

# Retrospective Evaluation of Return Rates in Pediatric Patients Treated With Inhaled Racemic Epinephrine for Croup

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## ABSTRACT

**Background:** Croup (viral laryngotracheitis) is a respiratory illness that often affects infants and young children.

**Objectives:** To determine if the length of observation (<2 hours vs ≥2 hours) following treatment of croup with inhaled racemic epinephrine in the emergency department (ED) is associated with return rates (within 48 hours after treatment) in pediatric patients.

**Methods:** We conducted a retrospective review of patients' medical records from February 2010 through June 2018 for pediatric patients (male and female, ≤12 years of age) diagnosed with croup in the ED, treated with racemic epinephrine, and discharged from the ED.

**Results:** We evaluated patients observed for less than 1 hour, 1 to 2 hours, and greater than 2 hours to determine difference in return rates within 48 hours. For patients with mild croup symptoms, 2% observed for less than 1 hour returned; 5% observed for 1 to 2 hours returned, and 3% observed for greater than 2 hours returned. Of the patients with moderate croup symptoms, 29% observed for less than 1 hour returned, 20% observed for 1 to 2 hours returned, and 20% observed for greater than 2 hours returned. A majority who returned for follow-up were not retreated with racemic epinephrine.

**Conclusion:** Based on our study results, we can conclude that observing patients following treatment of croup with inhaled racemic epinephrine in the ED for less than 2 hours did not increase their risk of deterioration or need to return. Our data did not show that a longer observation time resulted in lower return rates within 48 hours.

## INTRODUCTION

Croup (viral laryngotracheitis) is a respiratory illness that often affects infants and young children. It is characterized by inspiratory stridor, barking cough, and hoarseness. These symptoms occur due to inflammation in the larynx and subglottic airway.<sup>1</sup>

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In addition to inspiratory stridor, cough, and hoarseness, other common symptoms include those seen in any respiratory viral illness, such as nasal congestion and fever. Croup occurs most frequently between the ages of 6 months and 3 years, with most cases occurring during the second year of life.<sup>2</sup> Parainfluenza virus type 1 is the most common cause of acute laryngotracheitis.<sup>3</sup> Other less common causes of croup are respiratory syncytial virus, influenza, rhinovirus, and other respiratory viruses. Most cases of croup occur in the fall and early winter.

Although viruses cause most cases of croup, bacterial causes exist, and secondary bacterial infection also may occur.<sup>4</sup> Infection with croup is self-limiting in a majority of cases, and respiratory failure is uncommon, with fewer than 2% of cases requiring hospitalization.<sup>2</sup> In rare cases, significant respiratory distress and pulmonary complications may occur. Treatment

for croup usually includes a single dose of steroid and the addition of racemic epinephrine in selected cases. Corticosteroids—specifically dexamethasone—are recommended.<sup>1</sup> Corticosteroids are particularly important, as they can shorten the duration of croup-related symptoms.<sup>2</sup>

Several randomized controlled trials and meta-analyses have demonstrated the benefit of racemic epinephrine in reducing croup symptoms in children treated in the emergency department (ED). Racemic epinephrine has been shown to improve inspiratory stridor, retractions, and air entry when used in croup treatment.<sup>5</sup> However, there is no consistent evidence published to guide physicians on how long to observe patients in the ED before dis-

charge after receiving racemic epinephrine for those patients who require it. Traditionally, physicians are taught to observe patients for at least 2 hours after treating with inhaled racemic epinephrine for croup before discharge. This practice might have been derived because the effects of racemic epinephrine last 90 to 120 minutes and usually dissipate after 2 hours; therefore, observing patients for 2 hours or more would allow physicians to identify patients who might have a return of stridor and retractions. Despite this consensus, little is known about the optimal observation time.

In this study, looking specifically at patients who were treated with racemic epinephrine, we set out to determine whether the length of observation (<2 hours vs ≥2 hours) following treatment of croup with inhaled racemic epinephrine in the ED is associated with return rates within 48 hours after treatment in pediatric patients. The results of this study may help inform future guidelines for observation time following inhaled racemic epinephrine treatment for croup.

