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Full Length Research Article

THE LIDOCAINE PATCH- CAN IT HELP PATIENTS TOLERATE LONG TERM INTUBATION

[1*]George W. Williams, [2]Aanchal Sharma, [3]Golby Jalali, PharmD, [4]Dr. Bilal A. Rana, [5]Mahammad N Hussain,

[1,4]Department of Anesthesiology and Neurosurgery, The University of Texas Medical School at Houston, Houston, Texas, USA
[2,5]Department of Anesthesiology, The University of Texas Medical School at Houston, Houston, Texas, USA
[3]Memorial Hermann - Texas Medical Center Houston, Texas, USA

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ABSTRACT

Objective: To relieve the discomfort caused by an endotracheal tube in situ, which is a major concern in the management critically ill patients requiring mechanical ventilation. To facilitate ventilation, avoid increased airway pressures due to agitation, and minimize the risk of self extubation, critically ill intubated patients need to be given adequate sedation. Sedation and analgesics when given facilitates the mechanical ventilation but tend to affect the sensorium. Data Sources: ICU Team, Medical Record. Study Selection: Selected intubated patients requiring sedation. Data Synthesis: This case series reviews results from three patients with an endotracheal tube in situ that had a superior laryngeal nerve block via a lidocaine patch to evaluate if it results in improved tolerance of an endotracheal tube. Conclusions: Prospective studies evaluating the efficacy of the lidocaine patch for improved comfort of intubated patients should be considered.

INTRODUCTION

Pain is the most frequent memory which Intensive Care unit (ICU) patients have during their stay. (Stein-Parbury and McKinley, 2000) The endotracheal tube is a major cause of discomfort in ICU patients. Especially, if the patients are fully awake and require long term ventilation, an endotracheal tracheal tube in situ can frequently cause agitation. Agitation can precipitate accidental removal of endotracheal tubes (self extubation) or of intravascular catheters used for hemodynamic monitoring or administration of life-sustaining medications. Consequently, to control agitation, sedation and analgesics are administered which affect sensorium. Previous studies with the Lidocaine patch (LP) have shown it to be effective in relieving pain in various neuropathic and non-neuropathic conditions. (Hines *et al*., 2002; Desai *et al*., 2008 and Davies *et al*., 2004) Furthermore, Kim et al used the LP prophylactically and was able to successfully decrease venipuncture pain.

Corresponding author: George W. Williams
Department of Anesthesiology and Neurosurgery, The University of Texas Medical School at Houston, Houston, Texas, USA

(Kim *et al*., 2012) In effect, the application of a LP over a peripheral nerve territory allows the application of a peripheral nerve block (PNB), as applied in these chronic pain syndromes. Performing a PNB on the superior laryngeal nerve (SLN), though well described, may be technically challenging and not within the skillset of the non-anesthesiologist intensivist. (Iida *et al*., 2013 and Manikandan *et al*., 2010) Furthermore, even if training we pursued for intensivist in general, the risk of complications may outweigh the benefits. (Hsu CH *et al*., 2000) The LP has the benefit of easy placement over the anatomical area of interest. This case series reviews results from three patients with endotracheal tube in situ and use the Lidoderm patch over the SLN area to evaluate if it helps in tolerating endotracheal tube well. Figure 1 demonstrates the application of the patch on a model patient. Our institution does not require IRB permission for publishing case series.

Case 1

A 66-year-old 64kg female with a history of myasthenia gravis and hypertension diagnosed two years prior to admission presented to the Neuroscience Intensive Care Unit (NICU) with myasthenic crisis. She complained of gradually worsening diplopia, right eye ptosis and dysarthria. On presentation she

was noted to be in respiratory distress and hence was intubated and mechanically ventilated in the NICU. There was no respiratory or bulbar involvement prior to the hospitalization in question. The patient was being treated by her neurologist with Mestinone and Prednisone. With regards to her workup, CT of the chest was negative for thymoma. She was given intravenous immunoglobulin treatment for 5 days with continued prednisone and pyridostigmine. She was sedated with a propofol infusion at 10µg/kg/min. A LP was applied on day 7 of intubation. The patch was applied on the skin overlying SLN in the same fashion as shown in figure 1. It was applied for 12 hours on/12 hours off (per package insert instructions) for 3 days. Since the patient could clearly communicate and had no central neurologic deficits, we were able to stop her sedation during the application period to assess the efficacy of the patch. She reported better tolerance of endotracheal tube with the patch. Additionally, there was an improvement in her extraocular movement and right eye ptosis. The patient eventually failed extubation secondary to subglottic stenosis and tracheostomy was performed. Her FiO_2 was gradually decreased and she was transferred from ICU to inpatient rehabilitation with no residual neurologic or pulmonary deficits (besides the tracheostomy in situ).

