

ORIGINAL RESEARCH



Comparative study between oral acetaminophen and lidocaine spray on endotracheal tube-related sore throat in adult intensive care

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Abstract

Background/Purpose: Endotracheal tube (ETT)-related sore throat is a common source of stress in intensive care. Quantitative studies on therapy for ETT-related sore throat remain limited. The current study evaluated the therapeutic effects of oral acetaminophen (ACT) and lidocaine (LIDO) spray on pain relief for ETT-related sore throat in intensive care.

Methods: Patients who could communicate with caregivers non-verbally and who had acquired ETT-related sore throat at a medical intensive care unit (ICU) were enrolled. The medications were dispensed at the request of the patients. The intensity of ETT-related throat pain was recorded for quantitative comparison before and after patients received 500 mg of ACT orally or one dose of 10% LIDO spray locally. Before leaving the ICU, the patients were interviewed by a research nurse to assess the effect of these interventions on satisfaction with pain management for ETT-related sore throat.

Results: We enrolled 89 patients during the study period, and the intensity of ETT-related throat pain significantly decreased after treatment (6.97 in 5 min before vs. 3.60 in 120 min after oral ACT, $P < 0.001$; 8.56 in 5 min before vs. 4.12 in 120 min after LIDO application, $P < 0.001$). The degree of pain reduction over time differed between the ACT and LIDO groups. Patients in the LIDO group made more requests for additional therapy compared with patients in the ACT group (1 LIDO spray per request for an average of 4.7 requests vs. 1 ACT dose per request for an average of 1.3 requests, $P < 0.001$). Patients in both the ACT and LIDO groups reported high satisfaction with pain management for ETT-related sore throat (87.3 of 100 vs. 86.5 of 100, respectively, $P = 0.805$).

Conclusion: ACT and LIDO treatment can effectively attenuate ETT-related sore throat. Patients were highly satisfied with pain management for ETT-related sore throat after both oral ACT and local LIDO application.

Keywords

Endotracheal tube; Intensive care; Pain management; Quality of care

1. Introduction

Endotracheal tube (ETT) intubation is performed on patients who are unable to breathe independently. However, active ETT intubation is a stressor for patients in intensive care units (ICUs) [1–6].

ETT-induced sore throat often occurs after general anesthesia for surgery. Postoperative sore throat (POST) often occurs following ETT intubation and lasts for 1 or 2 days after ETT extubation [7–9]. Various pharmacological and nonpharmacological methods with variable success rates have been used for preventing or attenuating POST [9, 10].

Patients with critical conditions often experience ETT-related discomfort [11]. Patient age, disease type, emergent

intubation complications, [12–14] and prolonged intubation [15] potentially result in local tissue injury in the ETT placement area. Because POST is a potential indicator of ETT-related sore throat in patients with an emergent condition and studies on the presentation and pain management of ETT-induced sore throat remains limited [16, 17], management of ETT-related sore throat in critically ill patients is necessary.

Acetaminophen (ACT) and lidocaine (LIDO) are common pain relievers used in ICUs [18, 19]. In the current study, we evaluated the clinical effects of oral ACT and local LIDO application on ETT-related sore throat in patients with critical conditions.

2. Methods

2.1 Study participants

We conducted a year-long prospective study. Conscious patients with ETT intubation were asked to enroll. Patients with a history of allergy or adverse effects to LIDO or ACT were excluded. Patients who requested other sedatives or analgesics were excluded. Patients were enrolled after they provided informed consent. The current study was approved by the Institutional Review Board of MacKay Memorial Hospital, Taipei, Taiwan (protocol MMH-I-S-567). Pain management medication was administered immediately after the patients experienced ETT-related sore throat and requested treatment.

2.2 Definitions and data collection

2.2.1 LIDO 10% spray

LIDO 10% spray (50 mL/500 spray, AstraZeneca AB, Cambridge, UK) contains 5 g of lidocaine hydrochloride per container; 10 mg of LIDO per spray is applied topically for local anesthesia. When sprayed on the oropharyngeal mucosa, LIDO's onset of action is rapid, and the duration of activity is short (elimination half-life: 1.6 h in healthy patients and 6.6 h in patients with liver disease) [20]. Additionally, LIDO has a dose-dependent serum concentration [21] and concentration-dependent toxicity (the serum concentration of LIDO is measurable when 200 mg of LIDO is sprayed locally) [21, 22]. Therefore, the suggested maximum topical dose is 20 sprays (200 mg). Furthermore, local LIDO application may cause local mucosal irritation [23], and LIDO overdose causes central nervous system toxicity, which can result in seizures [22, 24, 25].