## METHODS

This study is an 8-year retrospective analysis of patients diagnosed with croup who received treatment with racemic epinephrine at 3 regional EDs in central Wisconsin. The EDs were Marshfield Medical Center-Marshfield, Marshfield Medical Center-Eau Claire, and Marshfield Medical Center-Rice Lake; all are similar in practice. This study focused only on patients who received racemic epinephrine. The use of racemic epinephrine was not standardized and was determined by the treating clinician. It was our intent not to determine who should get racemic epinephrine; however, if a clinician gave it, we looked at whether it was safe to discharge prior to 2 hours.

Electronic medical records for pediatric patients (male and female, ≤12 years of age) who were diagnosed with croup (International Classification of Diseases, Ninth Revision [ICD-9] code 464.4) in the ED and discharged from the ED from February 2010 through June 2018 were reviewed for analysis. Records for patients who were diagnosed at the same time with asthma, bronchiolitis, and/or pneumonia were excluded from the analysis. The principal investigator and study assistant manually cross referenced the corresponding admission/discharge records for date and time of admission to the ED for croup to link clinical data with ED event information.

Information abstracted included observational data from clinician notes to calculate croup severity score, croup treatment (ie, whether steroid was administered and, if so, steroid type), time of inhaled racemic epinephrine treatment, observation time, date and time of discharge from the ED, and returns for croup within 48 hours after treatment. Our study focused on a 48-hour return rate, because historically that was the recommended time frame. It does seem that if patients are going to return with persistent croup symptoms, they are more likely to return within the first 48 hours. In our institutions, the dose of racemic epinephrine used is 11.25 mg solution nebulizer. We defined observation time as the time from administration of first dose of racemic epinephrine

**Table 1.** Description of Study Sample

Number of visits	294
Number of patients	276
Average age, years	2.8 (2.1)
Average length of observation, hours	1.3 (0.7)
Maximum length of observation, hours	4.6
Observation length group	
<1 hour	45%
1-2 hours	42%
>2 hours	13%
Male	65%
Steroid treatment	93%
Westley croup score <sup>a</sup>	
Mild	93%
Moderate	7%
Time of day racemic epinephrine was administered	
Day (6:00-17:59)	27%
Night (18:00-5:59)	73%
Multiple doses of racemic epinephrine were administered	2%

Mean (SD) shown for numeric variables.

<sup>a</sup>Westley et al, 1978.<sup>6</sup>

until the time of discharge by clinician and identified any patient diagnosed with croup in the ED who returned to care with persistent symptoms within 48 hours from discharge. We also identified whether returned patients were retreated with steroid or another dose of racemic epinephrine. This included patients who returned to either the ED or were seen in the clinic or urgent care departments. Croup severity score was calculated using the Wesley Croup<sup>6</sup> scoring system based on patient's initial presenting symptoms as documented in the clinician's note.

Data were compiled in an Excel spreadsheet and validated by the principal investigator and study assistant before delivery to the biostatistician. Our primary outcome was to compare the return rate within 48 hours between patients observed for less than 2 hours with those observed for 2 hours or more. Visits were grouped as having observation less than 1 hour, 1 to 2 hours, and greater than 2 hours after treatment with racemic epinephrine. Subdividing visits into these groups provided a more granular understanding of return rates. Visit characteristics were described using means and SD for continuous variables and counts and percentages for categorical variables. Comparisons of visit characteristics across observation time groups were made using analysis of variance (ANOVA) for continuous variables, and chi-square tests for categorical variables. Return rates by observation time groups were further compared using chi-square tests after stratifying for croup severity. Retreatment among patients who returned within 48 hours of discharge also were tabulated. All statistical analyses were performed in SAS version 9.4. The Figure was generated using the ggplot2 package in R version 3.6.0.

## RESULTS

Over the 8-year period, 294 individual visits for 276 pediatric patients met inclusion criteria. The 294 visits were individual visits within the 8-year period and not repeat visits within the 48

**Table 2.** Patient and Clinical Characteristics by Observation Length Group

Characteristic	Observed <1 hour N=32	Observed 1-2 hours N=123	Observed >2 hours N=39	P value
Age, years	2.7 (2.1)	3.0 (2.2)	2.8 (2.2)	0.680
Male	64%	67%	62%	0.801
Steroid treatment	87%	98%	100%	0.001
Westley croup score <sup>a</sup>				
Mild	95%	96%	74%	<0.001
Moderate	5%	4%	26%	
Time of day RE was administered				
Day (6:00-17:59)	30%	24%	26%	0.639
Night (18:00-5:59)	70%	76%	74%	
Multiple doses of RE administered	1%	2%	8%	0.044

Abbreviation: RE, racemic epinephrine.  
Mean (SD) shown for numeric variables.  
P values are derived from ANOVA for continuous variables and chi-square test for categorical variables.  
<sup>a</sup>Westley et al, 1978.<sup>6</sup>

hours' time for 1 episode of croup. Table 1 highlights the demographic and clinical information for the sampled ED visits. The average age of our patients was 2.8 years, and 65% of the patients were male, for a male to female ratio of 1.9:1.

