

Viral Croup in Children in the Emergency Department: State of the Art

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Received: March 21, 2019; **Published:** April 01, 2019

Abstract

Viral croup is frequent under 3 years of age. It is characterized by inspiratory stridor, barking cough, hoarseness and different degrees of respiratory distress. Most cases do not endanger life, but if the obstruction of the upper airway progresses can lead to acute respiratory failure. The most frequent virus is parainfluenza-1. Other important causes are bacterial infections (epiglottitis and bacterial tracheitis), allergic reactions and aspiration of foreign bodies. Diagnostic tests are only necessary if differential diagnoses are suspected. Corticosteroids are the mainstay of pharmacological treatment. L-epinephrine is an option to achieve control of the airway in moderate and severe cases. Other important strategies are humid and warm air, optimal hydration and avoid pain and agitation. Heliox may be an option in selected cases. Among the most serious complications are severe obstruction of the airway and acute respiratory failure that can lead to collapse and death.

Keywords: Croup; Viral Infection; Corticosteroids; Children

Abbreviations

HiB: *Haemophilus influenzae* Type B; *S. aureus*: *Staphylococcus aureus*; IV: Intravenous; IM: Intramuscular; mg: Milligram; Kg: Kilogram; He: Helium; O₂: Oxygen; °C: Grades Centigrade; PICU: Pediatric Intensive Care Unit

Introduction

Viral croup is a common childhood disease. It is characterized by acute onset of barking cough, inspiratory stridor, hoarseness and variable degree of respiratory distress, resulting from partial upper-airway obstruction [1]. Croup is more common in males (1,4:1) from 6 months - 3 years old, with a high incidence in respiratory infections seasons [2,3]. It occurs in 5 to 20% of children with acute viral respiratory infections. The resolution of symptoms occurs before 48 hours in 60% of children and in the following 5 days in 95% of them. Only 5% need in-hospital treatment and 3% result in endotracheal intubation. The estimated mortality is of 1 per 30,000 cases annually [4]. We have made a review about this disease emphasizing in the current knowledge about its treatment.

Pathophysiology and clinical manifestations

Croup is secondary to viral infections in most cases [1]. The virus leads to inflammation and edema of the upper-airway mucosa and submucosa, with necrosis and epithelial cells shedding, resulting in increased thickness of the airway wall with narrowing and obstruction of the upper-airway lumen [5]. Infants suffer a more severe obstruction of the upper-airway due to the anatomical characteristics of their larynx with respect to the adult. The anatomical larynx position of the infant is upper and anterior, it has a conical shape with a smaller subglottic diameter and a collapsible structure due to its immature support tissue, and easily, the submucosa molecular structural

composition contributes to a large water accumulation. These characteristics facilitate that the subglottic edema due to inflammation triggered by viruses leads to a significant lumen obstruction in a short time [2,5]. Therefore, during a forced inspiration there is a great increase in resistance to the airflow that produces turbulence, increases the respiratory work and worsens the clinical manifestations [5]. If the obstruction worsens, stridor will be inspiratory and expiratory with progression to respiratory failure. If the airway is not secured, it can be fatal [4].

In most cases, high respiratory symptoms precede from 1 - 5 days the classical clinical manifestations of viral croup, sometimes accompanied by fever less than 39°C. Then appears the barking cough and hoarseness, and as the inflammation of the larynx progresses and obstructs the upper airway, inspiratory stridor and respiratory distress appear. In most children, croup resolves in 5 days. In general, children look good and most cases are mild [6]. The appearance of other symptoms depends on the organ involved; they can be limited to the larynx or extend to the ears, paranasal sinuses, nose, pharynx or the lower respiratory tract [2]. If there is hypoxemia and/or hypercapnia, it may be secondary to severe obstruction of the upper respiratory tract, inflammation of the small airway (bronchiolitis) or compromise of the pulmonary parenchyma with atelectasis, pneumonia or negative pressure pulmonary edema secondary to severe obstruction of the upper airway [1,5].