2.2.2 Numerical rating scale

Pain was defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage [26]. Pain is a sensory experience and involves affective and cognitive responses to body damage. Pain is interpreted subjectively, and the experience is unique. Therefore, patients who were able to self-report pain severity were enrolled in the study.

The intensity of ETT-related sore throat was evaluated and self-reported according to the Wong-Baker Faces Pain Rating Scale [27], which ranges from 0, "no hurt" (happy face), to 10, "hurts like the worst pain imaginable" (crying face). On the basis of the faces and written descriptions, the patient chooses the face that most accurately described their level of pain. This pain scale is appropriate for patients who do not know how to count or who may have impaired brain function. The reduction in ETT-related throat pain intensity was evaluated according to the difference between the score on the Wong-Baker Faces Pain Rating Scale 5 min before and 30, 60, and 120 min after each treatment in each group. One question answered on a typical 5-point Likert-type scale was designed to determine patient satisfaction with pain management for sore throat.

2.3 Investigation

The patients were randomly assigned into two groups: the ACT group, who received 500 mg of ACT orally, and the LIDO group, who received one dose of 10% local LIDO spray. Patients in each group were prescribed medication upon request. Pain severity was self-reported on a numerical rating scale 5 min before and 30, 60, and 120 min after each treatment [28]. The total duration required for ETT-throat pain relief was compared between 21 patients who requested a second dose in the ACT group with the patients in the LIDO group. Events were recorded after any adverse effects following LIDO administration, including consciousness changes, mucosal irritation [23, 29], seizures [24, 25, 30, 31], cyanosis [31], and electrocardiography changes, or after any adverse effects following ACT administration, including allergic reaction, liver failure, pneumonitis, agitation, skin rash, nausea, vomiting, constipation, and atelectasis. The treatment was withdrawn immediately, and the patient was promptly treated. Before leaving the ICU, patients were interviewed, and researchers helped them complete the questionnaire.

2.4 Statistical analysis

The primary outcome was the pain management effect of ACT and LIDO on ETT-related sore throat. The secondary outcome was the degree of patient satisfaction with pain management. All analyses were performed using the SAS 9.4 (SAS Institute Inc., Cary, NC). Continuous variables were reported as means \pm standard deviations. Categorical variables are described using frequency distributions and reported as numbers and percentages [n (%)]. Student's *t* test was used to evaluate the difference between the two independent samples. To determine the degree of pain reduction over time, the reported pain intensity before and after the first treatment in each group was analyzed. A paired *t* test was used to assess the difference in pain intensity 5 min before and 120 min after treatment in the same patient. A repeated-measures analysis of variance was used to compare the degree of pain reduction 30, 60, and 120 min after ACT or LIDO treatment. Both sets of data were then analyzed using the Bonferroni test, a post hoc analysis, to compare the degree of pain reduction after ACT or LIDO treatment between two time points. Statistical significance was set at an α value of 0.05.

3. Results

Table 1 presents the demographics and characteristics of the patients enrolled in the study. During the study period, 89 adult patients were enrolled; 26 were assigned to the LIDO group, and 63 were assigned to the ACT group. Age, gender proportion, ETT size, duration of ETT intubation, and length of ICU stay were similar between the groups. During the study period, patients in the LIDO group made more requests for additional therapy compared with patients in the ACT group (1 LIDO spray per request for an average of 4.7 requests vs. 1 ACT dose per request for an average of 1.3 requests, $P < 0.001$). The mean duration required for pain relief was 9.7 h in the ACT group and 37.5 h in the LIDO group ($P < 0.01$). No adverse physical effects were recorded in either group.

TABLE 1. Characteristics of the patients in the study

	Acetaminophen (n = 63; 70.8%)	Lidocaine (n = 26; 29.2%)	P-value*
Age, mean (SD), y	65.2 (12.7)	66.7 (11.1)	0.610
Gender, n (%)			
Man	32 (50.8)	13 (50.0)	0.946
Women	31 (49.2)	13 (50.0)	
Duration of ETT intubation, mean (SD)	7.9 (8.6)	7.8 (4.3)	0.926
ETT size, mean (SD)	7.5 (0.1)	7.5 (0.2)	0.577
ICU LOS, mean (SD)	10.2 (8.6)	9.9 (4.7)	0.822
Number of treatment required, mean (SD)	1.3 (0.5)	4.7 (0.5)	< 0.001
Duration required for pain relief, mean (SD), h	9.7 ^δ (3.8)	37.5 (47.2)	0.008

ETT, endotracheal tube; ICU, intensive care unit; LOS, length of stay; SD, standard deviations; ^δ21 cases.

*P-value estimated by Student's t-test for continuous variables or Pearson's χ^2 test for categorical variables.

The average score for pain intensity of sore throat in the ACT group before the first treatment was 6.97 ± 0.74 , which decreased to 6.35 ± 0.95 , 4.06 ± 0.74 , and 3.60 ± 0.68 at 30, 60, and 120 min after the first treatment, respectively. In total, 21 of 63 patients requested a second ACT dose. The average pain intensity before the second dose was 5.76 ± 0.83 , which decreased to 5.48 ± 0.93 , 3.24 ± 0.70 , and 2.19 ± 1.08 at 30, 60, and 120 min after the second treatment, respectively (Fig. 1A, left). The intensity of throat pain significantly decreased 120 min after ACT treatment ($P < 0.001$; Fig. 1B, left). The degree of pain relief after ACT treatment significantly increased over time and nearly plateaued 120 min after treatment ($P < 0.001$; Fig. 1C, left).

The average score for throat pain intensity in the LIDO group before the first treatment was 8.56 ± 0.72 , which decreased to 5.25 ± 0.51 , 3.70 ± 0.90 , and 4.12 ± 0.43 at 30, 60, and 120 min after the first treatment, respectively. The average pain intensity also declined each time after the second, third, fourth, and fifth LIDO application (Fig. 1A, right). The intensity of throat pain significantly decreased 120 minutes after LIDO treatment ($P < 0.001$; Fig. 1B, right). The degree of pain relief after LIDO treatment significantly increased over time ($P < 0.001$; Fig. 1C, right), and plateaued 60 min after treatment (4.85 ± 0.86 vs. 4.44 ± 0.76 60 min vs. 120 min after treatment, respectively; $P = 0.21$; Fig. 1C, right).

After comparing the effects of ACT and LIDO on pain relief for ETT-related sore throat, we observed that LIDO exhibited a greater maximum pain reduction than ACT did ($P < 0.001$, Table 2). Additionally, more patients in the LIDO group achieved maximum pain reduction than patients in the ACT group did 60 min after treatment (Table 2). Patient satisfaction with pain management for ETT-related sore throat at ICUs was high and similar between the ACT and LIDO groups (87.3 of 100 vs. 86.5 of 100; $P = 0.805$, Table 2).

4. Discussion

A one-year prospective analysis of 89 patients receiving pain relief medication for ETT-related sore throat at ICUs was performed. In this study, the intensity of ETT-related throat pain was moderate to extreme, which was effectively reduced

after ACT or LIDO treatment. Patients in the LIDO group made more requests for additional therapy and required longer duration for pain relief, compared to patients in the ACT group. No adverse physical effects were recorded in either group.

ETT is a life-sustaining device, but it is a common source of stress at ICUs and requires considerable carefulness [32–34]. The intensity of ETT-related throat pain in the study was moderate to extreme (6.9–8.5 out of 10 according to the Wong-Baker Faces Pain Rating Scale), which is comparable to the pain severity reported in previous studies [16, 35]. The intensity of pretreatment throat pain decreased over time. When the pain severity score decreased to 5–6 of 10, the patients discontinued their requests for additional treatment. The high pain tolerance of the patients in the current study toward ETT-related throat pain is consistent with the findings of a previous study [16]. Therefore, the severity of ETT-related throat pain should not be overlooked. Regular monitoring and aggressive care for ETT-related throat pain in critically ill patients is imperative.

ACT and LIDO behave differently according to pharmacometrics. LIDO is applied directly to sites where the ETT is located, whereas orally administered ACT takes time to absorb, distribute, metabolize, and start acting on regional lesions, which may contribute to the varying presentations of clinical pharmacokinetics between the two treatments in the current study. Local LIDO treatment had a faster onset of action in terms of pain relief compared with oral ACT. Additionally, the different pharmacodynamics between ACT and LIDO could affect the degree of pain relief for ETT-related sore throat in the current study. The mechanism of pain reduction in LIDO involves blocking regional electrical nerve impulses by inhibiting sodium channel influx [31]. By contrast, ACT exerts analgesic effects not only by preventing peripheral nociceptive signals to the spinal cord through stimulation of the descending serotonergic pathways [36] but also by elevating the pain threshold through the inhibition of central prostaglandin synthesis [37–39], which may extend its analgesic effects, thereby reducing the time required to mitigate ETT-related throat pain.

