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## **Subglottic laryngitis - changes in therapy approach over the past 20 years**

Ana Penezić, M.D.<sup>1</sup>, Mirko Ivkić, M.D., PhD<sup>1,2</sup>, Boris Ivkić, M.D.<sup>1</sup> and Tomislav Baudoin, M.D., PhD<sup>1,2</sup>

<sup>1</sup>Department of Otorhinolaryngology and Head and Neck Surgery, University Hospital Center “Sisters of Mercy”, Vinogradska cesta 29, 10000 Zagreb, Croatia

<sup>2</sup> Zagreb School of Medicine, Šalata 3b, 10000 Zagreb, Croatia

### **Corresponding author:**

Ana Penezić, M.D.

Department of Otorhinolaryngology and Head and Neck Surgery,

University Hospital Center “Sisters of Mercy”, Zagreb, Croatia

Vinogradska cesta 29, 10000 Zagreb, Croatia

e-mail: [apangercic@gmail.com](mailto:apangercic@gmail.com)

# Subglottic laryngitis - changes in therapy approach over the past 20 years

## Abstract

**Objective:** To show changes in the management of subglottic laryngitis over the last twenty years in Croatia.

**Methods:** We sent questionnaires to paediatricians and otolaryngologists (ENT) in 9 Croatian hospitals in 1993, 2003 and 2013. In the questionnaire we presented a case of a child with moderately difficult subglottic laryngitis, after which they had to answer questions about the management of this kind of a patient and common therapy practice in their hospitals. All data were categorical, described in absolute frequencies and with relative percentages. The Cochran–Armitage test for trend was used in analysis of different treatments over the years among ENT and paediatricians. Associations were statistically significant if  $p < 0.05$ .

**Results:** During a twenty-year period main novelties included the introduction of racemic epinephrine use (ENT from 3.3% in 1993 to 92.3% in 2013; paediatricians from 17.2% in 1993 to 100.0% in 2013) and downfall of humidification (ENT from 60.0% to 23.3%; paediatricians from 60.0% to 12.0%), antibiotic (ENT from 53.0% to 2.3%; paediatricians from 21.0% to 0.0%) and antihistaminic use (ENT from 67.7% to 0%; paediatricians from 43.2% to 2%), while corticosteroids (both parenteral and nebulized form) remained the cornerstone in treatment of moderately severe subglottic laryngitis.

**Conclusion:** Main novelties included the use of racemic epinephrine and downfall of antibiotic, antihistaminic and humidification therapy use, while corticosteroids remained the cornerstone in treatment of moderately severe subglottic laryngitis. Differences between approaches among specialities are minimized during 20-years period.

**Keywords:** subglottic laryngitis; history; therapy; racemic epinephrine; corticosteroids.

## **1. Introduction:**

Subglottic laryngitis is potentially a life-threatening condition with sudden onset and dramatic clinical presentation demanding prompt management and airway preservation [1-3].

Since the subglottic laryngitis is a viral disease, the treatment is mainly symptomatic, although some studies suggest there may be benefits from antiviral agents [3]. In history, the treatment of subglottic laryngitis consisted of mist therapy, humidification, intubation, and in more difficult cases, even tracheotomy was performed [3-7]. In search for the right therapy over the decades, antibiotics were commonly used, since it was believed they would prevent more difficult bacterial infections of the laryngotracheal area and because they could not rule out epiglottitis [3]. In the 1960s glucocorticoids usage became more common, but there were some controversies over selecting the best route of administration, deciding on good candidates and most of all, whether they would be safe [1, 3, 8-12]. Racemic epinephrine was later introduced giving fast resolution of symptoms even in difficult cases [1, 3, 13, 14]. Another recent modality is heliox, which shows short-term benefits when administered together with oral or intramuscular dexamethason in children with moderate to severe croup [15]. Treatment of croup is nowadays based on reducing the inflammation and swelling of subglottic area, with corticosteroids and racemic epinephrine as cornerstones of therapy [12, 13]. The aim of our study is to show changes in management of subglottic laryngitis over the last twenty years in Croatia.

