

## Primary research

# Do steroids prevent reintubation in children with laryngotracheobronchitis?

Jaishen Rajah, Jacinto Riera-Fanego, Janine Keeton, Aniel Ramjee,  
Rajanee Bhana, Lance Lasersohn and Hubert Hon

University of the Witwatersrand, Johannesburg, South Africa

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## Abstract

**Background:** Classic laryngotracheobronchitis (LTB) is an inflammatory process, with oedema and secretions that involve the entire laryngotracheobronchial tree. The severity of lower airway disease in African children with LTB has previously been documented. The aim of the present study was to determine whether steroids prevent reintubation in African children with classic LTB.

**Method and results:** The study was a retrospective analysis from January 1993 to December 1996. Eighty-two black children with LTB were mechanically ventilated in the intensive care unit (ICU). By univariate regression, the estimated B coefficients for variables such as age, pneumonia, days of intubation, arterial partial oxygen tension ( $\text{PaO}_2$ ) : fractional inspired oxygen ( $\text{FiO}_2$ ) ratio, atelectasis and antibiotic use were not statistically significant ( $P > 0.05$ ) as predictors for reintubation. Using multiple regression (all independent variables in combination), none of the variables acted as predictors of reintubation ( $P = 0.25$ ). Steroids were shown to have no effect alone or in association with other variables in altering reintubation rates. An increase in the days of intubation showed a tendency towards reintubation ( $P = 0.06$ ) in the univariate analysis (odds ratio 1.00–1.14), but showed no statistically significant difference in multivariate analysis. Of the variables used as predictors of reintubation, none acted either as a preventive factor or as a risk factor.

**Conclusion:** The present results suggest that steroids should not be recommended at any stage in treatment of intubated patients with classic LTB. Prospective studies should evaluate the major risk factors for reintubation: duration of intubation, trauma to the airway at intubation and during ICU stay, and dose and timing of steroids. They should also evaluate whether upper airway disease is present alone or in association with lower airway disease.

**Keywords:** croup, laryngotracheobronchitis, reintubation, risk factors, steroids

## Introduction

Classic LTB is an inflammatory process, with oedema and secretions that involve the entire laryngotracheobronchial tree. The severity of lower airway disease in African chil-

dren with LTB has previously been documented [1]. In 1979, Cherry [2] stated that steroid therapy could not be expected to offer benefit in classic LTB, and would probably be detrimental. Intubated patients with laryngotracheitis

have high risk of reintubation [3]. Also, the most clinically important end-point for intubated LTB patients is reintubation. The higher rate of airway complications that occur after extubation in children may be accounted for by their smaller airway diameter.

The usefulness of steroids in upper airway obstruction is debated. The major subgroups of individuals with upper airway obstruction in the intensive care setting to which the controversy of steroid use (ie do steroids prevent intubation or postextubation stridor?) pertains to are as follows: those with a normal airway on admission who may develop postextubation stridor; those with an airway at risk for airway oedema (multiple intubations, traumatic intubation, duration of endotracheal intubation >14 days); children intubated with laryngotracheitis (ie only upper airway abnormalities); children with laryngotracheitis who are not intubated; and those with LTB who are intubated [1,3, 4–18]. The question of steroid effectiveness has largely been addressed in the first four subsets [1,3,4–18]. No study has as yet documented the effectiveness of steroids in African children with classic LTB.

Steroids nonspecifically inhibit the inflammatory effects of many potentially harmful stimuli, including trauma [6,19]. They exert their benefit on the airway by decreasing airway swelling [6,19]. Our primary aim was to determine whether steroids, by reducing subglottic swelling, can reduce the reintubation rate in children with classic LTB. The impacts of other treatments (antibiotics), demographic features (age, duration of intubation) and pathophysiological features ( $\text{PaO}_2:\text{FiO}_2$  ratio, pneumonia, atelectasis) were also analyzed.

## **Patients and methods**

This is a retrospective study of patients with LTB who were intubated and ventilated in the ICU of our institution during the period January 1993 to December 1996. Over this 4-year period, 82 black children (58 males and 24 females) with a median age of 12.5 months (range 1–96 months) and median weight of 8.6 kg (range 3.7–25 kg) were treated. Of the 82 patients who were intubated, 85% were intubated in the operating room by a senior anaesthetist following a controlled gas induction. Patients with epiglottitis, spasmodic croup and a previous history of upper airway problems were excluded from the present study.

The upper airway component (laryngotracheitis) of the disease (LTB) was based on the following clinical and chest radiographic criteria: barking cough, coryza, fever, inspiratory stridor and the 'steeple sign' of the trachea in children who had a preintubation chest radiograph (which indicates upper airway narrowing). The following grading system for inspiratory stridor was used: grade 1, inspiratory stridor only; grade 2, as grade 1 plus expiratory stridor;

grade 3, as grade 2 plus pulsus paradoxus; and grade 4, as grade 3 plus cyanosis/mental obtundation [20]. All patients admitted into the ICU had either grade 3 or grade 4 stridor. The lower airway (bronchitic) component of the disease (LTB) was based on any of the following criteria either alone or in combination on admission to the ICU:  $\text{PaO}_2:\text{FiO}_2$  ratio; the need for positive-pressure mechanical ventilation; the presence of bronchopneumonia on chest radiography; atelectasis; and use of antibiotics.

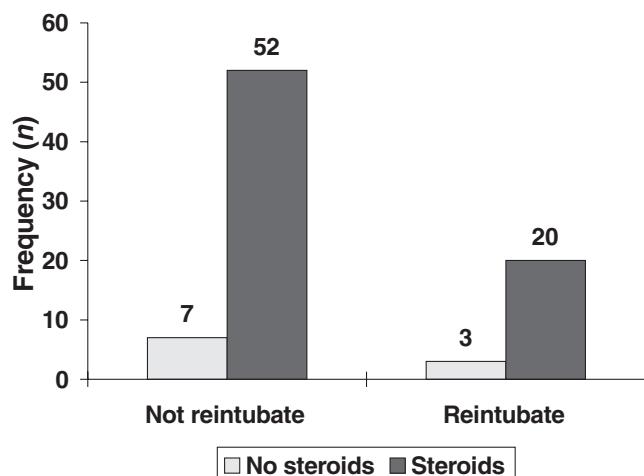
Bronchopneumonia was defined as an infiltrate in any one or more of the four quadrants on the chest radiograph. Specimens from the trachea were not routinely examined or cultured to detect viral or bacterial isolates.

Steroids given were dexamethasone in 44 patients (0.4 mg/kg every 12 h for four doses), hydrocortisone in 17 patients (2.1 mg/kg, every 6 h for 28 doses on average) and prednisolone (1 mg/kg daily for an average of 5 days) in nine patients. The timing of steroids was either from admission, from just before extubation, or both at admission and before extubation. Extubation criteria were not documented, even though it is unit policy to wait for an air leak of about 15–20% of the tidal volume (Siemens 900C ventilator; Siemens, Solna, Stockholm, Sweden) in patients with upper airway swelling in particular, as well as to adhere to traditional weaning criteria in general [21].

Antibiotics were started at admission to the ICU either empirically (for bronchopneumonia) or during ICU stay for proven or suspected infection, on the basis of chest radiography, blood cultures and blood counts. Atelectasis was diagnosed on the chest radiograph on the basis of tracheal deviation, shift of the lung fissures and infiltrates. The number of days of intubation was counted from the time of initial intubation to the time of extubation. The  $\text{PaO}_2:\text{FiO}_2$  ratio was used to document severity of shunt on admission (severity of lower airway disease). A grading system was used as follows: grade 4,  $\text{PaO}_2:\text{FiO}_2 < 100$ ; grade 3,  $\text{PaO}_2:\text{FiO}_2 < 200$ ; grade 2,  $\text{PaO}_2:\text{FiO}_2 < 300$ ; grade 1,  $\text{PaO}_2:\text{FiO}_2 > 300$ .

