

## ADVANCES

# Use of lidocaine and fentanyl premedication for neuroprotective rapid sequence intubation in the emergency department

Nick Kuzak, BSc, MD;\* David W. Harrison, MD;† Peter J. Zed, BSc, BSc(Pharm), PharmD‡

**ABSTRACT**

**Introduction:** Autoregulation is dysfunctional in the injured brain. Increases in intracranial and arterial pressure may therefore result in extension of the primary injury. Rapid sequence intubation (RSI) is a well-known cause of surges in both arterial pressure and intracranial pressure. Neuroprotective agents, namely lidocaine and fentanyl, have the potential to minimize the pressure surges implicated in secondary brain injury. The purpose of this study was to determine the frequency with which neuroprotective agents were used for neuroprotective RSI in the emergency department.

**Methods:** We conducted a retrospective chart review of all 139 patients intubated in the emergency department of Vancouver General Hospital between March and October 2003. Patients were eligible if there was an indication for neuroprotective agents defined as presumed intracranial pathology and a mean arterial pressure (MAP) > 85 mm Hg. Contraindications to fentanyl included MAP < 85 mm Hg or allergy to fentanyl.

**Results:** Seventy-seven patients were intubated for primary neurological indications. Indication for intubation included non-traumatic causes ( $n = 37$ ) (including cerebrovascular accident or intracranial hemorrhage) and closed head injury ( $n = 40$ ). The mean age ( $\pm$  standard deviation) was  $52.3 \pm 20.4$  years, and 31.4% were female. Fifty-seven (74.0%) patients had indications for neuroprotective agents, without contraindications. When neuroprotective agents were indicated, lidocaine was used in 84.2% (95% confidence interval [CI] 72.6%–91.5%) of patients while fentanyl was used in 33.3% (95%CI 22.4%–46.3%) of patients. Eleven percent of the intubations were performed with a fentanyl dose of  $\Delta 2$  mcg/kg, which is the lower limit considered effective.

**Conclusions:** Despite the potential benefit of using lidocaine and fentanyl in appropriate patients undergoing neuroprotective RSI in the emergency department, our study identified a significant underutilization of optimal premedication. The identification of barriers to use and the implementation of strategies to optimize use are necessary.

**Key words:** intubation; neuroprotection; lidocaine; fentanyl

\*R5 Emergency Medicine, University of British Columbia, Vancouver, BC

†Attending Physician, Department of Emergency Medicine, Vancouver General Hospital, Medical Director, Vancouver General Hospital Hyperbaric Unit, Clinical Associate Professor, Division of Emergency Medicine, Faculty of Medicine, University of British Columbia, Vancouver, BC

‡Pharmacotherapeutic Specialist - Emergency Medicine, CSU Pharmaceutical Sciences, Vancouver General Hospital, Clinical Associate Professor, Faculty of Pharmaceutical Sciences, Associate Member, Division of Emergency Medicine, Faculty of Medicine, University of British Columbia, Vancouver, BC

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**RÉSUMÉ**

**Introduction :** Dans les cas de traumatisme au cerveau, l'autorégulation devient dysfonctionnelle. L'augmentation des pressions intracrânienne et artérielle peut par conséquent entraîner une aggravation du traumatisme primaire. L'intubation en séquence rapide (ISR) est une cause bien connue de l'augmentation soudaine tant de la pression artérielle que de la pression intracrânienne. Les agents neuroprotecteurs, notamment la lidocaïne et le fentanyl, ont la capacité de minimiser ces poussées de pression responsables de traumatismes crâniens secondaires. La présente étude avait pour but de déterminer la fréquence à laquelle les agents neuroprotecteurs furent utilisés pour une ISR neuroprotectrice au département d'urgence.

**Méthodes :** Nous avons mené une étude de dossiers rétrospective des 139 patients intubés au département d'urgence du Vancouver General Hospital entre mars et octobre 2003. Les patients étaient admissibles s'il y avait une indication pour le recours à des agents neuroprotecteurs définie comme une pathologie intracrânienne présumée et une tension artérielle moyenne >85 mm Hg. Les contre-indications au recours au fentanyl comprenaient une tension artérielle moyenne <85 mm Hg ou une allergie à ce médicament.

**Résultats :** Soixante-dix-sept patients furent intubés pour des indications neurologiques primaires. L'indication pour une intubation comprenait des causes non traumatiques ( $n = 37$ ), (incluant l'accident vasculaire cérébral ou l'hémorragie intracrânienne) et le traumatisme crânien fermé ( $n = 40$ ). L'âge moyen ( $\pm$  écart-type) était de  $52,3 \pm 20,4$  ans et 31,4 % des patients étaient des femmes. Cinquante-sept patients (74 %) présentaient une indication pour recevoir des agents neuroprotecteurs, sans contre-indication. Quand les agents neuroprotecteurs étaient indiqués, la lidocaïne était utilisée dans 84,2 % des cas (intervalle de confiance [IC] de 95 % 72,6 %–91,5 %) et le fentanyl dans 33,3 % des cas (IC 95 % 22,4 %–46,3 %). Onze pour cent des intubations furent effectuées à l'aide d'une dose de fentanyl de >2 mcg/kg, ce qui représente la limite inférieure considérée comme efficace.

