**Appendix 2: Pretreatment in Head Injury**

**SUMMARY/RECOMMENDATIONS:**

* An *emergent* intubation should NOT be delayed for the administration of pretreatment agents.

* *Routine* use of pretreatment agents for intubation of patients with head injury will *no longer be recommended.*

* Pretreatment agents will be reserved for *special situations* when there are compelling reasons to use them as decided by the attending physician responsible for airway management. Special Situations may include (but are not limited to):
  - Lidocaine in the patient with *isolated* head injury with signs of increased ICP who is normovolemic and hypertensive.
  - Lidocaine and/or Fentanyl in a patient with a nontraumatic ICH/SAH with significant hypertension.
  - Lidocaine, fentanyl, and/or esmolol in a patient with brain mass causing signs of herniation/midline shift.
  - Fentanyl or esmolol in a medical patient with severe cardiac disease.

* The literature does not support the use of vecuronium or other defasciculating agents, and it is not standard of care to do so.

**Background**

At Grady Memorial Hospital, physicians traditionally have intubated patients with head injury using the “pretreatment” agents lidocaine and vecuronium. While many attending physicians recognize the lack of evidence to support the practice, these agents have been used because of the consensus that it is standard of care to do so. This guideline serves to examine the literature supporting or refuting the use of specific agents in intubation of patients with closed head injury.

**VECURONIUM**

A “defasciculating” dose of the competitive neuromuscular blocking agents (e.g., vecuronium 0.01 mg/kg) has traditionally been suggested to blunt the effect of defasciculations from succinylcholine on intracranial pressure. However, a systematic review revealed: 1) insufficient evidence that succinylcholine raises ICP; 2) no studies of patients with traumatic brain injury that evaluated the effect of a defasciculating dose of competitive neuromuscular blocking agents on ICP in patients intubated with succinylcholine; and 3) level 2 evidence that patients with brain tumors intubated in the operating room with succinylcholine can have the ICP response attenuated with a defasciculating agent. Based on the lack of support for defasciculating agents, more recent authorities on airway management have advised against routine use of these agents.1, 2

**LIDOCAINE**

Lidocaine is thought to blunt the rise in intracranial pressure associated with manipulation of the larynx during intubation. Additionally, lidocaine has been shown to decrease cerebral vascular resistance and cerebral blood flow as well as stabilize neuronal membranes via its sodium channel
blocking effects. Recent debates have been published regarding the strength of evidence for lidocaine use as well as the potential for harm.\textsuperscript{3,4} Supporters of lidocaine explain that it would be nearly impossible to obtain ICP measurements during intubation of head injury patients in the emergency department.\textsuperscript{4} Data to support the use of lidocaine has been extrapolated from intubation in the operating room of both healthy patients and those with brain tumors, as well as from endotracheal suctioning of patients with head injury in the ICU. Patients pretreated in the OR with lidocaine averaged a 12 mm Hg less rise in ICP compared to those who did not receive lidocaine in one study.\textsuperscript{5} Another study demonstrated that pretreatment of 10 patients with lidocaine before suctioning in the ICU attenuated the ICP rise (16-27 mm Hg in the placebo group; 10-22 mm Hg in the lidocaine group).\textsuperscript{6} A study of 30 patients undergoing VP shunt placement for increased ICP showed a decrease in ICP of 36% with hemodynamic stability when lidocaine was dosed at 1.5 mg/kg and given 2 minutes prior to intubation.\textsuperscript{7} Studies which document the reliability of lidocaine in blunting the sympathetic response are described below.

Critics cite a review in which the authors did not find any evidence that pretreatment with lidocaine improved neurologic outcomes or reliably decreased intracranial pressure in human patients with head injury.\textsuperscript{8} Critics also point out that a blunting of the hypertensive response may not be desirable if ICP is increased, or at least not reduced in proportion to the mean arterial pressure. This conclusion is based on the Monro-Kellie hypothesis leading to the equation: Cerebral Perfusion Pressure = Mean Arterial Pressure – Intracranial Pressure. While brief increases in ICP have not clearly been shown to affect outcome, decreases in MAP and CPP have been shown to adversely affect neurological outcome, as well as mortality.\textsuperscript{3} Chesnut et al. documented a 150% increase in mortality from one episode of hypotension in patients with severe head injury.\textsuperscript{9} Wald et al. also followed patients with severe head injury. Those who had an episode of hypoxia or hypotension had double the mortality and half the chance at returning to “good” neurological status compared to those who did not have hypoxia or hypotension.\textsuperscript{10}

\textbf{ESMOLOL and FENTANYL}

Three different studies have specifically compared esmolol to other agents with respect to attenuation of the sympathetic response. One randomized, double-blind study of non-cardiac patients undergoing elective surgery demonstrated that lidocaine, fentanyl, and esmolol all attenuated systolic blood pressure, but only esmolol reliably blunted tachycardia.\textsuperscript{11} Another randomized, double-blind study of gynecologic patients undergoing elective surgery compared lidocaine alone, esmolol alone, and a combination of both drugs. Esmolol alone, but not lidocaine alone, blunted tachycardia. Neither alone attenuated blood pressure. Only the combination of both blunted both tachycardia and hypertension.\textsuperscript{12} Another randomized, double-blind study of patients undergoing elective non-cardiac surgery showed that only esmolol blunted both tachycardia and hypertension; fentanyl blunted hypertension but not tachycardia; and lidocaine was not different than placebo.\textsuperscript{13} In a fourth study of elective surgery patients, esmolol significantly blunted the response to tachycardia and hypertension; lidocaine and nitroglycerin were not different than placebo.\textsuperscript{14}

One randomized, double-blind trial was done on emergency department patients with isolated closed head injury (multisystem trauma patients excluded). The trial demonstrated equal efficacy of lidocaine and esmolol in preventing increase in HR (mean increase 4.0), SBP (mean increase 1.3 mm Hg), and DBP (mean increase 2.6 mm Hg).\textsuperscript{15}

While it seems reasonable to use either esmolol or fentanyl in patients with isolated head injury—i.e., patients not suspected to be in hemorrhagic shock—textbooks seem to recommend fentanyl but not esmolol for unclear reasons.\textsuperscript{2} The evidence for both fentanyl and esmolol is stronger than that
It is also important to understand the well-documented significant effect of hypotension and decreased cerebral perfusion pressure on mortality and neurological outcome (as described above) when deciding to use these agents.

**STANDARD OF CARE??**

Despite the weak evidence for routine use of the pretreatment agents, physicians often support the use because they feel it is “standard of care.” However, review of the National Airway Registry III database revealed 1,128 intubations on patients with closed head injury from 2002 to 2006. Only 62.9% of patients (adults and pediatric patients) received any form of pretreatment. 56.9% of adults received lidocaine. 7.9% of patients received fentanyl. 7.1% of patients received a defasciculating dose of a competitive neuromuscular blocking agent. Eight cases of hypotension were observed, 4 out of 8 patients received fentanyl. Otherwise, there was no difference in adverse hemodynamic events in patients who received pretreatment agents and those who did not. The assertion that pretreatment is “standard of care” can therefore be challenged since nearly 40% of patients did not receive pretreatment. A defasciculating agent was used less than 10% of the time, and therefore one could argue that is standard of care not to use a defasciculating agent.

References:

