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L.I. Ho
H.J. Harn
T.C. Lien
P.Y. Hu
J.H. Wang

Postextubation laryngeal edema in adults Risk factor evaluation and prevention by hydrocortisone

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L.I. Ho (✉) · T.C. Lien · P.Y. Hu
J.H. Wang
Department of Respiratory Therapy,
Veterans General Hospital-Taipei
201, Sec 2, Shih-Pai Road,
Taipei, Taiwan. R.O.C. 11217
FAX: +886(2)8757455
Tel.: +886(2)8757456

H.J. Harn
Department of Pathology,
National Defense Medical Center
and Tri-service General Hospital-Taipei,
Taiwan, R.O.C.

Abstract *Objective:* To evaluate the risk factors for postextubation laryngeal stridor and its prevention by hydrocortisone in adult patients.
Design: Prospective, randomized, double-blind, placebo controlled study.
Setting: Medical and surgical ICU of a tertiary teaching hospital.
Patients: 77 consecutive patients of both sexes, who had undergone tracheal intubation for more than 24 h and fulfilled the weaning criteria, were eligible for the study. Patients were excluded if they were less than 15 years of age, had a disease or the surgery of the throat, or had been extubated during the current hospitalization.
Intervention: The control group received placebo (normal saline 3 cc) and the experimental group received hydrocortisone 100 mg by intravenous infusion 60 min before extubation.
Main outcome measures: Patients were observed 24 h after extubation for symptoms or signs of laryngeal edema or stridor: prolonged inspiration with accessory usage of respiratory muscles or crowing sound with inspiration or reintubation.
Results: The overall incidence of postextubation stridor was 22% (17/77). Only one patient (1%), who belonged to the control group, needed reintubation. 39% of female patients and 17% of male patients developed stridor. The relative risk of females developing this complication was 2.29. 7/39 of the hydrocortisone group and 10/38 of patients in the control group developed postextubation stridor.
Conclusions: Hydrocortisone did not significantly reduce the incidence of postextubation laryngeal edema or stridor. From the risk factors evaluated, we were unable to demonstrate a statistical correlation between postextubation stidor and the duration of the intubation, the patient's age, the internal diameter of the endotracheal tube, or the route of intubation. However, female patients were more likely to develop this complication.

Key words Endotracheal tube · Complications · Postextubation · Stridor · Laryngeal edema · Corticosteroids

Introduction

Endotracheal intubation for respiratory support of critically ill patients has become a standard life-saving form of therapy. It can be done safely and appears to be well tolerated for up to several days. However, it can cause many complications [1–3], both during intubation and after extubation, that result from injury to the hypopharynx, larynx, and trachea and are related to both the tube and the cuff. Evidence of injury, including mucosal

ulceration, mucosal inflammation and edema, is frequently found when assessed pathologically [3–5]. Edema of the laryngeal structure in the postextubation period is one of the most severe complications, because it can cause significant morbidity and even death [6, 7].

The purpose of this study was to determine the possible risk faktors and the prophylactic effect of steroids on the occurrence of postextubation stridor.

Materials and methods

All patients admitted to our medical and surgical intensive care units (ICUs) from 1 March through 31 August 1990, who had been intubated and had a planned elective extubation, were eligible for entry into this study.

Patients wer excluded if they were less than 15 years of age, had been extubated during the current hospital stay, or had throat disease or had throat surgery. Each patients was intubated by an ICU resident via the orotracheal or nasotracheal route with a low-pressure, high-volume cuff tube; prolonged or traumatic intubation was excluded. As part of routine airway management, the endotracheal tube cuffs were checked at least in every shift (8 h) by respiratory therapists, and the cuff pressure was kept at 25–30 cm H_2O.

For each patient, possible risk factors including age, sex, admission diagnosis, internal diameter (i.d.) of the endotracheal tube, and route and duration of intubation were recorded before extubation. Patients were then allocated randomly to receive either an intravenous infusion of 100 mg hydrocortisone sodium succinate (Mead Johnson) or a placebo (normal saline) 1 h before extubation. Randomization was balanced in both groups in blocks of four patients, according to a random table. This scheme was designed so that the number of patients in each group receiving hydrocortisone or placebo would be approximately the same. Placebo and hydrocortisone were packaged in identical volume and appearance by the hospital pharmacy to ensure that they were administered in a double-blind fashion. The protocol was approved by the Institutional Review Board on Human Research at our hospital and written informed consent was obtained from the patients or their relatives prior to entry into the study.

All patients were examined immediately after extubation and monitored in the ICU every 6 h for 24 h by one of the authors for signs and symptoms of respiratory distress and the occurrence of stridor. To overcome the inherent variability resulting from the use of clinical criteria as endpoints, the investigators reached a preliminary consensus regarding the threshold for diagnosis. Laryngeal edema was defined as clinical signs of upper airway obstruction [8, 9], i.e., prolonged inspiratory phase associated with the recruitment of accessory respiratory muscles (subcostal, suprasternal, or intercostal muscle retraction, or all three); stridor was defined as a crowing sound on inspiration. Patients who developed stridor and/or dyspnea were treated with epinephrine 2.25% solution, 0.05 ml/kg in 2.5 ml of a hypotonic solution delivered as an aerosol.

Data were analyzed by the chi-square test for qualitative results. Analysis of variance was used for quantitative data. Values were given as mean ± SD or median and range; $p < 0.05$ was considered statistically significant.

Results

The characteristics of the 77 patients studied are given in Table 1. The control and hydrocortisone groups were almost identical with respect to sample size and the distribution of risk factors of postextubation stridor, except that the control group had more orally intubated patients.

Seventeen patients developed postextubation stridor; the overall incidence was 22%. Their age, the median i.d. of the endotracheal tube, and the route and duration of intubation are listed in Table 2. Postextubation stridor developed in 7 of 39 patients given hydrocortisone and in 10 of 38 control patients given placebo. Most of our patients

Table 1 Characteristics of patients in treated and control groups

	Hydrocortisone ($n = 39$)	Control placebo ($n = 38$)
Mean age (years) ± SD	61 ± 14	64 ± 18
Gender (n)		
Male	29	30
Female	10	8
Duration of intubation (h) ± SD	146.5 ± 92.3	110.1 ± 112.1
Admission diagnosis (n)		
Respiratory failure	11	8
Sepsis	2	1
Acute pulmonary edema	3	6
Chest trauma	2	3
Drug overdose	1	5
Postoperative	9	6
Neurologic disease	3	2
Post cardiopulmonary resuscitation	4	3
Miscellaneous	4	4
Route of intubation (n)		
Oral	3	14
Nasal	36	24
Median (range) internal diameter of endotracheal tube	7.5 (7.0–8.0)	7.5 (6.5–8.0)

Table 2 Postextubation laryngeal edema risk factor analysis

	All patients ($n = 77$)	Laryngeal edema ($n = 17$)	p*
Mean age (years) ± SD	62 ± 16	64 ± 16	NS
Median (range) internal diameter of endotracheal tube	7.5 (6.5–8.0)	7.5 (6.5–8.0)	NS
Mean duration of intubation ± SD	139.4 ± 11.4	91.5 ± 58.85	NS
Route of intubation			
Oral	17	5	NS
Nasal	60	12	
Gender			
Female	18	7	< 0.05
Hydrocotrisone	39	7	NS
Placebo	38	10	

* Student's two-sample t-test for continuous variables; chi-square test for categorical variables

were intubated nasally (60 vs 17); 5/17 (29%) orally intubated patients and 12/60 (20%) nasally intubated patients developed laryngeal edema.

Gender was identified as a risk factor of postextubation stridor: 7/18 (39%) female and 10/59 (17%) male patients developed stridor. The relative risk of stridor in female patients was 2.29 ($p < 0.05$) (Table 2). Reintubation due to severe stridor was needed in one female patient from the control group.

Discussion

Postextubation laryngeal edema or stridor is thought to be the result of trauma to the laryngeal mucosa with resultant mucosa edema and swelling. Damage to the mucosa is a frequent finding due to endotracheal intubation, especially when examined with a bronchofibrescope. Stauffer et al., in a prospective study of intubated and tracheostomy patients, found that 21 of 39 (54%) intubated patients had ulcers on the posterior vocal cord and 49 of 52 (93%) patients had mucosal inflammation and/or edema at autopsy [1]. Since steroids can inhibit the early stage of the inflammatory process [10], they have been used to prevent and treat postextubation laryngeal edema. Biller et al. have demonstrated in monkeys that dexamethasone (4 mg/kg) suppresses of postintubation laryngeal edema and hastens its development once it has formed [11]. Woods et al. have reported that the administration of high-dose dexamethasone (4 mg/kg) and oxymetazoline is effective in the treatment of subglottic edema secondary to mucosal trauma in the ferret model [12]. However, in Way and Sooy's study, intramuscular injection of 4 mg dexamethasone at the time of extubation had no effect on edema formation [13]. A double-blind study mostly of adults, conducted by Goddard et al. failed to show benefit with the use of betamethasone to prevent postextubation inflammation [14]. Since the results of these studies were controversial and it is our routine practice to use hydrocortisone before extubation, we conducted this prospective, randomized, double-blind study to evaluate the risk factors and the prophylactic effect of hydrocortisone on the occurrence of postextubation stridor.