**Conclusions :** Malgré les bienfaits potentiels du recours à la lidocaïne ou au fentanyl chez les patients soumis à une ISR neuroprotectrice au département d'urgence, notre étude a révélé une sous-utilisation importante d'une prémédication optimale. La détermination des barrières au recours à cette prémédication et la mise sur pied de stratégies pour optimiser son utilisation sont nécessaires.

**Introduction**

Intracranial pathology, arising from spontaneous or traumatic causes, accounts for a significant proportion of visits to the emergency department (ED). The goal of ED care is to prevent secondary neurologic injury originating from hypoxia, hypercarbia, hypotension and further increases in intracranial pressure (ICP). Patients with significant intracranial pathology often require intubation for airway protection and/or optimization of ventilation and oxygenation. Intubation in these patients is often achieved using a rapid sequence intubation (RSI). Laryngoscopy and tracheal intubation are documented to cause sympathetic surges resulting in increases in ICP and arterial pressure.<sup>1–3</sup> Intracranial pressure and mean arterial pressure (MAP) have been shown to increase by 22 mm Hg and 25–58 mm Hg, respectively, following standard controlled anesthetic induction and intubation.<sup>1–3</sup> These effects are more pronounced with RSI when compared with a standard anesthetic induction.<sup>4</sup>

Control of the physiologic response to RSI may be important. Elevated ICP is associated with 50% of all head

injury deaths, and arterial hypertension is an independent predictor of hematoma enlargement and death in intracranial hemorrhage.<sup>5–8</sup> Unfortunately, human studies evaluating the response of ICP to intubation do not exist and are difficult to perform. Sympathetic stimulation is thought to correlate directly with ICP increases. Measures of sympathetic stimulation such as blood pressure, heart rate and plasma catecholamine levels are the ICP surrogates studied in the literature.

Minimizing sympathetic stimulation with appropriate depth of anesthesia, smooth laryngoscopy, and prevention of hypoxia and hypercarbia should be the goals for any intubation performed in an emergency setting. They are particularly important in patients with neurologic injuries. Once these technical factors have been optimized, pharmacologic agents can help with blunting the ICP and sympathetic response.

Numerous pharmacologic interventions have been evaluated to determine if the undesirable effects of intubation can be minimized. These medications are referred to as neuroprotective agents, due to their ability to blunt sympathetic and, presumably, ICP responses to intubation. Lido-

caine, esmolol, and synthetic opioids are the most widely studied neuroprotective agents. Lidocaine, at a dose of 1.5 mg/kg, has been shown to directly blunt ICP rises by approximately 15 mm Hg with tracheal suctioning in intubated patients.<sup>9,10</sup> However, studies evaluating the hemodynamic effects of lidocaine during laryngoscopy and tracheal intubation demonstrate that lidocaine has only small effects on suppressing sympathetic output.<sup>11,12</sup>

Human studies evaluating the effect of synthetic opioids and esmolol on the ICP response to laryngoscopy or tracheal manipulation are lacking. The attenuation of sympathetic and hemodynamic responses by these agents has been studied extensively during laryngoscopy and intubation. Both synthetic opioids and esmolol have been shown to be vastly superior to lidocaine in this regard.<sup>13–16</sup> Opioids studied as neuroprotective agents include sufentanil, remifentanil, alfentanil and fentanyl. The emergency literature deals almost exclusively with fentanyl, presumably because it has the advantages of being easily available, familiar, and less likely to produce adverse cardiovascular effects. Doses of 5–10 µg/kg will unequivocally cause sympatholysis and block arterial hypertension and tachycardia, but may cause hypotension.<sup>17,18</sup> Doses of 2.5–3 µg/kg have been demonstrated to be effective and superior to lidocaine, without risk of hypotension.<sup>14,15</sup> Esmolol 100–200 mg has sympatholytic actions that are slightly superior to fentanyl and markedly superior to lidocaine.<sup>13–15,17</sup> The combination of esmolol and fentanyl provided the greatest sympatholysis and hemodynamic stability.<sup>14,17</sup>

Despite the potential benefits of neuroprotective agents in patients undergoing RSI in the ED and their acceptance as standard of care, the actual use of these agents has not been evaluated at our centre. The purpose of this study was to determine the frequency with which neuroprotective agents are used for RSI in our ED when there are clear indications for use.