## **Statistical analysis**

Database management and statistical analysis were performed with SAS software, version 6.12 (SAS Institute Inc, Cary, NC, USA). The age, weight and intubation days (all non-normal distribution) as well as the  $\text{PaO}_2:\text{FiO}_2$  ratios (ordinal data) are expressed as median (range). Univariate and multivariate logistic analysis were tested for reintubation with the following predictive variables: age, steroids, pneumonia, intubation days,  $\text{PaO}_2:\text{FiO}_2$  ratio, atelectasis and antibiotics. The results were expressed as estimated coefficients,  $P$  value and odds ratio (95% confidence intervals) for each variable.  $P < 0.05$  was considered statistically significant.

**Figure 1**

Frequency distribution of steroid intake.

## Results

The frequency distribution of steroid intake is given in Fig. 1. Overall, 52 out of the 59 patients who were not reintubated were given steroids, whereas 20 out of 23 patients who were reintubated were given steroids. Out of the 23 reintubated patients, nine had bronchopneumonia diagnosed on admission (first day in the ICU), 16 were administered antibiotics during the ICU stay, and nine developed atelectasis during the ICU stay. In the same group, the median age was 11 months (range 2–36 months), the median  $\text{PaO}_2:\text{FiO}_2$  ratio on admission was grade 3 (range grades 1–3) and the median number of days intubated was 9 (range 1–38).

The overall mortality of the group as a whole was approximately 3.66% (three out of 82 patients). All of these patients died after extubation. The cause of death in two of these patients was septic shock, with underlying malnutrition. Both of these patients were recovering from measles acquired in the preceding 2 weeks. One of these patients was given steroids. The third patient had a cardiorespiratory arrest, which was sudden and unexpected. No immediate cause was identified. This patient did not receive any steroids.

An increase in the days of intubation showed a tendency toward reintubation ( $P=0.06$ ) in univariate analysis (odds ratio 1.00–1.14), but showed no statistically significant difference in multivariate analysis. Estimated B coefficients for variable such as age (Table 1) were not statistically significant ( $P>0.05$ ) in univariate regression. Using multiple regression, none of the independent variables acted as predictors for reintubation ( $P=0.25$ ; (Table 2).

**Table 1**

**Estimated coefficients, odds ratios and 95% confidence intervals for predictors of reintubation in univariate logistic regression**

Variable	Estimated coefficient	P	OR	95% CI
Age	-0.03	0.14	0.97	0.93–1.01
Steroids	-0.11	0.88	0.90	0.21–3.82
Pneumonia	-0.41	0.42	0.67	0.25–1.77
Intubationdays	0.06	0.06	1.07	1.00–1.14
$\text{PaO}_2:\text{FiO}_2$ ratio	0.12	0.41	1.12	0.85–1.48
Atelectasis	0.96	0.09	2.61	0.87–7.81
Antibiotics	0.93	0.08	2.53	0.91–7.05

CI, confidence interval; OR, odds ratio.

**Table 2**

**Estimated coefficients, odds ratios and 95% confidence intervals for predictors of reintubation in multivariate logistic regression**

Variable	Estimated coefficient	P	OR	95% CI
Intercept	-1.43	0.52		
Age	-0.03	0.27	0.98	0.93–1.02
Steroids	-0.39	0.64	0.68	0.13–3.42
Pneumonia	-0.39	0.50	0.68	0.22–2.10
Intubation days	0.04	0.36	1.04	0.96–1.12
$\text{PaO}_2:\text{FiO}_2$ ratio	0.16	0.28	1.17	0.88–1.57
Atelectasis	0.36	0.59	1.43	0.61–5.87
Antibiotics	0.63	0.28	1.88	0.61–5.86

$-2 \log L = 9.06$ , with seven degrees of freedom ( $P=0.25$ ). CI, confidence interval; OR, odds ratio.

Steroids showed no tendency toward a significant association with reintubation on either the univariate or multivariate analysis ( $P=0.88$  and 0.64, respectively). The negative B coefficient for steroids suggested that the greater the steroid use, the more likely it was that reintubation would be required. This trend is not surprising in the malnourished, septic child who embarks on a course of steroids, and whose disease process is potentially aggravated.

