the effective reversal of pruritis that occurs secondary to the use of epidural morphine or fentanyl for pain control. Recent studies have been published on the use of naloxone to counteract the problems of pruritis. Although this method has been quite effective, it generally requires the use of continuous infusion of naloxone due to its relatively short half-life. In addition, infusions of greater than 10 mg/kg/hr can reduce the analgesia produced by the epidural narcotics. Diphenhydramine (Benadryl®) has also been used to treat pruritis associated with the use of epidural narcotics. Although diphenhydramine tends to sedate patients it provides little symptomatic relief.16

Wakefield and Mesaros have conducted an initial study of fifty postcesarean section patients comparing the efficacy of nalbuphine 5 – 10 mg...
IV to that of diphenhydramine 25–50 mg IV. Preliminary results from their study indicated a success rate of over ninety percent in alleviating pruritis with nalbuphine. These and other investigators noted that nalbuphine offers some analgesia of its own and it may reverse some of the respiratory depression known to be associated with epidural morphine, as it does with fentanyl induced respiratory depression.

Since epidural narcotics have a delayed onset, the use of nalbuphine can provide analgesia until the epidural morphine becomes effective. In a preliminary study, Dadabhoy and co-workers looked at the use of intravenous nalbuphine doses of 0.21 ± 0.05 mg/kg in a balanced anesthesia technique for cesarean section. They found that despite rapid transplacental transfer of nalbuphine, APGAR scores are acceptable at 8.5 ± 2.1 when measured at 5 minutes. This would appear to support the safety of using intravenous nalbuphine to prophylactically treat pruritis caused by using fentanyl in local anesthetic solutions used to provide epidural analgesia in the management of labor and delivery. Specific recommendations for effective dose ranges of nalbuphine in patients receiving epidural morphine or fentanyl should be forthcoming in the anesthesia literature as investigators report from their controlled studies.

We hope our experience with nalbuphine in several unique anesthesia applications and the upcoming work of several investigators in new applications of nalbuphine will be helpful to the readers, along with the fine case study by Thomas McHugh, CRNA.

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REFERENCES
(17) Lecture by John K. Steen, MD "Anesthetic management of the shock-trauma patient" presented at Grand Rounds, Aultman Hospital, Canton, Ohio, October 2, 1985.

On oxygen monitoring...

To the Editor: In the February, 1986 issue of the AANA Journal, Nancy Gondringer and James Cuddeford present an excellent article for the AANA Journal Course #6 on monitoring in anesthesia. Their explanations of the complex monitors available to anesthesia providers and the importance of these monitors in ensuring safe anesthesia delivery were easy to comprehend. The following comments pertain to Table II: A brief description of monitoring modalities in relation to physical status categories. Unfortunately, these comments have led to the death of several patients.

During an anesthesia crisis, one of the first actions to take is to turn off all agents except oxygen. The only way to insure oxygen is being delivered is with an in-circuit oxygen monitor. The monitors mentioned in the cited AANA Journal are excellent for monitoring patient physiological functions, but it is equally important in the commonly used semi-closed anesthesia systems to at least monitor the percent oxygen delivered to the patient. Of course, the multiple gas analyzers now available will further assure quality control of all gases delivered to the patient.

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Response:
The comments by Mr. Hardesty as to the necessity of oxygen analyzers to monitor the fraction of inspired oxygen delivered to a patient are certainly true. Table II in our article is a suggested list of monitors of a patient's physiological functioning. Instruments to monitor the function of the anesthesia delivery system were not intended to be included.

We certainly believe that use of an oxygen analyzer during any anesthetic procedure is vital in assuring quality patient care. We would also add that use of an oxygen analyzer without appropriate documentation of continual monitoring and/or use of an oxygen analyzer which is not regularly calibrated and such calibration documented, constitutes less than quality anesthesia care.

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Editor’s note: The article being discussed here was part of the AANA Journal Course on Monitoring in Anesthesia. Chapter 4 of the course "Clinical application of monitoring gas and vapor delivery" (October, 1985 AANA Journal) and Chapter 5 "Clinical application of monitoring oxygenation and ventilation" also cover oxygen monitoring.