## **2. Materials and methods**

Following our institutional review board approval, we sent questionnaires to paediatricians and otolaryngologists (ENT) in 9 Croatian hospitals. Eight of them were county hospitals (with otolaryngology and paediatric departments) and one was the University Hospital Centre.

Questionnaires were first sent in 1993, then in 2003 and the last ones in 2013. The otolaryngologists and paediatricians filled out the questionnaires anonymously and sent them back to the authors. In the questionnaire we presented a case of a child with moderately difficult subglottic laryngitis (modified Westley croup score 5), after which they had to answer questions about the management of this kind

of a patient and common therapy practice in their hospitals. Nebulized racemic epinephrine is given without intermittent positive pressure breathing (IPPB) in Croatia. The questionnaire from the year 2013 is shown in Appendix 1, and it also includes questions about the place of treatment and cooperation between paediatricians and otolaryngologists in the treatment of subglottic laryngitis. All questions had multiple choice answers. The answers were recorded in Microsoft Office Excel Datasheets (ver.2003) and analysed. All data were categorical, described in absolute frequencies and with relative percentages. The results were shown in tables and graphs. The Cochran–Armitage test for trend was used in analysis of different treatments over the years 1993, 2003 and 2013 among ENT and paediatricians. Associations were statistically significant if  $p < 0.05$  (GraphPad Prism ver.6).

### **3. Results**

#### **3.1. Demographics**

In 1993 the questionnaire was filled out by 82 otolaryngologists and 81 paediatricians, in 2003 by 44 otolaryngologists and 40 paediatricians, and in 2013 by 43 otolaryngologists and 50 paediatricians. The study conducted in 2013, which included questions about the place of treatment this illustrative case (Appendix 1), found that most of otolaryngologists and paediatricians would treat the child with moderate subglottic laryngitis in an out-patient clinic (74.4% ENT vs.74.0% paediatricians) and all of them would treat this child with medicaments (100.0% both groups). Neither otolaryngologists nor paediatricians would have chosen intubation and/or tracheotomy as a treatment of choice in this particular case.

There was no reported death case from subglottic laryngitis in the last 20 years by interviewed otolaryngologists and paediatricians in Croatia.

#### **3.2. Treatment of subglottic laryngitis**

During 1993 in Croatia all otolaryngologists (100.0%) and most of paediatricians (63.0%) used corticosteroids for the treatment of a child with moderately difficult subglottic laryngitis as in the described case (Figure 1a). They also frequently chose antihistaminics as a treatment option (67.7%

ENT vs. 43.2% paediatricians), as well as air humidification (60.0% ENT and 60.0% paediatricians). 53% of ENT and 21% of paediatricians chose to use antibiotics in treatment of the described case. L-epinephrine (adrenaline) was chosen as a treatment modality by 3.3% of ENT and 17.2% of paediatricians.

In 2003, while investigating opinions on the treatment of the described case, we observed a downfall of antibiotic (9.1% ENT vs. 15.0% paediatricians) and antihistaminic use (22.7% ENT vs. 0.0% paediatricians). Opinions on the treatment of the described case in 2003 are shown in Figure 1b. In this year ENT and paediatricians had most commonly chosen to use corticosteroids for the described case. 27.3% of ENT and 47.5% of paediatricians would use it parenterally (intramuscular), while 31.8% ENT and 10.0% of paediatricians would use corticosteroids in a nebulized form. The study found that in 2003 racemic epinephrine was used by 40.9% of ENT and 42.5% of paediatricians. Humidification was used by 59.1% of ENT and 12.5% of paediatricians. Also 13.6% of the surveyed ENT and 2.5% of paediatricians used mucolytics in the treatment of the described case.