The major finding of our study was that 100 mg i.v. hydrocortisone 60 min before extubation did not affect the occurrence of postextubation stridor. Among the risk factors analyzed, only female gender was significant in influencing the occurrence of stridor. Recently, in a placebo controlled, double-blind, multicenter study [15], Darmon et al. reported that the risk factors for postextubation laryngeal edema include an intubation duration of more than 36 h and female gender. In addition, dexamethasone does not prevent postextubation laryngeal edema. Our result were consisted with theirs, except for the duration of intubation. The importance of the duration of intubation in producing laryngeal injury remains debatable [16, 17]. Bishop et al., using a dog model, found that laryngeal injury reaches maximum severity between days 1 and 7, with no clear correlation with the duration of intubation beyond that point [18]. Stauffer et al. reported no significant relationship between the duration of endotracheal intubation or tracheotomy and overall laryngotracheal injury at autopsy [1]. Moreover, prolonged intubation in humans may correlate with many factors, such as infection, poor nutrition, episodes of hypotension etc., all of which could contribute to more severe laryngotracheal injury than intubation alone. We were unable to demonstrate a statistical correlation between postextubation stridor and the duration of intubation. Other factors, such as route of intubation [4, 5, 8] or tube size [8, 9, 13], have all been reported to be associated with an increased risk of tracheolaryngeal after intubation, although some of the results were conflicting. In our study, no relationship could be found between the i.d. of the endotracheal tube, the route of intubation, the patient's age, and the occurrence of postextubation stridor.

Although trauma to the larynx and trachea is a frequent finding after intubation, the precise incidence of postextubation laryngeal edema or stridor in adults is still unknown. It has been reported to occur in 2 to 15.4% of intubated patients [4, 14–16]. Such variation can be ascribed to differences in the population studied or the criteria used for the diagnosis of laryngeal edema. Our study presented a higher incidence than was reported elsewhere. We used clinical observations as diagnostic criteria as others have [8, 9, 15], instead of bronchofiberscopic examination because it is invasive and may be dangerous for some patients. However, the incidence of reintubation for laryngeal edema was 1%, similar to that in other reports [14, 15, 19].

Female gender is the risk factor found in our study. Tonkin and others have also reported a higher incidence of this complication in female patients [17, 20–22], probably because the larynx is smaller in females [15, 16]. Also, the mucosal membrane in male patients tends to be more resistant to trauma [15, 21]; the mucosa covering the cartilage of the vocal process is significantly thinner in the female [23]. Further study is needed to evaluate the effect of different ratios of the outer diameter of the endotracheal tube to that of the vocal cord and larynx to confirm this hypothesis.

It can be argued that a different regimen could have been effective. However, our regimen was based on the reports of some experimental studies: the interval between dexamethasone injection and a measurable decrease in laryngeal edema varied from 15 to 60 min [11, 22]. Darmon et al. reported that 8 mg i.v. dexamethasone given 1 h before extubation did not prevent this complication in adults [15]. Tellez et al. found that i.v. dexamethasone (0.5 mg/kg) given 6 h before extubation and continued

every 6 h befor a total of six doses was ineffective in preventing postextubation stridor [24]. The regimen might, however, be irrelevant.

In conclusion, the prophylactic use of corticosteroids for the prevention of postextubation stridor in routine cases of intubation in the ICU is unwarranted. However, its effectiveness in specific identifiable patients at risk (such as females) needs further investigation. Though the fiberscopic examination is the "gold standard" in the diagnosis of laryngeal edema, it has potential hazards and it is not as feasible in clinical practice. A set of diagnostic criteria based on clinical observation should be established so that we can diagnose postextubation stridor in cases when no fiberscopic examination is available. Postextubation stridor remains unpredictable, thus, more studies are needed to identify the actual risk factors.