## Methods

### *Design and setting*

This was a retrospective chart review conducted on a convenience sample of adult patients undergoing intubation in the ED at Vancouver General Hospital (VGH). VGH is a 700-bed adult tertiary care and referral centre within the Vancouver Coastal Health region and the main teaching hospital affiliated with the University of British Columbia (UBC). VGH has an annual ED census of 62 000 patient visits and is staffed by physicians board-certified in emergency medicine by the Royal College of Physicians and Surgeons of Canada. The study was coordinated by the Re-

search Division of the VGH Department of Emergency Medicine. Ethical approval was obtained from the UBC Clinical Research Ethics Board.

### *Patient population*

VGH is a participating centre in the National Emergency Airway Registry (NEAR III), and all patients undergoing endotracheal intubation in the ED are therefore entered into this registry. All patients intubated in the ED and entered into the database in the 8-month period between March and October 2003 were evaluated for inclusion in the study. Data on patients intubated more than once during the study period were entered as discrete events.

### *Data collection*

A single investigator (N.K.) extracted data from the airway database, including patient demographics, indication for intubation, premedication/neuroprotective agents, induction agent and paralytic. Doses of medications, timing, and presence of contraindications to lidocaine or fentanyl use were also obtained. Blood pressure and heart rate were obtained pre- and post-intubation. Data were entered into a preformed Excel® spreadsheet (Microsoft Corp., Redmond, Wash.).

Indications for neuroprotective agents were based on the criteria of presumed intracranial pathology and MAP > 85 mm Hg. A threshold blood pressure value for the use of neuroprotective agents could not be found in the literature. A threshold value was calculated based on subtracting a conservative average blood pressure rise incurred with intubation and laryngoscopy (25 mm Hg) from the upper desirable limit of MAP, 110 mm Hg.<sup>19</sup> Suspicion of neurologic injury at the time of intubation was inferred from the decision to order an urgent CT scan of the head as part of the initial care of the patient. Contraindications to fentanyl included MAP < 85 mm Hg or a known allergy to fentanyl.

### *Statistical analysis*

Demographic data are reported using standard descriptive statistics reported as means with standard deviations (SDs). The primary outcomes for this study are reported as proportions, using percentages with 95% confidence intervals (CIs).

## Results

During the 8-month study period, 139 intubations were performed (Fig. 1). The mean age ( $\pm$  SD) of subjects was 52.3  $\pm$  20.4 years, and 31.4% were female. Seventy-seven (55%) intubations were for primary neurologic indications, all us-

ing the RSI approach. Indications for intubation included non-traumatic causes ( $n = 37$ ) (including cerebrovascular accident or intracranial hemorrhage) and closed head injury ( $n = 40$ ). In 57/77 (74%) of the intubations performed for neurologic etiology there was an indication for the use of neuroprotective agents, without contraindications. Indications for intubation were primarily for protection of the airway. Optimization of oxygenation and ventilation (hyperventilation) were common secondary indications.

Of the 57 intubations performed with an indication for neuroprotective agents, lidocaine was used in 48 (84.2%–95%, CI 72.6%–91.5%) and fentanyl in 19 (33.3%–95%, CI 22.4%–46.3%). Only 6 (11%) of intubations were performed with optimal doses of both lidocaine (1.5 mg/kg) and fentanyl ( $\geq 2$   $\mu\text{g}/\text{kg}$ ), which is the lower limit considered to be effective. The time interval from administration of neuroprotective drugs to administration of induction and paralytic agents was between 2–4 minutes in all cases.

