

Efficacy of montelukast for the treatment of pediatric allergic purpura

Li-ping Bai, MB^a, Jing Yu, MM^b, Ya-xin Sun, MM^c, Jiu-mei Wang, MM^{d,*}

Abstract

Background: This study aims to evaluate the efficacy and safety of montelukast for the treatment of patients with pediatric allergic purpura (PAP).

Methods: We will retrieve the following electronic databases from inception to the present: MEDLINE, Embase, CENTRAL, CINAHL, AMED, Chinese Biomedical Literature Database, China National Knowledge Infrastructure Database, Wanfang, and VIP database without language limitation. Two authors will carry out study selection, data extraction, and quality evaluation independently. RevMan V5.3 software will be used for statistical software.

Results: This study will summarize high-quality evidence-based medicine to evaluate the efficacy and safety of montelukast for the treatment of PAP.

Conclusion: This study will provide strong evidence to determine whether montelukast is an effective and safety treatment for PAP.

Systematic review registration: PROSPERO CRD42019145472.

Abbreviations: Ig = immunoglobulin, PAP = pediatric allergic purpura, RCTs = randomized controlled trials.

Keywords: efficacy, montelukast, pediatric allergic purpura, safety

1. Introduction

Pediatric allergic purpura (PAP) is a very common hemorrhagic disease among pediatric population in clinic.^[1–3] It is often characterized as a small-vessel nonthrombocytopenic systemic vasculitis with the deposition of immune complexes containing immunoglobulin (Ig) A.^[4–6] Such disorder manifests as a palpable purpuric rash, arthralgia, gastrointestinal, and renal disorders.^[7–9] It has been estimated that the annual incidence of PAP is about 14 cases per 100,000 children with male to female rate of 1.2 to 1.65.^[10,11] Unfortunately, its etiology is still unknown.

The current clinical management of PAP mainly includes rituximab, chylothorax, triptolide, fosinopril, prednisone, vitamin E, and Chinese herbal medicine.^[12–17] However, up to date, there is no ideal intervention to treat this disorder. Previous studies have reported that montelukast has been widely used for the treatment of PAP.^[18–33] However, there is still no consistent conclusion of its

efficacy for PAP. Therefore, this study will systematically explore the efficacy and safety of montelukast for treating PAP.

2. Methods

2.1. Ethics and dissemination

This study will not analyze individual data, thus no ethic approval is needed. The results of this study are expected to be published in a peer-review journal.

2.2. Inclusion criteria for study selection

2.2.1. Type of studies. We will include randomized controlled trials (RCTs) of montelukast for the treatment of PAP. Any other types of studies, including nonclinical studies and non-RCTs, will be excluded.

2.2.2. Type of participants. Any children diagnosed with PAP will be eligible for inclusion, regardless their race and gender.

2.2.3. Type of interventions. Any forms of montelukast will be included in the experimental group. However, we will exclude managements of montelukast combined with other therapies.

In the control group, participants can receive any treatments, except any types of montelukast.

2.2.4. Type of outcome measurements. Outcomes consist of levels of urinary beta-2 microglobulin; levels of serum IgA and IgE; disappearance time of abdominal pain, arthralgia, and purpura; quality of life (measured by any related scales, such as Quality of Life scale for Children); and adverse events.

2.3. Search methods for the identification of studies

2.3.1. Electronic searches. We will retrieve the following electronic databases from inception to the present: MEDLINE,

This study is partly supported by Heilongjiang Provincial Higher Education Fundamental Business Expenses Research Project (2018-KYYWFMY-0089).

The authors have no conflicts of interest to disclose.

^a Department of Pediatric Medicine, ^b Department of Endocrinology, Affiliated Hongqi Hospital of Mudanjiang Medical University, ^c Department of Library, Mudanjiang Medical University, ^d Department of Dermatology, Affiliated Hongqi Hospital of Mudanjiang Medical University, Mudanjiang, China.

* Correspondence: Jiu-mei Wang, Department of Dermatology, Affiliated Hongqi Hospital of Mudanjiang Medical University, No 5 Tongxiang Street, Aimin District, Mudanjiang 157011, China (e-mail: Jiumeiwang2000@outlook.com).

Copyright © 2019 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the Creative Commons Attribution License 4.0 (CCBY), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

How to cite this article: Bai LP, Yu J, Sun YX, Wang JM. Efficacy of montelukast for the treatment of pediatric allergic purpura. *Medicine* 2019;98:39(e17239).