References

1. Stauffer JL, Olson DE, Petty TL (1986) Complications and consequences of endotracheal intubation and tracheotomy. Am J Med 70:65–76
2. Bishop MJ, Weymuller EA, Fink BR (1984) Laryngeal effects of prolonged intubation. Anesth Analg 63:335–342
3. Kastanos N, Miro RE, Perez AM, Mir AX, Augusti-vidal A (1983) Laryngotracheal injury due to endotracheal intubation: incidence, evolution, and predisposing factors. A prospective long-term study. Crit Care Med 11:362–367
4. Burns HP, Dayal VS, Scott A, Peter Van Nostrand AW, Bryce DP (1979) Laryngotracheal trauma: observations on its pathogenesis and its prevention following prolonged orotracheal intubation in the adult. Laryngoscope 89:1316–1324
5. Donnelly WH (1969) Histopathology of endotracheal intubation. Arch Pathol Lab Med 88:511–520
6. Mackenzie CF, Shin B, McAslan TD, Blanchard CL, Cowley RA (1979) Severe stridor after prolonged endotracheal intubation using high-volume cuffs. Anesthesiology 50:235–239
7. Jordan WS, Grave CL, Elwyn RA (1970) New therapy for postintubation laryngeal edema and tracheitis in children. JAMA 212:585–588
8. Koka BV, Jeon JS, Andre JM, MacKay I, Smith RM (1977) Postintubation croup in children. Anesth Analg 56:501–505
9. Deming MV, Oech SR (1961) Steroid and antihistaminic therapy for postintubation subglottic edema. Anesthesiology 22:933–936
10. Haynes GR Jr, Murad F (1985) Andrenocorticotropic hormone: adrenocorticosteroids and their synthetic analogs: inhibitors of adrenocortical steroids biosynthesis. In: Gilman AG, Goodman LS, Rall TW, Murad F (eds) The pharmacological basis of therapeutics. McMillan, New York, pp 1459–1489
11. Biller HF, Bone RC, Harvey JE, Ogura JH (1970) Laryngeal edema: an experimental study. Ann Otol Rhinol 174:1084–1087
12. Woods CI, Postma DS, Prazma J, Sidman J (1987) Effects of dexamethasone and oxymetazoline on "postintubation croup": a ferret model. Otolaryngol Head Neck Surg 96:554–558
13. Way WL, Sooy FA (1965) Histologic changes produced by endotracheal intubation. Ann Otol 744:799–813
14. Goddard JE, Phillipa OC, Marcy JH (1967) Betamethasone for prophylaxis of postintubation inflammation. Anesth Analg 46:348–353
15. Darmon JY, Rauss A, Dreyfuss D, Bleichner G, Elkharrat D, Schlemmer B, Tenaillon A, Brun-Buisson C, Huet Yann (1992) Evaluation of risk factors for laryngeal edema after tracheal extubation in adults and its prevention by dexamethasone. Anesthesiology 77: 245–251
16. Whited RE (1984) A prospective study of laryngeal sequelae in long-term intubation. Laryngoscope 94:367–377
17. Gaynor EV, Greenberg SB (1985) Untoward sequellae of prolonged intubation. Laryngoscope 95:1461–1467
18. Bishop MJ, Hibbard AJ, Fink BR, Vogel AM, Weymuller EA (1985) Laryngeal injury in a dog model of prolonged endotracheal intubation. Anesthesiology 62:770–773
19. Dixon TC, Sando MJW, Botton JM (1968) A report of 342 cases of prolonged endotracheal intubation. Med J Aust 2:529–533
20. Hedden M, Ersoz CJ, Donelly WH (1969) Laryngotracheal damage after prolonged use of orotracheal tubes in adults. JAMA 207:703–708
21. Harrison GA, Tonkin JP (1968) Prolonged (therapeutic) endotracheal intubation. Br J Anaesth 40:241–248
22. Hawkins DB, Crockett DM, Shum TK (1983) Corticosteroids in airway management. Otolaryngol Head Neck Surg 91:593–596
23. Balestrieri F, Watson CB (1982) Intubation granuloma. Otolaryngol Clin North Am 15:567–579
24. Tellez DW, Galvis AG, Storgion SA, Amer HN, Hoseyni M, Deakers TW (1991) Dexamethasone in the prevention of postextubation stridor in children. J Pediatr 118:289–294