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The clinical use of hypertonic saline/salbutamol in treatment of bronchiolitis

Zastosowanie roztworu soli hipertonicznej w leczeniu zapalenia oskrzelików

Karolina Ratajczyk-Pekrul [1,*], *Paweł Gonerko* [1], *Jarosław Peregud-Pogorzelski* [2]

[1] *Department of Pediatrics, Allergology and Pulmonology, Hospital of Zdroje, Szczecin, Poland*
[2] *Department of Pediatric Oncology, Pomeranian Medical University, Szczecin, Poland*

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ABSTRACT

Aim: To compare the efficacy of nebulised 3% saline solution (with salbutamol) or 0.9% saline solution (with salbutamol) in the treatment of mild to moderate bronchiolitis. **Methods:** It was a randomised, double-blind trial. Seventy-eight children (up to 18 month of life) with mild to moderate bronchiolitis hospitalised in Pediatric Unit Hospital of Zdroje were enrolled. The infants received inhalation of salbutamol (0.15 mg/kg, max. 1.5 mg = 1.5 ml) dissolved in 3 ml 3% saline – treatment group ($n = 41$), or 3 ml 0.9% saline – control group ($n = 37$). The therapy was repeated six times daily until discharge. The duration of hospital stay and rapidity of clinical improvement were assessed. **Results:** Taking the significance level specified at 0.05 into account, there were no statistically significant differences in the length of hospital stay, with 3.06 ± 1.613 days in the treatment group and 3.11 ± 1.634 days in the control group ($p = 0.43$). Neither were observed statistically significant differences in clinical severity scores after 24, 48 and 72 h ($p_{24} = 0.192$, $p_{48} = 0.425$, $p_{72} = 0.220$). The positive rate for RSV was 53%. No significant adverse events, such as bronchospasm, were observed. **Conclusions:** Nebulised 3% saline (with salbutamol) is not superior to 0.9% (with salbutamol) in the treatment of mild to moderate bronchiolitis.

Introduction

Bronchiolitis is the most frequent clinical manifestation of lower respiratory tract infection in small children and toddlers, with viruses being the most common aetiological factor among which respiratory syncytial virus (RSV) is responsible for 75–90% of infections. At the same time the RSV infection is responsible for the most severe clinical presentation of bronchiolitis [1, 2]. Typical symptoms are:

* *Corresponding author at*: Department of Pediatrics, Allergology and Pulmonology, Hospital of Zdroje, ul. Mączna 4, 70-780 Szczecin, Poland. Tel.: +48 691961925.
E-mail address: krpekrul@wp.pl (K. Ratajczyk-Pekrul).
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elongated expiration with the presence of wheezes and crepitations in chest auscultation preceded by several days of upper respiratory tract infection. In the course of the disease the small bronchi are inflamed, with oedema and congestion of mucous and submucous membranes as well as necrosis and exfoliation of respiratory syncytial cells which leads to accumulation of a thick mucus in large volume. All above mentioned changes lead to massive bronchial obstruction, in which smooth muscle cells play a minor part [3, 4].

It has been proven that the disturbance of mucociliary transport plays a significant role in pathogenesis of bronchiolitis, similarly as in cystic fibrosis and other chronic respiratory tract disorders [5, 6].

Respiratory tract's epithelium is covered by liquid airway surface layer (ASL), which is composed of two parts – external mucus layer (ML) and situated beneath it periciliary layer (PCL). Effective mucociliary transport is dependant mainly on the proper width of PCL (about 7 μm) which ensures correct movement of the cilia. The role of ML is to absorb and transport impurities and to regulate proper hydration of PCL [6, 7].

Maintaining a constant, optimal composition of an ASL is possible due to multiple conductance regulators localised on the proximal end of epithelial cells [8]. Impaired function of one of them – cystic fibrosis transmembrane conductance regulator (CFTR) – is an underlying cause of cystic fibrosis. As proposed by Mandelberg et al. [5], in RSV bronchiolitis aside above-mentioned pathological changes, there is a disturbed function of the channels that regulate ASL's composition which in consequence disrupts arrangement of ML/PCL layers and leads to inappropriate mucociliary transport.

In vitro and clinical research have shown the beneficial influence of concentrated saline nebulisations on mucociliary transport, with the greatest influence in patients with cystic fibrosis [9]. This solution, due to its osmotic properties, draws water out from submucous membrane, reduces oedema and restores appropriate composition of an ASL. Additionally saline in hypertonic concentrations improves rheological properties of the mucus, stimulates excretion of PGE2 which promotes the movement of cilia and induces cough to further clear the airways mechanically [10–12]. Since 2002 several clinical studies have been published, most of which positively evaluated the clinical effectiveness of concentrated saline nebulisations (3–5–7%) in patients with bronchiolitis [13]. The present publication is consecutive to above-mentioned ones.

Methods

Patients

Children with clinical diagnosis of bronchiolitis were enrolled into the research. The main author was the only one to qualify patients to take part in the study. Bronchiolitis was diagnosed based on clinical symptoms: prolonged expiration, wheezes and crepitations in patients with a few-day-long history of viral infection of upper respiratory tract. Additional criteria were: age 0–18 months of life, haemoglobin oxygen saturation ≤95% or Wang Index ≥5 upon admission (Table I) [14]. Pre-term babies <34 Hbd, children with chronic cardiac or respiratory disease, immunological deficiencies, two or more episodes of bronchial obstruction, children treated with systemic glucocorticosteroids, or ones that did receive a hypertonic saline nebulisation in last 24 hrs prior to admission, or with saturation <85% were excluded. Children with bronchial obstruction in history, but not fulfilling any of the major (parental asthma – medical diagnosis, patient egzema – medical diagnosis) and more than one of the minor criteria (allergic rhinitis – medical diagnosis, eosinophilia ≥4%, wheezing apart from colds) of Asthma Predictive Index (API) were qualified [15]. The parents or legal guardians gave signed consent for their children to participate in the study. The research was approved by the local Bioethical Committee.

Study design

The research took place during two periods of seasonal increase in bronchiolitis incidence in years 2011–2013, in the Department of Pediatrics, Allergology and Pulmonology, Hospital of Zdroje in Szczecin. For every patient a random variable from a binomial distribution was generated by a computer. Based on this number patient was given a nebulisation. The number patient enlisted under was known only to the personnel preparing the nebulisations, and it was not revealed to the doctors and nurses taking care of patient, or to legal guardians. The unblinding took place after the research programme was completed.

Upon enrolling patients had to undergo: immunochromatic test for RSV, throat cultures, complete blood count, CRP, serum ions, urinalysis, arterial blood gas, A-P chest radiograph. All patients were examined twice a day – in the morning and in the evening. Patients were evaluated

Table I – Wang scale[a]

	0	1	2	3
Respiratory rate	<30	31–45	46–60	>60
Wheezing	None	Terminal expiratory or only with stethoscope	Entire expiration or audible on expiration without stethoscope	Inspiration and expiration without stethoscope
Retraction	None	Intercostal only	tracheosternal	Nasal flaming
General condition	Normal			Irritable, poor feeding, lethargic

0–4 mild disease; 5–8 moderate disease; 9–12 severe disease.
[a] Adapted from Wang et al. [14].