Received: 20 August 2019 / Accepted: 26 August 2019

<http://dx.doi.org/10.1097/MD.00000000000017239>

Table 1	
Search strategy used in MEDLINE database.	
Number	Search terms
1	Pediatric allergic purpura
2	Henoch–Schönlein purpura
3	Henoch–Schönlein purpura
4	Spring fever
5	Children
6	Or 1–5
7	Montelukast
8	Singulair
9	Leukotriene inhibitor
10	Leukotriene antagonist
11	Or 7–10
12	Randomized controlled trials
13	Randomized controlled trials
14	Clinical trial
15	Randomized
16	Randomly
17	Allocation
18	Blind
19	Control
20	Comparator
21	Placebo
22	Sham
23	Or 12 and 22
24	6 and 11 and 23

Embase, CENTRAL, CINAHL, AMED, Chinese Biomedical Literature Database, China National Knowledge Infrastructure Database, Wanfang, and VIP database without language limitation. The detailed strategy for searching the MEDLINE database is shown in Table 1. Equivalent search strategy will be adapted in other electronic databases.

2.3.2. Other resources. Literature records, such as conference proceedings, dissertations, research projects, and reference lists of relevant reviews will also be searched.

2.4. Data collection and analysis

2.4.1. Selection of studies. Prior to the study selection, an eligibility criteria and later procedures will be built by all authors through discussion. All literature records will be confirmed by 2 independent authors based on the previous designed eligibility criteria. Any discrepancies between 2 authors will be solved by consensus with the help of a 3rd author. Authors will read the titles and abstracts of all search records to select studies suitable for inclusion. Then, all irrelevant and duplicated literature will be excluded. After that, all remaining studies will be read by full-texts to check if they meet the final inclusion criteria. The procedure of study selection will be presented in the flow diagram with specific reason for each excluded study at different stages.

2.4.2. Data collection and management. Before data extraction, a standard data collection sheet will be created after discussion among all authors. Two independent authors will collect data using such previous designed form. If 2 authors have different views, this issue will be solved through consultation with a 3rd author. The collected items consist of title, 1st author, publication time, region, patient characteristics, study setting, sample size, study methods, details of interventions in the experimental and control group, outcome measurements, adverse events, and any other detailed information.

2.4.3. Risk of bias assessment. Two authors will independently evaluate seven domains of bias using Cochrane risk of bias tool. Each domain will be further classified into 3 levels of bias: high, unclear, and low risk of bias. Any differences regarding the risk of bias assessment between 2 authors will be solved by discussion or consultation with a 3rd independent author in this study.

2.4.4. Treatment effect measurement. Discontinuous outcome data will be calculated with risk ratio with 95% confidence intervals. Continuous outcome data will be calculated with mean difference or standardized mean difference with 95% confidence intervals.

2.4.5. Dealing with missing data. The 1st authors will be contacted by email or telephone to require the missing data if possible. If that data cannot be inquired, we will analyze the available data and will discuss its potential influence in the discussion section.

2.4.6. Assessment of heterogeneity. Higgins I^2 test will be utilized to test inconsistencies among eligible studies. The cutoff point for I^2 test is 50%. $I^2 \leq 50\%$ indicates acceptable heterogeneity among studies. $I^2 > 50\%$ means the existence of substantial heterogeneity among studies.

2.4.7. Assessment of reporting biases. If more than 10 eligible RCTs will be included in this study, potential reporting bias will be investigated by funnel plot^[34] and Egger regression test.^[35]

2.4.8. Data synthesis and analysis. RevMan V5.3 software will be utilized for data synthesis and meta-analysis. If $I^2 \leq 50\%$, a fixed-effect model will be used for data synthesizing, and meta-analysis will be carried out if the same outcome of sufficient studies are included. If $I^2 > 50\%$, a random-effects model will be applied for data pooling, and subgroup analysis will be conducted. If there is still significant heterogeneity after subgroup analysis, we will not perform meta-analysis. Instead, we will report outcome results as a narrative summary.

2.4.9. Subgroup analysis. Subgroup analysis will be performed to identify possible reasons for significant heterogeneity based on the different location, treatments, comparators, and outcomes.

2.4.10. Sensitivity analysis. When sufficient data are available, sensitivity analysis will be carried out to explore the stability of pooled outcome results after eliminating low-quality studies.

3. Discussion

Due to the increasing incidence of PAP among the pediatric population, and consequently the rise in need for the management, it is very essential for both clinicians and patients to explore an effective therapy with satisfied safety profile such as montelukast. However, there is still lack of evidence-based medicine support regarding the efficacy and safety of montelukast for children with PAP. Through this study, we hope to eliminate this gap, and will offer an up-to-date evidence of montelukast for the treatment of PAP. In the event of inconclusive evidence, this study will explore an area for both clinical practice and further research. Thus, we believe this study is very helpful for children who have PAP and are keen to try montelukast therapy.