In 2013 racemic epinephrine was used for the described case by 92.3% of ENT and all surveyed paediatricians. 61.5% of ENT and 41.7% of paediatricians used corticosteroids parenterally (intramuscularly), and 30.8% of ENT and 33.3% of paediatricians used the nebulized form of corticosteroids in the treatment of the described case. Nebulized racemic epinephrine and corticosteroids together (whether intramuscular or in nebulized form) chose 74.4% of ENT and 68.0% of paediatricians. Opinions on the treatment of the described case in 2013 are shown in Figure 1c. Humidification was used by 23.3% ENT and 12.0% paediatricians. It is interesting that only 2.3% of ENT used antibiotics (and 0.0% of paediatricians). There is also a clear downfall of antihistaminic use (0% ENT; 2% of paediatricians).

Trend analysis of different treatment options among ENT and paediatricians from 1993 until 2013 was calculated and shown in Figure 2. Figure 2a shows trends among otolaryngologist in prescribing different treatments for subglottic laryngitis during 1993, 2003 and 2013. Figure 2b shows these trends

among paediatricians. There is a significant difference ( $p < 0.05$ ) in the usage of racemic epinephrine, humidification, antibiotics and antihistaminics as a treatment modality during the period of 20 years.

### **3.3. Paediatric and otolaryngology cooperation**

We asked ENT and paediatricians where a child with subglottic laryngitis is usually treated in their facilities. In 86.0% of cases children with subglottic laryngitis are treated in a paediatric ward. The opinion of ENT and paediatricians regarding the place of the treatment of a child with severe subglottic laryngitis is shown in Figure 3. We asked them to evaluate the cooperation between ENT and paediatricians regarding the treatment of subglottic laryngitis in their hospitals, and 60.2% evaluated it as great, 30.1% as good, and 9.7% think it could be better.

## **4. Discussion**

Opinions on the treatment of moderate subglottic laryngitis in the study have shown trends in management over the past 20 years in Croatia. The main novelty was introducing racemic epinephrine in the therapy during the period of 1993-2003, while glucocorticoids remained the mainstay in the therapy. The study also found that in 2013 in Croatia children with moderate croup received racemic epinephrine inhalations as first-line treatment in 92.3% of cases by ENT and by 100.0% of paediatricians. Nebulized racemic epinephrine and corticosteroids together (whether intramuscular or in nebulized form) chose 74.4% of ENT and 68.0% of paediatricians.

During the war in Croatia (1991-1995) adrenalin (L-epinephrine) was used in a nebulized form in the treatment of subglottic laryngitis. Among therapeutic options in the questionnaire during 1993 there was only L-epinephrine, and it was chosen as a treatment modality by 3.3% of ENT and 17.2% of paediatricians. During the period of twenty years racemic epinephrine became recognized as a first-line treatment of moderate subglottic laryngitis in emergency care departments both by ENT and paediatricians. There was a decrease in number of hospitalizations at otolaryngology departments in Croatia due to subglottic laryngitis, which might be related to the more frequent use of racemic epinephrine and steroids in emergency department [15]. This trend of using nebulized racemic

epinephrine in outpatient settings corresponds to the management of croup in other countries [13, 17]. A systematic review by Bjornson et al. has shown that nebulized epinephrine was associated with croup score improvement 30 minutes post-treatment, but this effect was not significant two and six hours post-treatment [13]. Epinephrine also bears a risk of rebound phenomenon and heart tachyarrhythmia, which are reasons for observing a child who received nebulized epinephrine in emergency care [1, 3, 13, 17, 18].

