Critical Review Form

Therapy

ICP Change during RSI, Swine Model—*J Trauma* 2005; 58: 278-283

Objectives: To report the development of a model in pigs to measure intracranial pressure (ICP) during laryngoscopic intubation while using a variety of common emergency rapid sequence intubation (RSI) induction agents (p. 278).

Methods: Pigs were sedated with intramuscular ketamine then intubated and mechanically ventilated with isoflurane anesthesia. Next, a fiberoptic intracranial parenchymal pressure monitor was placed with subsequent continuous monitoring of ICP, electrocardiography, arterial pressure, end-tidal carbon dioxide, and temperature.

Four intubation regimens were subsequently tested reflecting common intubation agent utilization. The regimens were thiopental alone, thiopental + succinylcholine (1 mg/kg IV), thiopental + succinylcholine + lidocaine (1 mg/kg IV), and thiopental + succinylcholine + lidocaine + pancuronium (0.01 mg/kg). Similar to existing recommendations, induction agents were administered three minutes before induction. Intubation occurred about 60 seconds after administration of induction agents. Since each regimen was to be tested on each of the eight experimental pigs (for a total of 32 RSI attempts), a 30-minute washout period occurred after regimens #1 & #2 and 2.5 hours after regimen #3 (p. 279).

The outcomes reported included mean arterial pressure, cerebral perfusion pressure, ICP during RSI of the swine model using each of these four regimens.

Guide		Comments
I.	**Are the results valid?**	
A.	**Did experimental and control groups begin the study with a similar prognosis (answer the questions posed below)?**	
1.	Were patients randomized?	No “patients” and no “control pigs”. Rather each pig received each RSI regimen and then compared with one another. Several potential difficulties were anticipated with this model: agitation in response to near-awakening, difficult intubations, and malignant hyperthermia (p. 279).
2.	Was randomization concealed (blinded)?	No randomization reported.

3.	Were patients analyzed in the groups to which they were randomized?	No randomization reported.
4.	Were patients in the treatment and control groups similar with respect to known prognostic factors?	No treatment & control groups; the lack or randomization introduces the possibility of bias.

B.	**Did experimental and control groups retain a similar prognosis after the study started (answer the questions posed below)?**	
1.	Were patients aware of group allocation?	The pigs were unlikely aware of the study protocol or their group allocation.
2.	Were clinicians aware of group allocation?	Yes, no blinding stated.
3.	Were outcome assessors aware of group allocation?	Yes, again introducing the potential for bias.
4.	Was follow-up complete?	Yes, all pigs were monitored in a similar fashion until all four regimens employed. Of significance, 13/32 intubation attempts were discarded because of a priori study design issues (difficult intubation or malignant hyperthermia).
II.	**What are the results (answer the questions posed below)?**	
1.	How large was the treatment effect?	1) All three regimens using succinylcholine demonstrated three-fold higher increases in mean peak changed in ICP during RSI (increasing from 3.6 mm Hg to 12-16 mm Hg). 2) No pre-treatment agent affected this increase in mean peak ICP. 3) MAP increased concurrently with ICP. 4) All regimens demonstrated increased ICP during intubation peaking at one minute after the start of laryngoscopy and intubation. (p. 280).
2.	How precise was the estimate of the treatment effect?	The 95% CI on Table 3 (p. 280) are quite wide (imprecise) reflecting the small number of animals studied.

III.	How can I apply the results to patient care (answer the questions posed below)?	
1.	Were the study patients similar to my patient?	No, I haven't cared for pigs in quite some time. Additionally, the authors did not induce head injuries (the population on which lidocaine is typically advocated) or use induction agents we usually use. The swine model makes sense, though, because no IRB would approve a similar study in humans and no alternative animal model currently exists. "Swine were chosen for this model because of low cost, size, and compatibility with standard equipment and available laboratory facilities. In addition, contrary to canines, swine have a laryngeal anatomy that is relatively difficult to orally intubate, making swine an excellent model for a study in which laryngeal manipulation is an important stimulus." (p. 280)
2.	Were all clinically important outcomes considered?	No. For humans the most important outcome is not ICP or MAP changes, but rather neurological outcomes (functional status, independent activities, etc.).
3.	Are the likely treatment benefits worth the potential harm and costs?	A novel animal model offering the potential to further test these long-standing, highly contentious, prophylactic interventions during RSI in larger numbers to better understand potential efficacy and mechanisms of action.

Limitations

1) These pigs had no head injuries, so cannot yet be extrapolated to the utility of these agents (or of this model) in head injured humans. Usually, lidocaine is recommended in the setting of potential brain injury so future trials of this animal model should include induced brain trauma with the resulting inflammatory cascade and secondary brain injury.

2) ICP is a surrogate marker. The real outcome of importance to patients and clinicians is the neurological recovery. Additional surrogate markers for future study include cerebral oxygenation and metabolism, but ultimately researchers will need to assess the long term neurological recovery and functional independence of these animals (and ultimately patients).

3) Small sample sizes preclude making definitive conclusions about the various RSI regimens, but the current data should permit future study with more precise power calculations. Future research should also include other commonly utilized RSI agents (Etomidate, Versed, etc.).

4) 13/32 intubations were excluded! Future studies will include a tracheostomy arm to allow standardized oropharyngeal and laryngeal stimulation.

Bottom Line

The swine model offers a novel opportunity to assess the long-held belief that pre-treatment agents like lidocaine and a defasiculating dose of a non-depolarizing paralytic can alleviate the ICP elevation noted during emergent laryngoscopic intubation. The current results, although limited by small numbers, seem to suggest no benefit of pre-treatment medications on ICP anytime that succinylcholine is utilized.