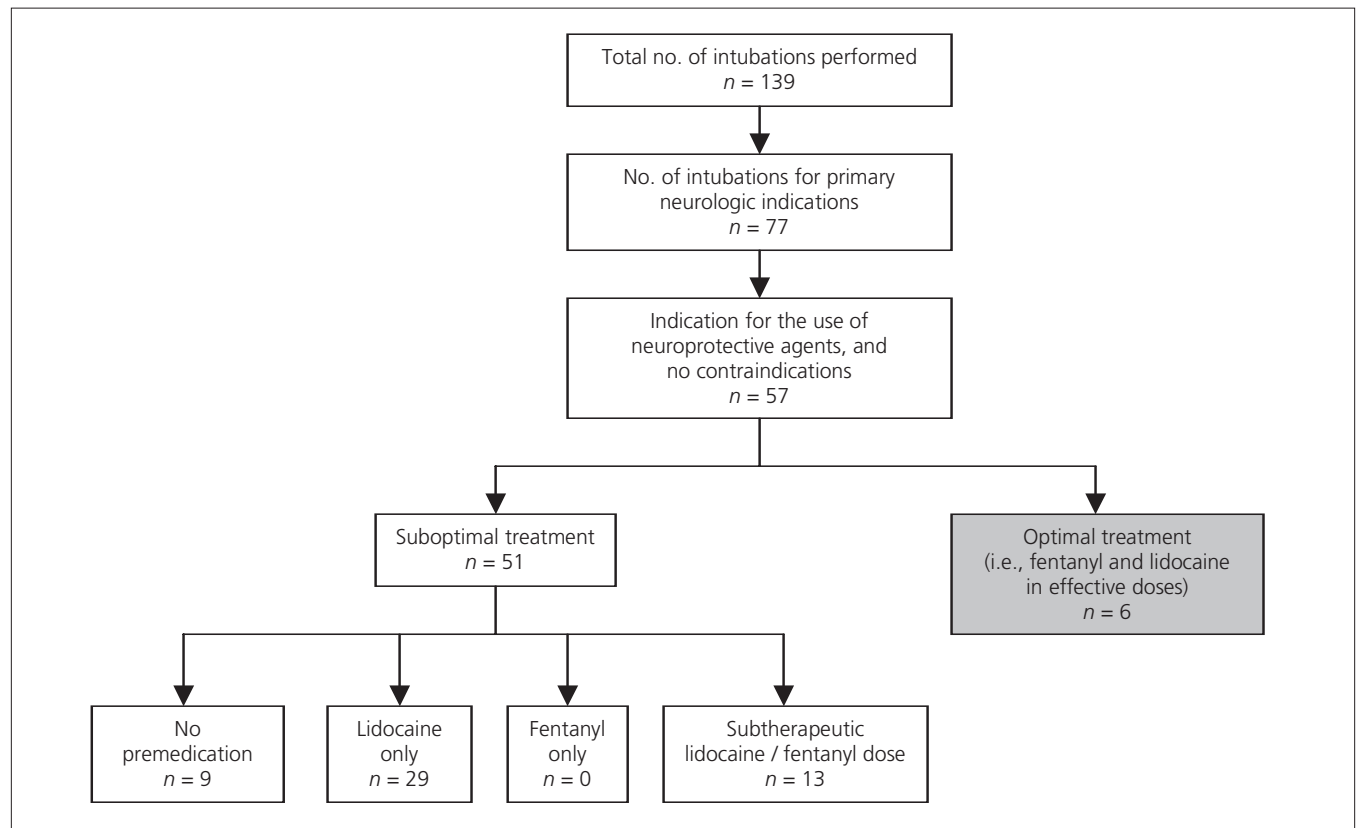
## Discussion

This study identified a significant underutilization of fen-

tanyl in hemodynamically stable patients with suspected neurologic injury. Despite both agents being indicated during neuroprotective RSI, fentanyl was used less than half as often as lidocaine. Furthermore, when fentanyl was used, doses were subtherapeutic in two-thirds of those patients treated. Only 6 of 57 hemodynamically stable patients with suspected neurologic injury received the optimal available RSI pretreatment drugs in the ED.

The cause for this underutilization and underdosing cannot be identified by our study. However, subsequent polling of the ED staff was undertaken to identify barriers to the appropriate use of neuroprotective agents, specifically fentanyl. Major concerns raised were those of hypotension with fentanyl administration (particularly with doses of 3 mcg/kg or greater), lack of knowledge of fentanyl efficacy and concern over delay in intubation.

The second phase of this study will identify and attempt to rectify the perceived barriers to the use of fentanyl. These will include providing each emergency physician with a concise literature review of the topic and presenting the issue at academic rounds. In addition, creation of a standardized intubation pre-printed order form is currently being designed and will serve as a reminder when pre-



**Fig. 1.** Patient flow of the 139 patients intubated in the emergency department of Vancouver General Hospital between March and October 2003.

scribing medications for RSI in the ED. Once this has been implemented, the compliance to fentanyl premedication in neurologically compromised patients requiring intubation will be reassessed.

### Limitations

Limitations of this study lie in its retrospective nature. It is difficult to assess by chart review alone the acuity with which the patient needed to be intubated. Perhaps it was felt on certain occasions that the 2–3-minute delay required for administration of the neuroprotective agent before administration of the induction agent and paralytic was too long and that more benefit would result from immediate control of the airway. However, this would account for only the 12% of cases where no neuroprotective agent was used (all others received at least lidocaine).

### Conclusion

Despite the potential benefit of using lidocaine and fentanyl in appropriate patients undergoing neuroprotective RSI in the ED, our study identified a significant underutilization of premedication, particularly fentanyl. Identification of barriers to the use of these agents and implementation of strategies to optimize their use are necessary to improve the care of patients undergoing emergency intubation for neurologic pathology in the ED.

**Competing interests:** None declared.

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**Correspondence to:** Dr. Peter J. Zed, CSU Pharmaceutical Sciences, Vancouver General Hospital, 855 West 12th Ave., Vancouver BC V5Z 1M9; 604 875-4077, fax 604 875-5267, zed@interchange.ubc.ca