

## A290

**TITLE:** A NATIONAL SURVEY ON THE PRACTICE PATTERNS OF ANESTHESIA INTENSIVISTS IN THE USE OF MUSCLE RELAXANTS**AUTHORS:** Heidi T. Klessig, M.D., H. Jack Geiger, A.B., Michael J. Murray, M.D.,\* Douglas B. Coursin, M.D.**AFFILIATION:** Departments of Anesthesiology and Internal Medicine University of Wisconsin CSC Madison, WI 53792 ,

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**Introduction:** Muscle relaxants (MRs) are some of the most commonly used drugs in anesthesia practice. Recent literature indicates that the use of MR in the intensive care unit (ICU) may be associated with various problems.<sup>1-4</sup> Currently, there seems to be a paucity of information available on actual utilization of MRs in the ICU. With this in mind, a survey was developed to establish ICU practice characteristics.

**Methods:** We developed a 22 question survey which was constructed on a FOXBASE + / Mac DATA BASE to allow for ease of data entry and manipulation. A list of all current anesthesiologists with the special certificate of competence in critical care was obtained and cross referenced with the membership of the ASCCA, ASA, and SCCM to facilitate contact. Contacts were initially made by phone with a 5-10 minute interview of the practitioner. This was found to be overly time consuming and inefficient. A mass mailing was undertaken. Practitioners were asked to respond to a variety of inquiries which centered on the type of facility where they practiced, size of their ICU, indications for MR use, agent(s) used, mode of administration, monitoring techniques, concurrent use of sedatives and analgesics, methods of determining adequacy of analgesia and indications for discontinuing or reversing the relaxant.

**Results:** 176 out of 368 (48%) eligible anesthesia intensivists completed the survey. 72% of these were associated with a university or university-affiliated center. The majority practice in a surgical or combined medical/surgical ICU. Most (51%) indicated that vecuronium was the primary MR used in their ICU, while 30% used pancuronium most frequently. Atracurium was selected as the primary MR by only 2% of respondents. The most preferred method of delivery was intermittent bolus (34%), followed by continuous infusion (20%). Neuromuscular blockade was most commonly monitored using clinical criteria or not at all (66%) rather than with a nerve stimulator. The most common indications for MR use were facilitation of mechanical ventilation, increased intracranial pressure, shivering, and facilitation of procedures or diagnostic studies in the ICU. All respondents indicated that they use concurrent sedatives, narcotics, or hypnotics during MR use. Utilization of MR by respondents practicing in pediatric ICUs was twice that of the group as a whole.

**Discussion:** Our goal in this survey was to determine current practice patterns of MR use in the ICU to provide a basis for further study on the optimal use of MRs in this setting. We began by studying anesthesia intensivists, a small group of experts familiar with the use of MRs. Neuromuscular blockade in the ICU under their direction is most commonly provided by intermittent bolus injection of vecuronium. Of interest, neuromuscular blockade is not usually monitored with a nerve stimulator. This is in contradistinction to recent recommendations.<sup>1,2</sup> If nerve stimulator monitoring is infrequent among this group, it is presumably even less commonly used by other intensivists. The increased use of MRs in pediatric ICUs was an unexpected finding, and appears to represent the more frequent use of pressure controlled ventilation and the higher incidence of surgery requiring postoperative immobilization in this population.

**Summary:** We surveyed 368 anesthesia intensivists to determine their practice patterns with MRs in the ICU. Of the 176 responding, the majority use vecuronium by intermittent bolus and administer repeat doses based on clinical parameters rather than on the basis of peripheral nerve stimulation. MRs are not used in the absence of sedation or analgesia by this practitioner population.

**References:** 1. Crit Care Med 1990; 18:1177-79. 2. Anesthesiology 1990; 72:566-70. 3. Ped Neuro 1990; 6:190-6. 4. Anesth Analg 69; 1989:518-21.