The study found that the preferable route of corticosteroid administration during 2013 in Croatia was intramuscular (ENT 61.5%; paediatricians 41.7% in 2013). Corticosteroids in nebulized form are also frequently chosen for the treatment of moderately severe subglottic laryngitis by ENT (30.8%) and paediatricians (33.3%). Unfortunately we have not investigated the dosage of given glucocorticoids, nor would it have been dexamethasone or prednisolone. This limitation of our study could be a point for further investigation. A recent review by Russell et al. showed that corticosteroids had a beneficial impact after six hours upon administration, lessened the need for repeated visits and (re)admissions [12]. The preferred practice is to use single oral dose of dexamethasone (0.6mg/kg), and in vomiting children nebulized budesonide or dexamethasone (0.6mg/kg) given intramuscularly [1, 3, 9, 11, 12, 17, 19-21]. In Croatia there is no oral solution of dexamethasone, which would be a preferable choice for children. Over the last few years in Croatia there has been an increase in usage of rectal prednisone (100mg) for treatment of croup. Exact data on the widespread use of this route of steroid treatment in Croatia are currently unknown and further investigation in this direction could be carried out. It is important to stress that single dose corticosteroid treatment is preferable, because of possible complications of prolonged (or multiple) corticosteroid use such as bacterial and fungal infections [1, 3, 11, 12, 21].

In this study we observed downfall of antibiotic use for the treatment of subglottic laryngitis (ENT from 53.0% to 2.3%; paediatricians from 21.0% to 0.0%). In history, there was a belief that bacteria (especially *Corynebacterium diphtheriae*) had the main role in etiology of croup [3]. Over the years etiology of croup has been clarified, and it is known that bacteria represent a very small piece of the



puzzle of etiology [3, 22, 23]. Bacterial croup is usually secondary infection with *Staphylococcus aureus*, or other common bacterial pathogens like *Streptococcus pyogenes*, *Streptococcus pneumoniae*, *Haemophilus influenzae* or *Moraxella catarrhalis* [23]. It usually involves spreading of the infection and regarding pathology there is extensive exudate and pseudomembrane formation at the bronchial and bronchiolar levels, which results with progressive airway obstruction [23]. Over the decades there was a trend of antibiotic use, which was believed to prevent this obstruction. The fall of antibiotic use in the treatment of subglottic laryngitis suggests a better understanding of pathophysiology and etiology of the disease, as well as raising awareness of preventing antibiotic resistance.

The pathology of laryngotracheitis represents combined influence of cytopathological effect of parainfluenza virus and host response to viral infection [3, 23]. One of the studies on recurrent croup and allergy showed that children with specific parainfluenza IgE antibodies who had croup more frequently released histamine into the airway than children with upper respiratory tract infection caused by the same pathogen [23, 24]. The possible correlation between allergy and croup was investigated over the years, and this may have resulted in the usage of antihistaminics in treatment of croup [25-28]. Since treatment with antihistaminics did not bring any significant improvement, it was abandoned, which can also be seen in our study. There is a significant decrease in antihistaminic use by otolaryngologists (from 67.7% in 1993 to 0.0% in 2013) and paediatricians as well (from 43.2% in 1993 to 2.0% in 2013). Although there was a clear link between atopy and recurrent laryngitis, one of the recent studies which tried to connect recurrent croup and allergy showed that positive RAST did not correlate with clinical symptoms [23, 25-30].

It is interesting that humidification therapy is still used in the treatment of moderate subglottic laryngitis in Croatia (in 2013 23.3% of ENT and 12.0% of paediatricians used it). In this particular case it was combined with other treatment and neither ENT nor paediatricians used it as the only treatment option. Current literature shows no evidence that humidification therapy alone could be useful in the treatment of moderate to severe subglottic laryngitis [3-5, 31].

Among trends in the treatment of subglottic laryngitis tracheotomies and intubation as a treatment modality were often utilized at the beginning of the past century. If there is suspicion on bacterial infection or a patient presenting with severe laryngotracheitis there is an indication for intubation [32]. These patients require intensive care monitoring in the paediatric intensive care unit (PICU), so they make ground for decision where to treat a child with severe infection [3, 23, 32]. When we asked about the place of treatment patients with severe subglottic laryngitis, otolaryngologists replied they would also send these patients to be treated in a paediatric ward (Figure 3). However, moderately severe croup is mainly treated at paediatric emergency departments (860% of respondents) in Croatia. The results of good and excellent cooperation between otolaryngologists and paediatricians in the study show the importance of good interpersonal relationships in emergency care setting.