Case 2

21 year old 52 kg female s/p bilateral gunshot wound to the chest and left thigh was brought to our hospital. On arrival her Glasgow Coma Scale score (GCS) was 3 and endotracheal tube was in situ. The injuries included left 1st rib fracture, posterior left 4th rib fracture, bilateral pneumothorax, lung contusions, spleen laceration, left proximal femur fracture which was open comminuted. She was taken to the operating room (OR) upon admission and during surgery, the left upper lobe, right upper lobe, right middle lobe lung was resected followed by chest tube placement bilaterally. The patient was transferred to the Shock Trauma Intensive Care Unit (STICU) for further management. Post-operative day (POD) #1 a T 3-4 corpectomy, decompression, T 2-5 anterior spinal fusion and intermedullary nailing left femur was done. In the ICU her GCS gradually improved and she started responding to commands. Due to her respiratory failure she continued to remain on the ventilator. She was kept on a continuous midazolam infusion and *pro re nata*(PRN) fentanyl for sedation and endotracheal tube tolerance. On POD #6 a LP was applied as described above in case 1 for 3 days. She did not receive any fentanyl in the 3 day period and her midazolam infusion was stopped during the 12 hour application period but had to be started 2 hours following patch removal on POD #7 and #8. The patient was able to communicate and reported to have decreased discomfort from the presence of endotracheal tube during the application period of the patch. Later she had a tracheostomy placed and gradually weaned from the ventilator. She was transferred from the STICU to the floor and was eventually discharged to rehabilitation.

Case 3

A 48 year old 80kg female s/p severe motor vehicle accident was intubated in the field and brought to our hospital. On arrival, her GCS score was 3 and was hypotensive requiring pressors. A subdural intracranial pressure monitor ('bolt') was placed by neurosurgeons in the emergency department with an initial pressure of 8 mmHg and seizure prophylaxis was initiated. She was transferred to STICU for mechanical ventilation and further management. She was diagnosed with bilateral pedicle and lamina fractures at C6 with joint diastasis at C6-C7, left medial orbital wall fracture, right tibial fracture with knee subluxation, left side radius and ulna fracture. Her neurological status and hemodynamic status gradually improved and she was weaned from norepinephrine. On post admission day (PAD) # 2 underwent an uneventful anterior cervical discectomy, fusion of C6-C7 with allograft bone graft along with anterior plate and screw construction, right tibia and fibula fixation, left medial orbital wall fixation. Following the above surgery, she gradually became conscious and oriented in the STICU. Acetaminophen and hydromorphone was scheduled and PRN for pain; during this time period, the patient required 10 mg of hydromorphone/day on average. LP was applied on PAD #5 of continued for next three days as described in case #1. On day 1 of LP application she did not require any PRN sedation; on days 2 and 3 she did not require any PRN sedation during the 12 hour period of patch application. While intubated, she was lucid and communicated increased comfort with LP placement. Later she had a tracheostomy placed and was weaned from the ventilator. At the time of manuscript submission, the patient remains in the hospitalized awaiting transfer to a facility in Mexico.

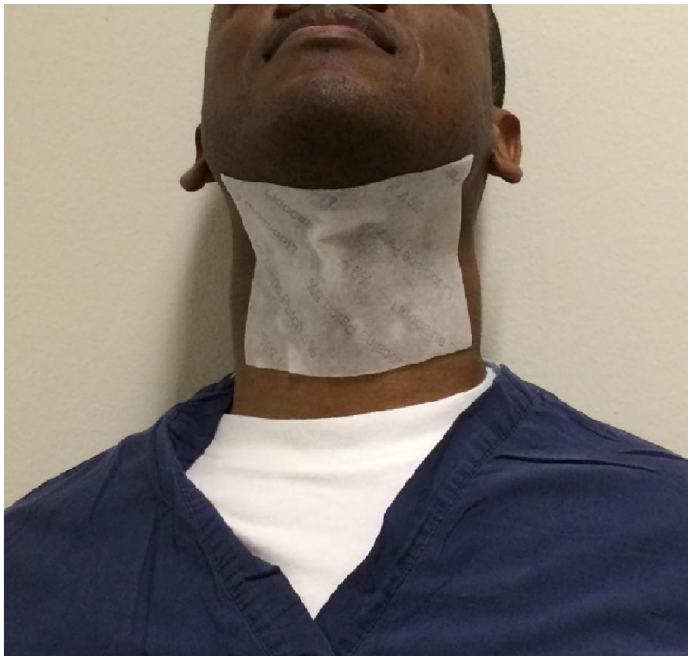

Figure. 1 Patch applied to member of ICU team

DISCUSSION

The presence of endotracheal tube in situ is a major stimulus for the patients in ICU. This is even more concerning in patients requiring long term ventilation. To facilitate ventilation, avoid increased airway pressures due to agitation, and minimize the risk of self extubation, critically ill intubated patients need to be given adequate sedation. Options to achieve this include a wide variety of drugs including opiates, benzodiazepines, hypnotics (ie- propofol) or α-2 agonists (ie- dexmetatomidine) and others are used to help patients tolerated endotracheal intubation and facilitate mechanical ventilation. These medications are known

