International Immunopharmacology 54 (2018) 198–209

Contents lists available at ScienceDirect

International Immunopharmacology

journal homepage: www.elsevier.com/locate/intimp

Review

Broncho-Vaxom in pediatric recurrent respiratory tract infections: A systematic review and meta-analysis

Ju Yin[a], Baoping Xu[a], Xiantao Zeng[b,c,d], Kunling Shen[a,*]

[a] Department of Respiratory, Beijing Children's Hospital, Capital Medical University, China National Clinical Research Center for Respiratory Diseases, 100045 Beijing, China
[b] Center for Evidence-Based and Translational Medicine, Zhongnan Hospital of Wuhan University, Wuhan 430071, China
[c] Center for Evidence-Based and Translational Medicine, Wuhan University, Wuhan 430071, China
[d] Department of Evidence-Based Medicine and Clinical Epidemiology, The Second Clinical College, Wuhan University, Wuhan 430071, China

ARTICLE INFO

Keywords:
Broncho-Vaxom
Pediatric recurrent respiratory infections
Meta-analysis
Efficacy
Safety

ABSTRACT

Objectives: Assess the efficacy and safety of Broncho-Vaxom in pediatric recurrent respiratory tract infections (RRTIs).

Methods: Published randomized controlled trials (RCTs) of Broncho-Vaxom for pediatric RRTI were searched using PubMed, Embase, Cochrane Library, CBM, CNKI, WanFang Data, and VIP databases up to January 2017. Risk of bias was evaluated in accordance to the guidelines of the Cochrane collaboration and the level of evidence was graded according to the GRADE.

Results: 53 RCTs involving 4851 pediatric patients were included in this meta-analysis. It showed that Broncho-Vaxom was positively correlated with a reduction in the frequency of respiratory infection [MD = −2.33, 95% CI (−2.75, −1.90), P < 0.00001] compared to the control group. The Broncho-Vaxom group was more effective than control groups in relation to the duration of antibiotics course, infections, fever, cough, and wheezing, increasing serum immunoglobulin levels (IgG, IgA or IgM), and T-lymphocytes subtype (CD3+, CD4+, or CD8+). However, Broncho-Vaxom had higher adverse event rates [RR = 1.39, 95% CI (1.02, 1.88), P = 0.04]; these were not serious and did not influence the treatment course.

Conclusion: Broncho-Vaxom shows a good efficacy for pediatric RRTIs on the basis of routine therapy (e.g. anti-infection and antiviral therapy). However, the level of evidence was low and more international multicenter clinical trials are needed to explore the efficacy and safety of Broncho-Vaxom.

1. Introduction

Recurrent respiratory tract infections (RRTIs) are one of the common diseases that are seen in children. It is defined as any upper or lower respiratory tract infections (RTIs) that occurs frequently per year, however, the concept of recurrence remains unclear since there is no generally agreed definition globally. China defines RRTIs through not only considering numbers but also ages (≥7 upper RTIs per year, ≥3 tracheobronchitis per year or ≥2 pneumonias per year if age is 0–2 years, ≥6 upper RTIs per year, ≥2 tracheobronchitis per year or ≥2 pneumonias per year if age is 2–5 years, ≥5 upper RTIs per year, and ≥2 tracheobronchitis per year or ≥2 pneumonias per year if age is 5–14 years) [1]. According to the guidelines of the Dutch College of General Practitioners referral for recurrent RTI is indicated if acute otitis media occurs > 4 times per year, sore throat occurs > 5 times per year, or if otitis media with effusion persists for > 6 months [2]. The duration of RRTIs is longer and it may affect children's growth as well as increase the chances of them suffering from other respiratory diseases as they enter adulthood.

The pathogenesis of RRTIs is complicated by the variety of antimicrobial causes as well as immunological and respiratory diseases [3]. There are no specific guidelines for the treatment of RRTIs at the moment. However, from an epidemiologic point of view, it has been shown that the prevalence of IgA and/or IgG subclass deficiency was 25% in patients with recurrent upper respiratory tract infections, 22% in patients with recurrent pulmonary infections, and 12.3% in patients with recurrent bronchiolitis [4]. IgG subclass deficiency is quite prominent in young children but rare in older children, suggesting a transient immaturity of the immune system as one of the possible pathogenic factors. Defects in the immune system such as common variable immunodeficiency and selective IgA deficiency are known to be linked with frequent respiratory infections by bacteria and viruses [5].

* Corresponding author at: No.56 Nanlishi Road, Xicheng District, 100045 Beijing, China.
E-mail address: kunlingshen1717@163.com (K. Shen).

https://doi.org/10.1016/j.intimp.2017.10.032
Received 16 June 2017; Received in revised form 10 October 2017; Accepted 30 October 2017

Table 1
Clinical data of included studies.