Diagnosis

The diagnosis of croup is clinical. The laboratory or radiology tests helps to rule out differential diagnoses or to detect complications if there is clinical deterioration [4]. The characteristic radiological sign of croup is the pencil sign on the proximal trachea evident in the X-ray of the anteroposterior film of the neck, but its absence does not exclude the diagnosis [5]. In cases of rapid airway obstruction, wheezing, aphonia, toxic appearance, high fever, sialorrhea, dysphagia, recurrent or prolonged stridor, poor response to treatment, croup in children younger than 3 months or in immunodeficient patients, other non-viral causes of croup must be sought. The differential diagnoses are bacterial infections (epiglottitis and bacterial tracheitis), non-infectious etiologies like those that alter the anatomy, foreign body aspiration, tumors, vascular malformations, and malacias [7]. Also burns, neurological problems (central or peripheral lesions), metabolic (hypocalcemia, hypothyroidism), allergic reactions, gastrointestinal (gastroesophageal reflux), among others [5]. Differential diagnoses are summarized in table 1.

- Foreign-body aspiration.
- Non-viral infections: laryngeal diphtheria, candidiasis, retropharyngeal or peritonsillar abscess, papillomatosis, epiglottitis, bacterial tracheitis.
- Pseudo-croup (spasmodic/allergic reaction), angioneurotic edema, anaphylaxis.
- Congenital malformations: diaphragms, fissures, malacia, vascular rings, stenosis, cysts or hemangiomas.
- Paralysis or dyskinesia of vocal cords (central or peripheral neurological lesions).
- Myasthenia gravis.
- Extrinsic compression by tumor, mass or other
- Acquired injuries: Subglottic stenosis, granulomas, fibrosis, edema, laceration, bruises, thermal or chemical burns, among others.
- Gastroesophageal reflux.
- Hypocalcaemia, hypothyroidism.

Table 1: Differential diagnosis.

Etiology

Eighty percent of cases are secondary to viral laryngitis. Parainfluenza-1 is the etiology in 75%; less common are parainfluenza-2 and 3. Others viruses that can be found are rhinovirus, respiratory syncytial virus, influenza A and B, adenovirus and metapneumovirus [8].

Among the non-viral infectious causes of croup, it is worth mentioning bacterial epiglottitis and bacterial tracheitis due to its severity. In most cases, bacterial epiglottitis is associated with *Haemophilus influenzae* type B (HiB) infection and less frequent with *Streptococcus*

pyogenes, non-encapsulated *Haemophilus influenzae* and *Staphylococcus aureus* (*S. aureus*) [5]. The manifestations of bacterial epiglottitis are rapid evolution, severe obstruction of the airway, high fever, toxic aspect, sialorrhea, inability to swallow, protrusion of the tongue and sniffing position. Is important early endotracheal intubation with minimal manipulation and the empirical antibiotic treatment starts with a third-generation cephalosporin [5,9]. Bacterial or purulent tracheitis is an infection mainly caused by *S. aureus* and HiB [7]. It affects children from 5 - 13 years old more frequently. In bacterial tracheitis there is acute inflammation of the tracheal mucosa with the presence of abundant purulent membranes that obstruct its lumen [10]. The clinical manifestations are less severe than those of epiglottitis and its clinical course is slower than that of viral croup before the obstruction becomes significant [11]. The treatment consists of antibiotics against *S. aureus* and HiB, guaranteeing the permeability of the airway and, if necessary, perform endotracheal intubation [10,11].

Among the noninfectious causes of croup, the spasmodic croup, also known as false or pseudo-croup (laryngismus stridulus) is common. The clinical manifestations are like those of viral croup. It is characterized by an inflammation of allergic origin of the laryngeal mucosa and its symptomatology is disproportionate in relation to the inflammatory process [1]. It occurs usually at night with sudden and rapid onset, in children from 1 - 3 years without symptoms in previous hours or days, recurrence is frequent and patients respond adequately to treatment with cold air, inhaled or systemic corticosteroids and antihistamines. Some triggers are insects, viruses, food and environmental contaminants [8].

Classification

Croup can be classified according to the anatomical segment involved: supraglottic (epiglottitis, laryngeal diphtheria), glottic (viral or allergic, paralysis of vocal cords) [7] or infraglottic (bacterial tracheitis, foreign body) [12]. Also, it can be classified by the degree of severity of the clinical manifestations [1,7]. The most popular classification is the Westley scoring system (Table 2) [13]. This score classifies the severity of the clinical manifestations and has four categories of severity: mild, moderate, severe and impending respiratory failure (Table 3).

Feature	Category	Score
Stridor	None	0
	When agitated	1
	At rest	2
Retractions	None	0
	Mild	1
	Moderate	2
	Severe	3
Air entry	Normal	0
	Decreased	1
	Markedly decreased	2
Cyanosis	None	0
	Cyanosis with agitation	4
	Cyanosis at rest	5
Level of Consciousness	Normal (including sleep)	0
	Disoriented	5

Table 2: Westley Scoring System [13]. In 1978, Westley, et al. created and applied this scoring system to assess the initial severity and response to treatment in the clinical trial they performed. It is the most popular scoring system for croup. It has 5 features, with a minimum score of 0 and a maximum of 17. The features are: 1) stridor in inspiration and/or expiration, 2) retractions of the chest wall: the severe category refers to the use of abdominal muscles, 3) the entry of air (in the auscultation), refers to the intensity of lung murmur, 4) cyanosis with ambient air, and 5) level of consciousness: disorientated is equivalent to any degree of alteration of consciousness.

Score	Category
0 - 2	Mild
3 - 5	Moderate
6 - 11	Severe
≥ 12	Impending respiratory failure

Table 3: Classification: Westley Scoring System. Each category results from the Westley croup severity score [13].

Treatment

The aim of the treatment is to relieve the obstruction of the airway and keep its patency [7]. There are pharmacological and non-pharmacological options.

Position, nutrition and rest: The child should be allowed to adopt their most comfortable position or to rest on their mother's arms, avoiding any source of anxiety and pain (venipuncture, X-rays, noise, sleep interruption, feeding tubes, hunger) [14]. Fever should be controlled to reduce respiratory distress. Oral feeding should not be stopped if the respiratory distress is mild or moderate. If the child accepts and tolerates the oral route, there is no justification for administering parenteral medications, since the oral route is the best option [7,14].

Hydration: An adequate state of hydration should be conserved. The parenteral route is an option if the patient is dehydrated and does not accept or tolerate the oral route, has severe respiratory distress or respiratory failure, otherwise, the oral route is the first option. Use isotonic fluids and avoid hypotonic solutions to prevent the onset of hyponatremia [4].

Humidified air/oxygen: When supplementary oxygen (or any medicinal gas) is used especially in croup, it should be humidified and warmed to avoid airway injuries, decrease flow resistance and optimize respiratory work [15]. Although warm and humid oxygen must always be used, humidity and heat do not change the clinical course of the croup because it has no direct action on the mechanisms that produce it [16].

Cold air: The relief of the upper airway obstruction has been related to breathe cold air, but until now, its effectiveness on croup has not been demonstrated. On the other hand, exposure to cold air generates bronchospasm and increases respiratory work [4].

Oxygen: If croup or other associated pathology generates hypoxemia, its use is necessary. If there is no hypoxemia but the supplementary oxygen decreases the respiratory distress, it should be continued [4].

Corticosteroids: They have a pivotal role in the treatment with a proven beneficial effect [17,18]. Different corticosteroids have been used for their anti-inflammatory action in the upper airway [19,20]. The corticosteroids used in croup have a powerful anti-inflammatory effect with long duration. The most commonly used inhaled corticosteroid is budesonide, which is lipophilic and accumulates in the respiratory mucosa and from there releases continuously with a sustained clinical effect. Dexamethasone is the most used non-inhaled corticosteroid, administered orally, intravenously (IV) or intramuscularly (IM), with properties in its structure that give it a longer half-life [17,21]. Most of the corticosteroids starts its actions at 0.5 - 4 hours, with a maximum action at 6 - 12 hours and a length of action from 24 - 36 hours [20,22]. The effect of inhaled budesonide (1 mg) was compared with dexamethasone. Two clinical studies showed that inhaled budesonide and dexamethasone had the same effectiveness [20,23]. Prednisolone (1 mg/Kg, single dose) was also compared with dexamethasone (0.15 mg/kg or 0.6 mg/Kg, single dose), without differences [24-26]. The classically recommended dose of dexamethasone is 0.6 mg/Kg, however, there is evidence that a single dose of 0.15 mg/Kg has the same efficacy as a dose of 0.6 mg/Kg [27,28]. In addition, the use of two or more corticosteroids by the same or different route does not improve the results [24]. The most recent evidence concludes: 1) corticosteroids are better than placebo, 2) budesonide, dexamethasone or prednisolone have the same clinical efficacy for the improvement of stridor and respiratory distress, 3) its clinical effects remain from 6 - 24 hours [17,24] and 4) reduce hospitalization and length of hospital stay with its main clinical effect at first 2 hours [29]. Corticosteroids should always be used at any degree of severity of croup. A single dose of oral, IV or IM dexamethasone (0.15 - 0.6 mg/Kg) or nebulized budesonide (1 mg) or prednisolone (1 mg/Kg), are equally, considering the oral or inhaled route in first place and the availability of the medication in the patient environment. Two or more

corticosteroids by different routes of administration are not more effective than one. Taking into account the pharmacological characteristics of corticosteroids, is not useful to administer more than 1 dose before 24 hours [17].

Epinephrine: It is recommended to administer nebulized L-epinephrine in cases of moderate and severe croup and impending acute respiratory failure, since it is better than placebo with a significant clinical benefit additional to the corticosteroids [30]. Racemic epinephrine is not more effective or safer than nebulized L-epinephrine 1: 1000 [31]. Currently, no study has proven the benefit of a specific dose, however, most studies use a single dose of 0.5 mg/Kg up to 5 mg, with the maximum clinical benefit at 30 minutes and a length of 6 hours with proven safety [31]. After the nebulization of a single dose, the patient must remain under medical observation for 4 hours, since when the effect of the medication is exhausted, the obstruction of the airway may reappear, a situation known as rebound effect. Because the goal of epinephrine is to relieve transient obstruction while the corticosteroid acts, it should never be used as monotherapy. There is no additional clinical benefit of giving repeated doses of nebulized epinephrine within 2 hours [32]. In fact, most studies and clinical practice guidelines recommend a single dose (0.5 mg / kg up to 5 mg). If a second dose is administered, it should be applied only if the severity worsens after a period of improvement, that is, only if necessary and not at predetermined intervals. Using repeated doses in short intervals increases the risk of adverse effects, mainly cardiac arrhythmias [32]. Among the contraindications of epinephrine are glaucoma, cardiopathies that generate obstruction to the outflow tract of the left ventricle and syndromes of cardiac pre-excitation.

Heliox: It is a mixture of helium and oxygen (He:O₂). The usual presentations have the following concentrations: 60:40, 70:30 and 79:21 (He:O₂). Since helium and heliox (79:21) have lower density (0.179 g/L and 0.43 g/L, respectively) than oxygen (1429 g/L) and air (1293 g/L), its flow through the proximal airway has less resistance than other gases, especially in obstructive pathologies such as croup [33], therefore, decreases respiratory work, improves oxygenation and increases the elimination of CO₂. Unfortunately, it is expensive, requires a high-flow system, causes hypothermia (if it is not heated properly), and if the patient needs an inspired fraction of oxygen greater than that provided by the heliox mixture, worsens the hypoxemia [33,34]. Heliox in croup has a relieving effect with transient improvement of respiratory distress. Like L-epinephrine, the main goal is to gain time while the corticosteroid acts. It is recommended to use it in moderate cases that get worse, in severe cases and in impending respiratory failure, since in mild cases it does not provide additional benefits to corticosteroid [33].

Other treatments: Antihistamines, antitussives, sedatives, mucolytics, expectorants and antibiotics, have no proven benefit in the treatment of viral croup. Antihistamines only take place in the treatment of allergic croup in selected cases [4].

Depending on the degree of severity, the treatment recommendations are [4,6]:

Mild Croup: Do not stop oral feeding, ensure adequate hydration and avoid the generation of pain or anxiety. Nebulized L-epinephrine is not recommended. One dose of corticosteroid (inhaled or orally) should be administered with new evaluation to the patient after 4 hours. If the evolution is favorable, the patient can go home, ensuring adequate care and the detection of warning signs with medical supervision in the next 24 to 48 hours [6].

Moderate Croup: Do not stop the oral feeding, guarantee and adequate hydration and avoid the generation of pain or anxiety. One dose of corticosteroid (inhaled or orally) should be administered with new evaluation to the patient after 4 hours [6]. If there is hypoxemia or respiratory distress and the stridor worsens, use supplementary oxygen and nebulized L-epinephrine 1:1000, 0.5 mg/kg up to 5 mg, single dose. If the stridor disappears, the respiratory difficulty decreases and there is good oxygenation, the patient can go home. If the patient is not going well, must receive in-hospital treatment [14].

Severe croup and impending respiratory insufficiency: Stop the feeding initially (4 - 6 hours) without placing a feeding tube. Once the permeability of the airway is assured, restart the feeding by the oral route. If the patient needs endotracheal intubation, install a feeding tube later. Try to achieve adequate stabilization and transfer the patient to the pediatric intensive care unit in safe conditions, preparing for a difficult airway protocol [6]. The goal is to maintain and guarantee patency of the airway and relieve obstruction. Humidified and warm supplementary oxygen should be administered by a high-flow system. The heliox could be administered by a high flow system if there is no hypoxemia that contraindicates its use. Use a single dose of parenteral corticosteroid should. Administer nebulized L-epinephrine 1: 1000 undiluted 0.5 mg/Kg up to 5 mg in a single dose, and if necessary, repeat it as many times as necessary, but at intervals longer than 2 hours. If there is no improvement 30 minutes after the first dose of L-epinephrine 1:1000 or if the patient progresses to respiratory failure, endotracheal intubation should be performed. Do not forget that the patient with croup has a difficult airway.

The figure 1 shows the treatment algorithm.