The average length of observation in our patient population was 1.3 hours, with 45% observed for less than 1 hour; 42% observed for 1 to 2 hours; and only 13% observed for greater than 2 hours. The maximum length of observation was 4.6 hours in our study sample. The majority of patients (93%) had mild croup symptoms, while 7% had moderate croup symptoms. No patients in our study sample had severe croup symptoms. A majority of our patients (93%) received steroids—specifically dexamethasone 0.6 mg/kg—as part of their treatment. It is not clear from the medical records why the other 7% did not receive steroids.

Preliminary evaluation of clinical characteristic by observation time did not reveal a statistically significant difference in patient ages among the different observation periods (Table 2). In the less than 1 hour observation group, 95% had mild symptoms, while 5% had moderate symptoms. In the 1 to 2 hours observation group, 96% had mild symptoms, and 4% had moderate symptoms. In the greater than 2 hours observation group, 74% had mild symptoms, while 26% had moderate symptoms. Regarding steroid treatment, 100% of patients observed for greater than 2 hours were treated with steroid, compared to 87% of patients in the less than 1 hour group and 98% of the 1- to 2-hour group. Given these data, a greater percentage of those observed for less than 1 hour had milder symptoms compared to those observed for greater than 2 hours. In addition, of those who received more than 1 dose of racemic epinephrine, 8% were in the greater than 2 hours observation (Table 2).

Further cohort analysis was performed to determine whether return rates were associated with initial observation time. The return rates within 48 hours were compared between the different observation times (Table 3, Figure). In the greater than 1 hour

observation group, only 5 patients with croup symptoms returned for additional care within 48 hours. Of these 5 patients, 3 had initial mild symptoms, while 2 had moderate symptoms. None of the patients who returned were retreated with racemic epinephrine, though 2 of them received steroids. The age of these patients ranged from 20 months to 3 years, and a majority (4 out of 5) were male.

In the 1- to 2-hour observation group, 7 patients returned to care within 48 hours with persistent croup symptoms. Only 1 of these patients was retreated with racemic epinephrine, and this was a patient with initial moderate symptoms by croup score. Three out of the 7 patients received steroids. In the greater than 2 hours observation group, only 3 patients returned, and 1 was admitted to the hospital for further treatment. Only 1 out of the 3 patients received steroids. When comparing the total return rate based on observation times in our study population, we found no significant association.

## DISCUSSION

Croup is a common pediatric illness often encountered by ED physicians. Although much is known regarding the treatment of croup, the appropriate observation time after administration of racemic epinephrine is not well established. The current recommendation is to observe patients for at least 2 hours prior to discharge, though this practice was not adapted from well-conducted studies. Several studies have attempted to define an appropriate length of observation in this population. A small observational study conducted at a children's hospital in Atlanta, Georgia suggested that selected patients with croup can be safely discharged after observation for 2 hours following racemic epinephrine administration.<sup>7</sup>

Our study aimed to compare patients observed for less than 2 hours versus those observed for 2 hours or more to see if there is an association in return rates within 48 hours. Croup symptoms are mild in most cases and, as such, the return rate in croup cases is low. When we compared return rates based on observation time, there was no association between return rates and observation time ( $P=0.538$ ) among mild cases. Similarly, when looking at return rates among moderate cases, there was no statistically significant difference in return rates based on observation time ( $P=0.905$ ); however, there were too few cases to detect small differences in readmission rate. In those patients who did return within 48 hours, the majority were not retreated with racemic epinephrine. The majority of our patients were male. This sampling result corresponds to observations in the general population, where there is slight male predominance with croup, with a male to female ratio of approximately 1.4:1.<sup>4</sup> Consistent with a typical presentation of croup—which generally occurs during the night/early morning

hours due to resting secretions and edema building without clearing during sleep—in our patient population, a majority of cases presented to the ED at night (73%).<sup>8</sup>