The positive B coefficients of atelectasis, antibiotic use, intubation days and  $\text{PaO}_2:\text{FiO}_2$  ratio, which together indicate infection and lower airway disease, suggest a greater likelihood of reintubation in the presence of these factors, although none of these associations was statistically significant. This tendency is to be expected in sick, intubated children.

## Discussion

No studies have documented a benefit for steroids in preventing reintubation in classic LTB. The present study indicates that steroids are ineffective in preventing reintubation in children with LTB. The doses of steroids employed in most studies involving patients with upper airway obstruction are contentious. The ideal dose is possibly 0.6 mg/kg [11]. However numerous studies [10–12] have documented that lesser doses of 0.2–0.3 mg/kg have been successful in decreasing upper airway inflammation. Tibballs *et al* [18] stated that the dose of prednisolone used in their study, although less than the suggested ideal, was nevertheless effective. The mean dose of dexamethasone in the present study of 0.4 mg/kg was therefore acceptable. However, the lack of standardization of steroids with respect to timing of onset of use, the dose used and the types used are major limitations to this study.

Steroids were shown to have no effect alone or in association with other variables in preventing reintubation. Of the variables used as predictors of reintubation, none acted either as a preventive or as a risk factor.

The natural history of classic LTB is different from that of laryngotracheitis. Apart from significant lower airway disease, a major factor is that patients with LTB have endotracheal tubes in place for a longer period, and are therefore at risk of ongoing upper airway inflammation and nosocomial infection. The fact that steroids did not alter the frequency of reintubation in classic LTB does not proscribe against their use in patients with laryngotracheitis as the primary diagnosis on admission to hospital.

Other variables, including patient age, pneumonia, days intubated, atelectasis, antibiotic use and  $\text{PaO}_2 : \text{FiO}_2$  ratio, were shown to have no effect on the incidence of reintubation. In the present group of patients, it is probable that these factors in combination rendered steroid use non-beneficial, by acting as cocontributors to lower airway pathology. Steroids would not be expected to be of benefit in such a group.

A major concern with steroid use in African children, who are possibly malnourished and who may present with bacterial tracheitis and bronchopneumonia, is their propensity toward sepsis and nosocomial infection. Failure to recognize the particular historical, ecological, aetiological and clinical perspectives in such patients could potentially worsen their morbidity and mortality. Tunnessen and Feinstein [4] designed a prospective study model in laryngotracheitis and steroid usage, and outlined all areas of controversy.

The major limitations of the present study are that the timing of onset of steroid use varied, the dose of steroids was not standardized, different types of steroids were

used, and the duration of steroid use differed. Prospective studies should evaluate carefully the major risk factors for reintubation, including the following: duration of intubation; trauma at time of intubation and during ICU stay; dose of steroids; and timing of steroids. They should also evaluate what particular subset of patients is involved with respect to upper airway involvement. The use of the term croup should be avoided as it is often used interchangeably to describe distinctly different clinical entities. The side effects of acute steroid therapy should also be documented. Every effort should be taken to prevent nosocomial infection and maintain proper airway care (humidification and proper sedation to minimize airway trauma), because these factors may act as confounding variables for reintubation. In addition, the degree of airway leakage should be standardized, because this may further act as a confounding variable for reintubation. Tracheal aspirates at the time of intubation should be routinely examined because bacterial isolates may predict the lack of response to steroids or the need for earlier antibiotic therapy.

The results of the present retrospective study suggest that steroids may not be beneficial in the treatment of African patients who are intubated for classic LTB. A prospective randomized controlled trial needs to be undertaken in this particular population group to support these findings.

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**Authors' affiliation:** Intensive Care Unit, Chris Hani Baragwanath Hospital, University of the Witwatersrand, Johannesburg, South Africa

**Correspondence:** Dr J Rajah, Intensive Care Unit, Chris Hani Baragwanath Hospital, PO Bertsham 2013, Johannesburg, South Africa. Tel/fax: +27 11 938 1595; e-mail: 092raj@chiron.wits.ac.za