Despite several studies indicating that LIDO application effectively reduces ETT-related local pain [10, 17, 40], other

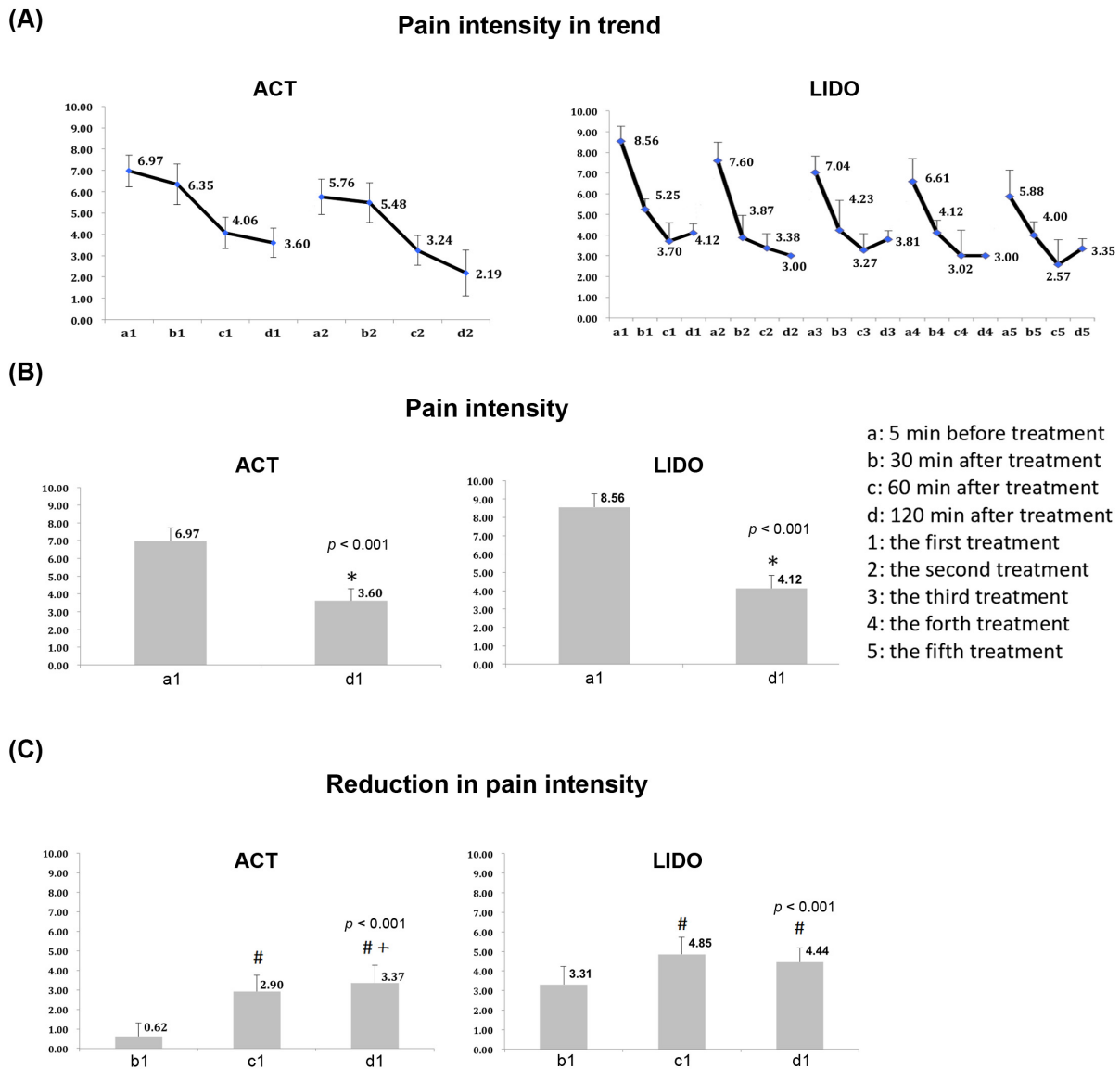


FIGURE 1. The effects of ACT medications and LIDO application on ETT-related sore throat. (left) The pain management effects of ACT medication on ETT-related sore throat. (A) Intensity of throat pain over time. (B) Intensity of throat pain before and after ACT treatment. $*P < 0.001$ vs. a1. (C) Pain intensity reduction after ACT treatment at different time points ($P < 0.001$). $\#P < 0.001$ vs. b1, $+P < 0.001$ vs. c1. (right) The pain management effects of LIDO application on ETT-related sore throat. (A) Intensity of throat pain over time. (B) Intensity of throat pain before and after LIDO treatment. $*P < 0.001$ vs. a1. (C) Pain intensity reduction after LIDO treatment at different time points ($P < 0.001$). $\#P < 0.001$ vs. b1. ACT: acetaminophen, LIDO: lidocaine, ETT; endotracheal tube, a1, b1, c1, d1: time points at 5 min before, and 30, 60, 120 min after the first treatment.

studies have demonstrated that local LIDO application prior to tracheal intubation increased the intensity of POST [29, 41]. Because local LIDO application reduces the incidence of persistent cough [10, 42, 43], LIDO can effectively block electrical impulses from peripheral nerves around the laryngopharynx and larynx. Therefore, complications resulting from ETT-related pain management through local LIDO application may be caused by LIDO-induced chemical irritation or other additives such as ethanol and methanol. Furthermore, the mucosal inflammation and injury caused by ETT intubation and extubation may augment a patient's perception of noxious stimuli. This condition (hyperalgesia) may increase tissue sen-

sitivity to local irritation [44]. Therefore, a careful assessment of localized pain immediately following LIDO application is crucial for treating ETT-related sore throat.

The current study had several limitations. First, we did not include a placebo arm to determine the placebo effect because several clinical considerations such as the safety of the placebo agent and spray costs have limited the manufacturer's capacity to produce placebo sprays. Additionally, participants in a placebo arm without standard pain management would receive a low standard of care, which would be ethically untenable. Therefore, we conducted this study and attempted to compare two validated, standard ICU practices to determine

TABLE 2. Comparison of the pain management effect on ETT-related sore throat between the ACT and LIDO groups