## **5. Conclusions:**

During a twenty-year period main novelties include the use of racemic epinephrine and downfall of antibiotic, antihistaminic and humidification therapy use, while corticosteroids remained the cornerstone in treatment of moderately severe subglottic laryngitis. Differences between approaches among specialities are minimized during this period.

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**Disclosure Statement:**

**Conflict of interests:** none.

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## Appendix 1

### Questionnaire for subglottic laryngitis

**Case presentation:** In your emergency ambulance, right after midnight, parents come with a 2-year old boy. You find out that problems occurred suddenly, while the boy was asleep, and that he had coryza the day before. Parents said that he had normally swallowed.

In clinical exam you found that he is subfebrile (axillary measured temperature 37,9° C), he is breathing stridorously, with „barking“ cough, but without retractions in jugulum or supraclavicular areas. He is not cyanotic.

Your working diagnosis is: subglottic laryngitis.

#### Questions:

1. Your work specialty: a) paediatrician, b) otorhinolaryngologist (ENT).
2. You decided to treat this child: a) ambulatory, b) observe him in a ward, c) in an intensive care unit.
3. How would you secure his airway? a) Medicamentous treatment, b) endotracheal intubation, c) tracheotomy.
4. In your opinion, does this child need an ENT exam? a) Yes, b) No.
5. In your opinion, which of the following therapy would you use in the treatment of this child: (multiple choice)
  - a) cold humidification,
  - b) antibiotic,
  - c) antihistaminic,
  - d) adrenalin (parenterally),
  - e) recemic epinephrin (inhalation),
  - f) corticosteroids (parenterally),
  - g) corticosteroids (inhalation),
  - h) mucolytics,
  - i) other (which): \_\_\_\_\_.
6. If the child had a more severe clinical picture of subglottic laryngitis, you would treat him:
  - a) In the paediatric ward, b) in the ENT ward.
7. In your opinion, subglottic laryngitis should be treated by:
  - a) paediatricians, b) ENT, c) both paediatricians and ENT.
8. In the hospital where you work, children with subglottic laryngitis are treated :
  - a) In the paediatric ward, b) in the ENT ward.
9. How would you evaluate the cooperation between paediatricians and ENT in treating subglottic laryngitis in the hospital where you work:
  - a) bad, b) it could be better, c) good, d) excellent.

10. Were there any death cases caused by subglottic laryngitis in the hospital where you work in the last 10 years: a) no/I don't know, b) if yes- how many? \_\_\_\_\_