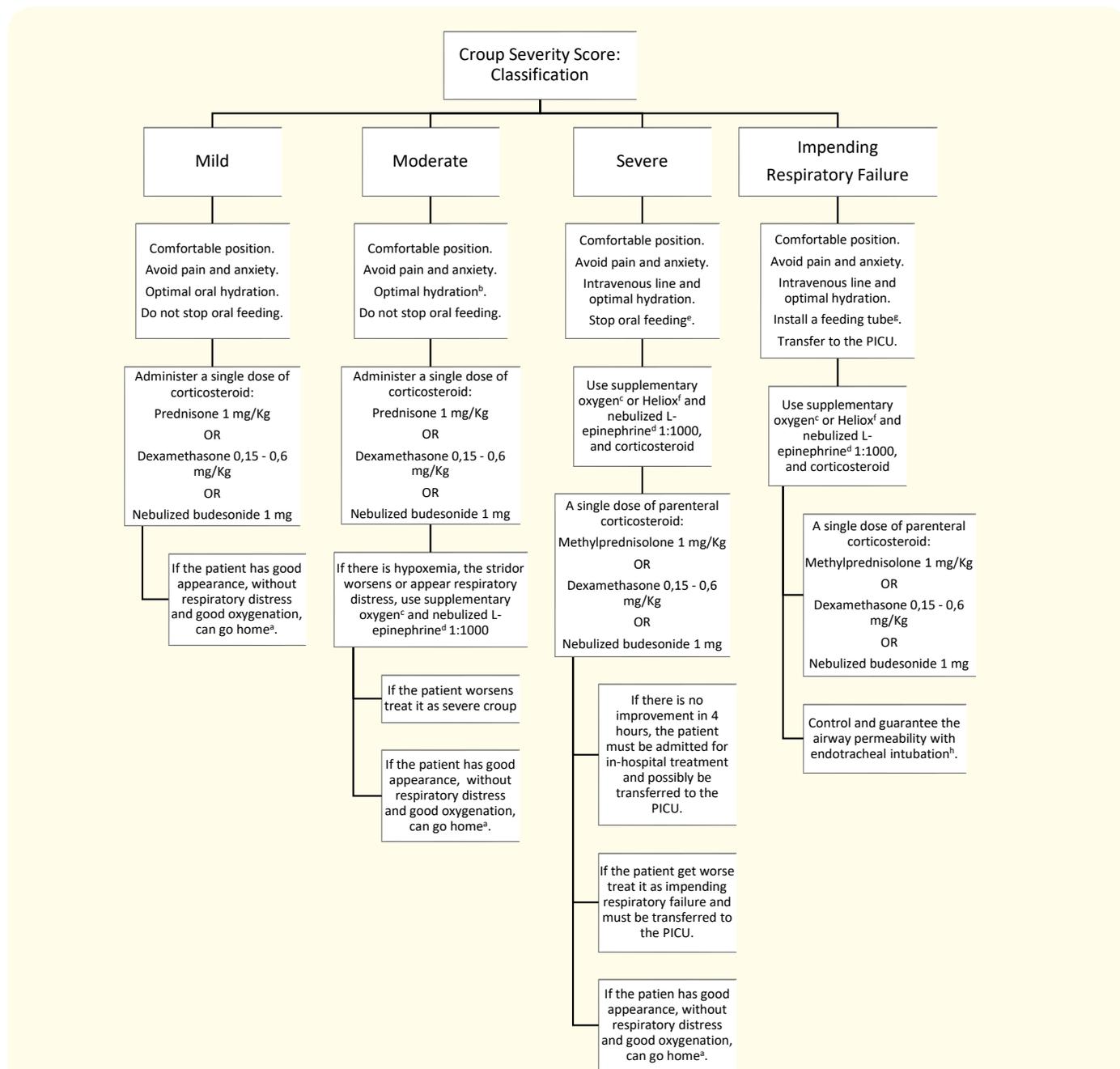


Figure 1: Treatment algorithm.

^aIf the evolution is favorable, the patient can go home, ensuring adequate care and the detection of warning signs with medical supervision in 24 to 48 hours.

^bThe first option for optimal hydration is the oral route. In cases of respiratory deterioration or difficulties with maintaining adequate oral acceptance, optimal parenteral hydration should be ensured.

^cWhen supplemental oxygen is used, it should be warmed and humidified and delivered with a high flow system.

^dAdminister Nebulized L-epinephrine 1: 1000 undiluted up to a single dose of 5 mg, and if necessary, repeat it, but at least every 2 hours.

^eThe feeding should be suspended for 4 to 6 hours initially without placing a feeding tube. Once the permeability of the airway is assured, restart the feeding by the natural route.

^fHeliox can be administered by a high flow system if the patient does not have hypoxemia that can worsen and contraindicate its use.

^gIf endotracheal intubation is necessary, install a feeding tube later.

^hIf endotracheal intubation is necessary, do not forget that it is a difficult airway

Complications

The most serious complication is obstruction of the airway with progression to respiratory failure, hypoxemia, circulatory collapse and death. Babies younger than 6 months can develop apneas. Another serious complication is pulmonary edema due to negative pressure, also known as post-obstructive pulmonary edema. The viral infection can also spread to the ear, bronchioles and the lung parenchyma [1,35]. Croup should never be underestimated. Mild croup can progress earlier than expected to a severe obstruction, so observation and anticipation play a critical role in good treatment. Remember: if you promote situations that generate anxiety and pain, the obstruction will get worse.

Conclusions

Most of the cases of croup are mild or moderate, but a mild degree of laryngeal obstruction can progress earlier than expected to a severe airway obstruction and respiratory failure. The most important strategies for its management are early intervention, avoiding anxiety, pain and crying, and the administration of a single dose of oral or inhaled corticosteroid: dexamethasone, prednisone or budesonide. Nebulized L-epinephrine 1:1000 is a good strategy to relieve upper airway obstruction transiently, while corticosteroids act, controlling and relieving the severity of the obstruction. The heliox may be an option for severe cases if is administered using a high flow system. An appropriate and early management can reduce hospital admissions, complications, intubations, fatality and return visits to receive hospital care.

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Volume 8 Issue 4 April 2019

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