Studies	Sample (T/C)	Interventions		Endpoints	Age (years)[a]	Follow-up time (months)
		T	C			
Maestroni [62]	11/9	1 course	Placebo	①②	1–16	6
Ahrens [61]	83/72	1 course	Placebo	①③	2–16	6
Schaad [60]	45/49	1 course	Placebo	①③	0.67–12	6
Zagar [59]	29/22	1 course	Placebo	①③	4–12	6
Paupe [58]	61/55	1 course	Placebo	③	T6.6 ± 5.3 C7.6 ± 5.3	6
Gomez-Barreto [57]	26/30	1 course	Placebo	①③	T4.7 ± 1.7 C4.0 ± 1.8	6
Jara-Perez [56]	99/100	1 course	Placebo	①③	6–13	6
Tingxi Zhang [55]	15/15	1 course	Routine therapies	①②③⑤⑥	T4.1 ± 1.6 C13.8 ± 1.6	5
Gutierrez-Tarango [54]	26/28	2 courses	Placebo	①③	1–12	12
Schaad [53]	120/100	1 course	Placebo	①	3–8	6
Del-Rio-Navarro [52]	20/20	1 course	Placebo	①③	T4.0 ± 0.9 C4.1 ± 0.9	6
Jie Gao [51]	19/19	1 course	Routine therapies	②	T3–10 C3–10	3
Lihua Huang [48]	38/34	1 course	Routine therapies	②⑥	T3–10 C3–10	6
Junhui Yuan [49]	15/15	1 course	Routine therapies	①②③⑥⑦⑧⑨⑩	T4.0 ± 1.2 C7.1 ± 1.5	6
Huiyu Zhang [50]	36/37	1 course	Routine therapies	①②③⑥⑧⑨⑩	0.5–2.9	6
Jinsong Li [45]	39/38	1 course	Routine therapies	①②⑤⑧	0–8	6
Yu Tan [46]	45/44	1 course	Routine therapies	①③⑥⑧⑨⑩	1–10	6
Yongli Wu [47]	45/45	1 course	Routine therapies	①③⑤⑥	T6.5 ± 1.3 C6.2 ± 1.4	12
Ying Liao [41]	50/49	1 course	Routine therapies	①②③⑤⑥	T1–5 C1–6	12
Haiying Mo [42]	52/52	1 course	Routine therapies	①②③⑤⑦⑧⑨	T4.5 ± 1.5 C5.0 ± 1.5	6
Aiqi Zhang [43]	30/30	1 course	Routine therapies	①②	Not reported	3
Xin Zhao [44]	100/100	1 course	Routine therapies	②	T4.5 ± 1.1 C4.3 ± 1.2	6
Razi [40]	40/35	1 course	Placebo	①③	1–6	12
Hua Fu [36]	50/49	1 course	Routine therapies	①③⑤⑦⑧⑨	T2.3 ± 0.5 C1.9 ± 0.7	3
Yuan Gao [37]	76/83	1 course	Routine therapies	①③⑤⑦⑧	2–5	12
Min Song [38]	32/32	1 course	Routine therapies	②	T4.6 ± 1.9 C4.4 ± 2.0	6
Guoying Ye [39]	50/45	1 course	Routine therapies	③	T4.3 ± 0.7 C4.9 ± 0.9	6
Mingxia Chao [32]	31/30	1 course	Routine therapies	①②③	1–7	12
Beiling Hu [33]	47/46	1 course	Routine therapies	①③⑤⑦⑧	5–12	3
Aiping Liang [34]	36/37	1 course	Routine therapies	①④⑤	1–5	12
Yujing Zhang [35]	46/20	1 course	Routine therapies	①②③⑨	0.75–5	12
Xiongxiong Huang [25]	65/65	1 course	Routine therapies	①②③④⑤	0.58–3	6
Huiqun Ji [26]	35/31	1 course	Routine therapies	①	T3.7 ± 1.5 C3.3 ± 1.7	6
Juhong Li [27]	30/30	1 course	Routine therapies	②③	1.5–3	3
Zhihong Lou [28]	33/33	2 courses	Routine therapies	①④	T3.7 ± 1.9 C3.6 ± 2.0	12
Yuping Zhao [30]	50/50	1 course	Routine therapies	①②④⑤	1–7	12
Diqian Zhuang [31]	60/60	1 course	Routine therapies	②③	5.6 ± 2.8	6
Manfeng Zuo [29]	35/33	1 course	Routine therapies	①②③⑤⑦⑧	1–6	6
Guolin Chen [24]	75/75	1 course	Routine therapies	①②③⑦⑧⑨	T4.3 ± 1.8 C4.5 ± 1.5	6
Guie Li [22]	66/66	2 courses	Routine therapies	①②⑤⑦⑧	4.2 ± 1.6	6
Lancui Lu [23]	55/54	1 course	Routine therapies	①②④⑤	T1–10 C2–9	6
Jiayi Liao [19]	31/31	2 courses	Placebo	①②③	1–12	12
Ya Shen [20]	48/48	1 course	Routine therapies	①②⑤⑦⑧⑨	T3.5 ± 1.6 C3.8 ± 1.8	12
Ling Su [21]	84/84	1 course	Routine therapies	①②④⑤⑥	0–14	12
Shenfeng Gu [14]	40/40	1 course	Placebo	①③⑤⑦⑧	1–12	12
Fei Liu [15]	73/67	1 course	Routine therapies	①②⑦	T5.91 ± 0.38 C5.84 ± 0.34	6
Wei Zhang [16]	17/16	1 course	Routine therapies	①	1–12	12
Hongwen Zhu [17]	30/30	1 course	Routine therapies	①②③④⑤	T1–5 C1–6	6
Shaoxiong Zhuang [18]	30/30	1 course	Placebo	①②④⑤⑥⑦	0.5–4	6
Shiyan Luo [11]	45/45	1 course	Routine therapies	①②③④⑤	T1–14 C1–15	6

(*continued on next page*)