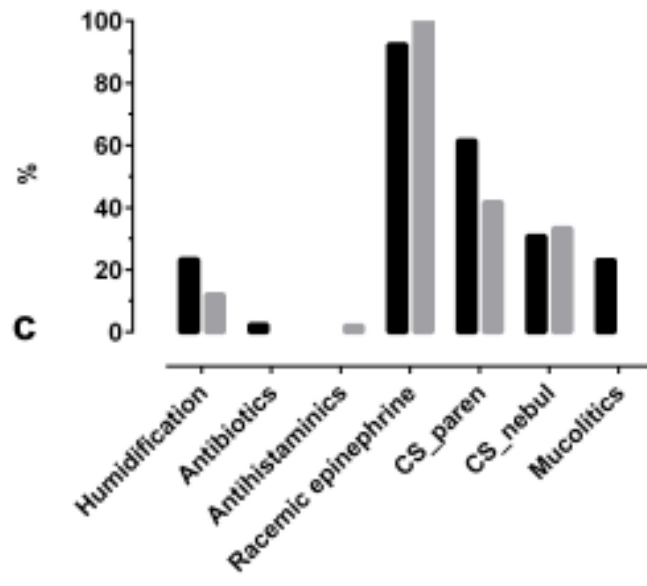
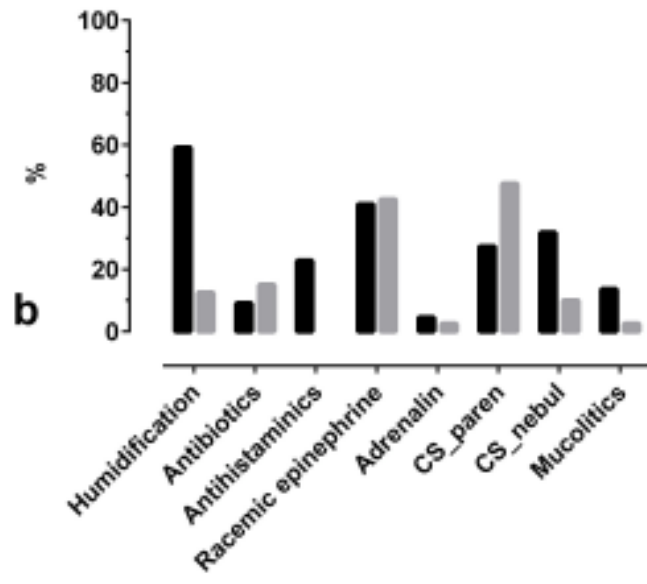
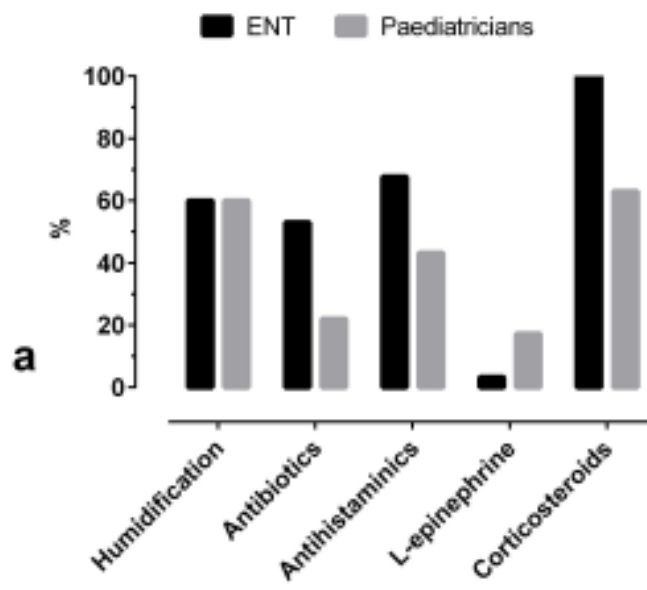
11. Comments and suggestions: \_\_\_\_\_