	Acetaminophen (n = 63; 70.8%)	Lidocaine (n = 26; 29.2%)	<i>P</i> -value*
Maximum degree of pain reduction, mean (SD)	3.4 (0.9)	5.3 (0.7)	< 0.001
Duration required to achieve maximum effect, n (%)			
30 min after treatment	1 (1.6)	4 (15.4)	NA
60 min after treatment	34 (54.0)	21 (80.8)	
120 min after treatment	28 (44.4)	1 (3.8)	
Degree of patient satisfaction with the pain management, mean (SD)	87.3 (12.6)	86.5 (14.5)	0.805

ACT, acetaminophen; ETT, endotracheal tube; LIDO, lidocaine; NA, not available; SD, standard deviations. **P*-value estimated by Student's *t*-test for continuous variables.

their effectiveness. Second, to compare the duration required for the pain relief between the two groups, we were compelled to enroll 63 patients in the ACT group because only 21 patients in the group requested a second ACT dose; otherwise, the number of patients would match the number of patients (26) in the LIDO group (Table 1). Because the pain intensity before and after the first ACT treatment was similar between the single-dose and two-tablet groups, all patients enrolled in the ACT group were analyzed for other outcomes to avoid data manipulation. Third, the pretreatment pain levels of patients in the LIDO group were higher than those of patients in the ACT group. The baseline differed, so caution should be exercised when interpreting the finding that LIDO conferred greater maximum pain reduction than ACT did (Table 2).

5. Conclusions

Both ACT and LIDO effectively attenuated ETT-related throat pain. Patients were highly satisfied with their pain management plan after both oral ACT and local LIDO application. Because ACT and LIDO exhibit different pharmacokinetics and pharmacodynamics, we expect that a combination of ACT medication and LIDO application could produce a synergetic effect in reducing ETT-related throat pain; this is worthy of further study.

AUTHOR CONTRIBUTIONS

Shih-Yi Lee and Hui-Chun Ku designed the study. Shih-Yi Lee, Hwee-Kheng Lim, and Che-Wei Wu collected the data. Shih-Yi Lee, Hwee-Kheng Lim, and Jerry Cheng-Yen Lai analyzed the data. Shih-Yi Lee and Che-Wei Wu analyzed the results and drafted the manuscript. Shih-Yi Lee and Hui-Chun Ku completed and proofread the article.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The current study was approved by the Institutional Review Board of MacKay Memorial Hospital, Taipei, Taiwan (protocol MMH-I-S-567).

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this article. Shih-Yi Lee is member of the Editorial Board of this journal.

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