## A291

**TITLE:** LEVELS OF MESSENGER RNA (mRNA) CODING FOR PHOSPHOENOLPYRUVATE CARBOXYKINASE (PEPCK) ARE INCREASED IN RAT PERITONITIS/SEPSIS**AUTHORS:** C.S. Deutschman, M.S., M.D., M.G. Clemens, Ph.D., T.G. Buchman, Ph.D., M.D.**AFFILIATION:** Depts. of Anesthesiology/Critical Care Medicine and Surgery, The Johns Hopkins Medical Institutions, 600 North Wolfe Street, Baltimore, MD 21205

Both sepsis and starvation stimulate hepatic gluconeogenesis<sup>1</sup>. In starvation both transcriptional control and post-transcriptional stabilization are involved. This process is hormonally mediated with insulin playing a dominant role<sup>2</sup>. Sepsis is regarded as a state of relative "insulin resistance"<sup>1</sup> but molecular mechanisms regulating gluconeogenesis in sepsis have not been investigated. This study tests the hypothesis that: 1) the increased rate of hepatic gluconeogenesis in sepsis is associated with elevations in the level of mRNA coding for PEPCK, the rate-limiting step in gluconeogenesis, and 2) this elevation of mRNA is greater than that noted in starvation.

**METHODS:** Sepsis was induced in three pentobarbital-anesthetized overnight-fasted adult rats by cecal ligation and single puncture with an 18-gauge needle. This results in rapid development of a persistent hypermetabolic state<sup>3</sup>. Control animals were subjected to sham laparotomy. Following surgery, animals were given free access to water but not food. Twenty-four hours later, the animals were re-anesthetized and the liver isolated and perfused with a collagenase containing buffer to disrupt non-cellular elements. Cells were removed from the hepatic skeleton and hepatocytes separated from non-parenchymal cells by 10 G centrifugation. Hepatocytes were lysed with guanidinium thiocyanate buffer and total RNA separated from genomic DNA by ultracentrifugation across a cesium chloride gradient.

A 500 base pair (BP) DNA probe complementary to a portion of rat PEPCK mRNA was synthesized and enzymatically amplified using the polymerase chain reaction (PCR). The probe was labelled with <sup>32</sup>P dCTP using a random-primed labelling kit<sup>4</sup>.

Equal amounts of total RNA from control and septic animals were subjected to Northern Blot analysis with the radiolabelled PCR probe. Autoradiography of the membrane and microdensitometry were used to detect differences in the isotopically generated hybridization signal between fasted and septic animals.

**RESULTS:** A single band of radiodensity was noted in both septic and control RNA lanes on the membrane. Septic animals generated a signal four times as dense as that from sham operated animals. Thus, more mRNA coding for PEPCK was present in septic than control animals.

**DISCUSSION:** Transcription of PEPCK mRNA in starvation is stimulated by compounds which increase intracellular levels of cyclic AMP (c-AMP)<sup>5</sup>. Fed animals have undetectable levels of PEPCK mRNA, primarily reflecting insulin mediated inhibition of transcription<sup>2</sup>. This insulin effect overrides c-AMP effects<sup>5</sup>. Sepsis is associated with elevations of epinephrine and glucagon (which increase intracellular c-AMP) but also levels of insulin which should be sufficient to override c-AMP effects<sup>1,5</sup>. This study reveals that the level of mRNA coding for PEPCK is increased in this model of sepsis. Therefore, the "insulin resistance" of sepsis may involve failure of insulin to inhibit transcription of PEPCK mRNA.

<sup>1</sup>Wolfe RR, Shaw JHF: Am J Physiol 248:E236-E243, 1985.<sup>2</sup>Granner D, Pilkis S: J Biol Chem 265:10173-10176, 1990.<sup>3</sup>Yohanda A, et al: FASEB J 1:A711, 1989.<sup>4</sup>Feinberg AP, Vogelstein B: Anal Biochem 132:6-13, 1983.<sup>5</sup>Sasaki et al: J Biol Chem 259:15242-15251, 1984.