## **Figure legends:**

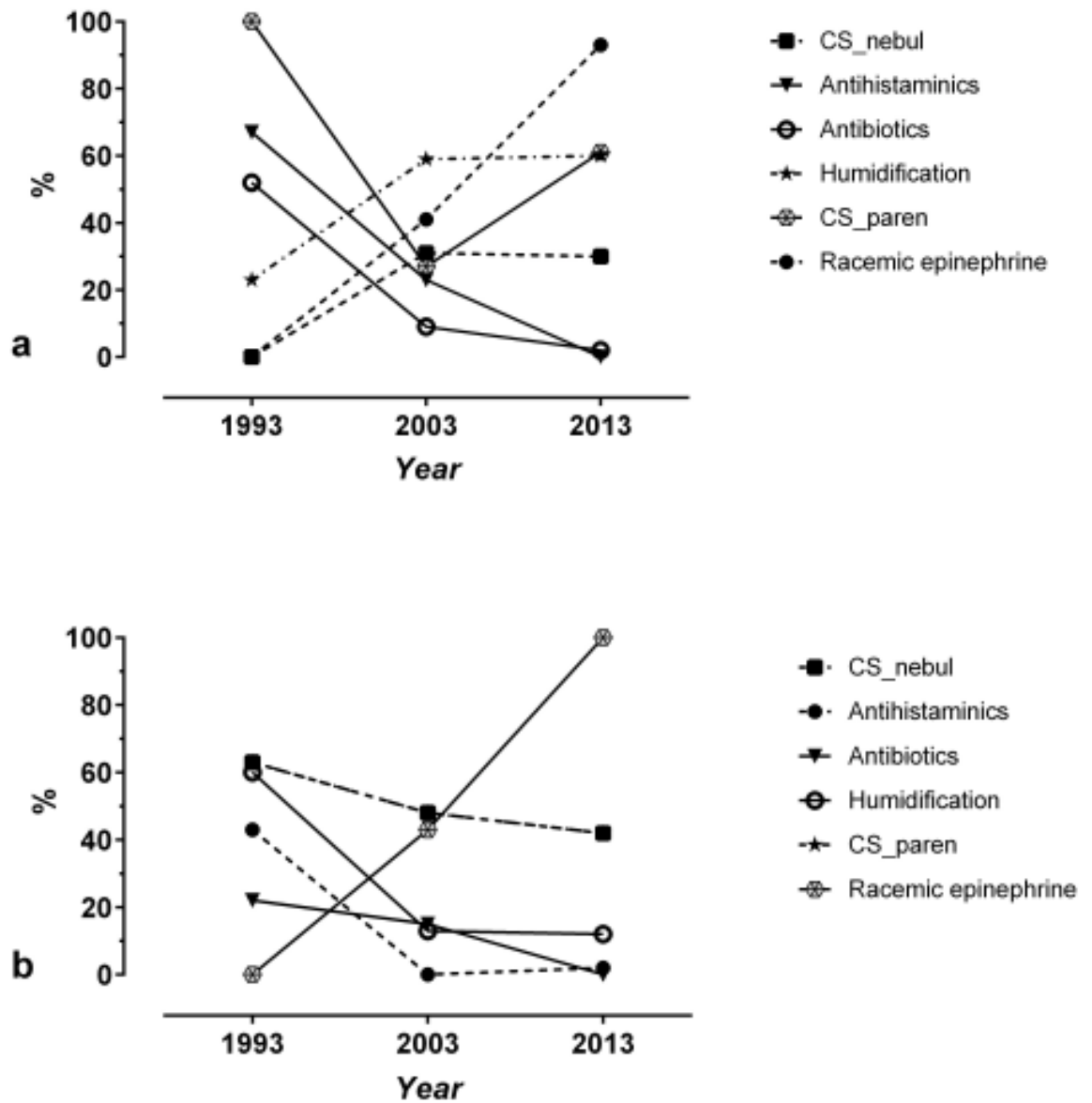
**Figure 1.** Trends in opinion among otolaryngologists (ENT) and paediatricians regarding treatment of moderately severe subglottic laryngitis: a) year 1993, b) year 2003, c) year 2013.

**Legend:** ENT-otolaryngologists; CS\_paren-corticosteroids applied parenterally; CS\_nebul-corticosteroids applied in nebulized form.





**Figure 2.** Trend analysis of different treatment options from 1993 to 2013 among: a) otolaryngologists, b) paediatricians. Y-axis shows the percentage of otolaryngologists (Fig.2a) and paediatricians (Fig.2b) who used specific treatment option. X-axis shows years of the study. The Cochran–Armitage test was used for trend analysis. **Legend:** CS\_paren - corticosteroids applied parenterally; CS\_nebul - corticosteroids applied in nebulized form.



**Figure 3.** Opinions of otolaryngologists and paediatricians regarding the place of the treatment of a child with severe subglottic laryngitis. **Legend:** ENT-Otolaryngologists; Dept.-Department.