to attenuate airway reflexes but the administration over a long term period of time may cause persistently impaired level of consciousness. (Coplin *et al*., 2000; Breen *et al*., 2005 and Mason P. Remifentanil, 2002) In one randomized controlled trial patients who received less sedation, spent fewer days undergoing mechanical ventilation and less overall ICU days. (Kress *et al*., 2000) Studied such as this have led to the commonly applied sedation interruption approach to caring for mechanically ventilated ICU patients. (Barr *et al*., 2013) The approach of withholding sedation has to be carefully balanced with the risk of causing long term psychological injury to a patient (Samuelson *et al*., 2007 and Kress *et al*., 2003) Long term untreated pain can lead to post traumatic stress disorder. (Myhren *et al*., 2010) Reade et al in their review article concluded that management of sedation and delirium can have an important effect on the outcomes of patients who are treated in ICUs. They suggested that best outcomes are achieved with the use of a protocol in which the depth of sedation and the presence of pain and delirium are routinely monitored, pain is treated promptly and effectively, the administration of sedatives is kept to the minimum necessary for the comfort and safety of the patient, and early mobilization is achieved whenever possible. (Reade *et al*., 2014)

We used the LP as a novel pharmacologic approach to help tolerating stimulus of endotracheal tube. The LP 5% (Lidoderm, Watson Lab Inc., Salt lake city, UT, USA) consists of an adhesive material containing lidocaine 5% (700 mg/patch) applied to a non-woven polyester felt backing and covered with a polyethylene terephthalate film-release liner. According to the package labelling, up to three patches ($420cm^2$) may be applied once daily for a maximum of 12 hours/day. It is not necessary to titrate the dosage, preventing the risk of overdose. (Hsu *et al*., 2000) The observations that we have documented in our patients indicate that while the LP is on, patients do not require as much sedation. The mechanism behind that could be the stabilization of neuronal membrane in superior laryngeal nerve through inhibition of the sodium flux required for initiation and conduction of impulses. Superior laryngeal nerve block provides anesthesia of the larynx from the epiglottis to the level of the vocal cords. The depth of anesthetic effect depends on the duration for which patch was applied. In various studies when the topical anesthetic was applied for 60 min, the depth of the anesthetic effect was found to be 3 mm, and for 120 min of application time, the depth of the anesthetic effect was found to be 5 mm. (Bjerring P, Arendt-Nielsen L, 1990 and Wahlgren CF, Quiding H, 2000) We applied it for 12 hours so we expect the lidocaine to reach around superior laryngeal nerve vicinity considering its superficial position in the neck. The duration and depth necessary may vary depending on the degree obesity of treated patients; our patient population did not include patients with a BMI > 50 kg/m2. We used the patch for a three day trial period in these patients who required long term ventilation and were awake enough to share their experience. All the three patients reported to have better tolerance of the endotracheal tube after the 2-3 hours of application and the overall experience was good. The most frequent adverse events reported by the manufacturer with the LP 5% are mild skin rash, redness or irritation at the application site, which have also been reported with the vehicle patch alone in clinical trials. (Lidoderm, ? and Comer, Lamb, 2000) None of our patient reported any irritation nor did we observe any redness or rash at the site of LP application. Another concern commonly attributed with lidocaine usage is its toxicity. It has been reported that the systemic absorption rate of lidocaine from a 5% LP applied to the skin in humans is very low. The toxicity symptoms of lidocaine start at the concentration of 5 µg/ml. Pharmacologically, maximum plasma lidocaine concentration is approximately 0.186 µg/ml with 4 LPs applied for 24 h, which is approximately 12–15% of the lidocaine concentration necessary to influence cardiac activity and 4–5% of that necessary to achieve systemic toxicity. (Gammaitoni *et al*., 2002) Thus, the risk of any adverse systemic event with 5% LP is very low even with the continuous application of up to 4 patches per day. Furthermore, Gammaitoni et al reported no loss in sensation at the application site. Conceivably, the LP could be continuously applied for 24 hours at a time given that in our patient population, two of our three patients indicated a difference in relief once the LP was removed.

The cost of one LP is $9.39 (applied for 12 hours then off for 12 hours). When compared per our institutions dosing routine for an 80 kg patient, propofol at 30 mcg/kg/min would cost $124.42/24 hour period, dexmetatomidine at 0.5 mcg/kg/hr would cost $475.20/24 hour period, and midazolam at 0.05 mg/kg/hr would cost $37.65/24 hour period. On a relative scale the cost of utilizing an LP is minimal and the potential benefit from reduced need for the more expensive infusions listed is substantial. In conclusion, the results from these patients suggest that the LP 5% may help patients tolerate endotracheal tube in critically ill patients. Prospective, randomized control trials should be conducted to further evaluate the utility of the LP for critically ill mechanically ventilated patients requiring sedation.

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