### Limitations

There are several limitations to our study, including that it is a retrospective study dependent on chart review from different clinicians at different EDs. In addition, we only included charts from 3 institutions in Wisconsin, which might limit the generalization of our study results to other populations. Another limitation is that the croup severity score was not assigned/standardized prior to treatment. We had to extrapolate/calculate croup severity score based on patients' presenting symptoms from the charts. Furthermore, there were only a few cases of patients who returned with croup symptoms after receiving racemic epinephrine. To account for these differences, there is a need for a larger prospective study with standardized croup severity scoring prior to treatment with racemic epinephrine to determine appropriate observation times after its administration. Another limitation in our study is that we had very few cases with moderate croup symptoms; and although it does not appear that observing these group of patients for less than 2 hours leads to an increase in return rate within 48 hours, we recognize that there were too few cases to detect small differences in return rate.

### CONCLUSION

From our study results, we can conclude that observing patients with mild croup symptoms for less than 2 hours did not increase their risk of deterioration or need to return. In patients with moderate croup symptoms, there was no statistically significant difference in return rates based on observation time; however, there were too few cases to detect small differences in return rate. Our data did not show that a longer observation time in patients with mild and moderate croup symptoms results in lower return rates within 48 hours. Despite the recommendations to observe patients for greater than 2 hours, it seems that clinicians are safely discharging patients after observing for less than 2 hours, and this is not leading to worse outcomes.

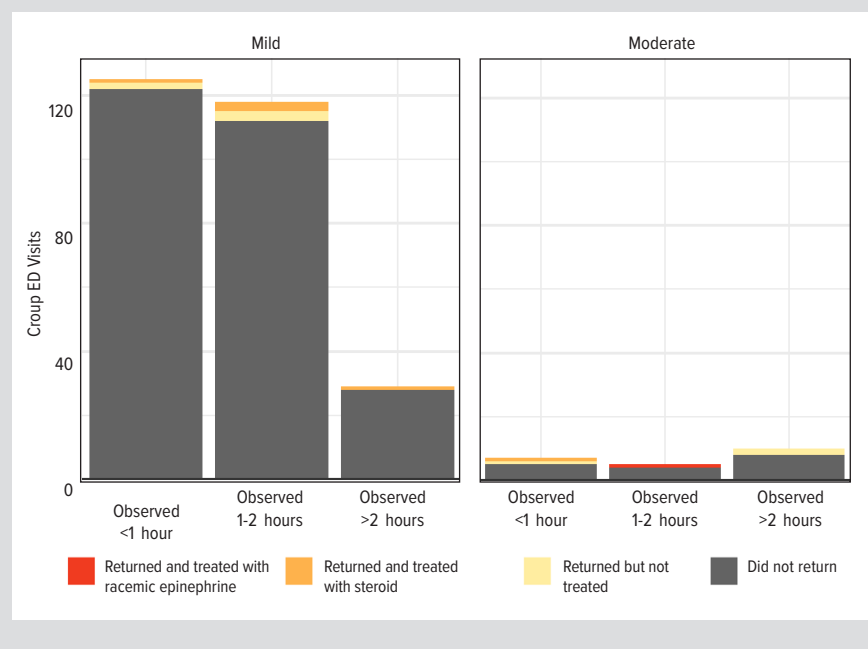
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**Table 3.** Rate of Return Within 48 Hours by Observation Length Group

	Observed <1 hour	Observed 1-2 hours	Observed >2 hours	P value
<b>Total (N = 294)</b>				
Did not return within 48 hours	127 (96%)	116 (94%)	36 (92%)	
Returned within 48 hours	5 (4%)	7 (6%)	3 (8%)	
<b>Mild cases (N = 272)</b>				
Did not return within 48 hours	122 (98%)	112 (95%)	28 (97%)	0.538
Returned within 48 hours	3 (2%)	6 (5%)	1 (3%)	
<b>Moderate cases (N = 22)</b>				
Did not return within 48 hours	5 (71%)	4 (80%)	8 (80%)	0.905
Returned within 48 hours	2 (29%)	1 (20%)	2 (20%)	

**Figure.** Comparison of Return Rates Within 48 Hours Between the Different Observation Times



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