Author contributions

Conceptualization: Ya-xin Sun, Jiu-mei Wang.

Data curation: Jing Yu, Jiu-mei Wang.

Formal analysis: Jing Yu, Ya-xin Sun.

Funding acquisition: Jiu-mei Wang.

Investigation: Jiu-mei Wang.

Methodology: Jing Yu, Ya-xin Sun.

Project administration: Jiu-mei Wang.

Resources: Jing Yu, Ya-xin Sun.

Software: Jing Yu, Ya-xin Sun.

Supervision: Jiu-mei Wang.

Validation: Jing Yu, Ya-xin Sun, Jiu-mei Wang.

Visualization: Jing Yu, Ya-xin Sun, Jiu-mei Wang.

Writing – original draft: Jing Yu, Ya-xin Sun, Jiu-mei Wang.

Writing – review & editing: Jing Yu, Ya-xin Sun, Jiu-mei Wang.

References

- [1] Hetland LE, Susrud KS, Lindahl KH, et al. Henoch-Schönlein purpura: a literature review. *Acta Derm Venereol* 2017;97:1160–6.
- [2] Dalpiaz A, Schwamb R, Miao Y, et al. Urological manifestations of Henoch-Schönlein purpura: a review. *Curr Urol* 2015;8:66–73.
- [3] Xiong LJ, Mao M. Current views of the relationship between *Helicobacter pylori* and Henoch-Schönlein purpura in children. *World J Clin Pediatr* 2016;5:82–8.
- [4] Pohl M. Henoch-Schönlein purpura nephritis. *Pediatr Nephrol* 2015; 30:245–52.
- [5] Davin JC. Henoch-Schönlein purpura nephritis: pathophysiology, treatment, and future strategy. *Clin J Am Soc Nephrol* 2011;6:679–89.
- [6] Saulsbury FT. Henoch-Schönlein purpura. *Curr Opin Rheumatol* 2010;22:598–602.
- [7] Tizard EJ, Hamilton-Ayres MJ. Henoch-Schönlein purpura. *Arch Dis Child Educ Pract Ed* 2008;93:1–8.
- [8] Ebert EC. Gastrointestinal manifestations of Henoch-Schönlein purpura. *Dig Dis Sci* 2008;53:2011–9.
- [9] Pillebout E, Niaudet P. Henoch-Schönlein purpura. *Rev Prat* 2008;58:507–11.
- [10] Rostoker G. Schönlein-Henoch purpura in children and adults: diagnosis, pathophysiology and management. *Biodrugs* 2001;15:99–138.
- [11] Yang YH, Hung CF, Hsu CR, et al. A nationwide survey on epidemiological characteristics of childhood Henoch-Schönlein purpura in Taiwan. *Rheumatology* 2005;44:618–22.
- [12] Crayne CB, Eloseily E, Mannion ML, et al. Rituximab treatment for chronic steroid-dependent Henoch-Schönlein purpura: 8 cases and a review of the literature. *Pediatr Rheumatol Online J* 2018;16:71.
- [13] Cogar BD, Groshong TD, Turpin BK, et al. Chylothorax in Henoch-Schönlein purpura: a case report and review of the literature. *Pediatr Pulmonol* 2005;39:563–7.
- [14] Zhang J, Lv J, Pang S, et al. Chinese herbal medicine for the treatment of Henoch-Schönlein purpura nephritis in children: a prospective cohort study protocol. *Medicine (Baltimore)* 2018;97:e11064.
- [15] Wu L, Mao J, Jin X, et al. Efficacy of triptolide for children with moderately severe Henoch-Schönlein purpura nephritis presenting with nephrotic range proteinuria: a prospective and controlled study in China. *Biomed Res Int* 2013;2013:292865.
- [16] Xu J, Cong H, Sheng Y. Efficacy of foscipril on proteinuria in children with Henoch-Schönlein purpura nephritis [in Chinese]. *Zhongguo Dang Dai Er Ke Za Zhi* 2009;11:229–30.
- [17] Erdoğan O, Oner A, Aydın A, et al. Effect of vitamin E treatment on the oxidative damage occurring in Henoch-Schönlein purpura. *Acta Paediatr* 2003;92:546–50.
- [18] Khanna S, Uniyal B, Kumar D, et al. Henoch-Schönlein purpura probably due to montelukast presenting as subacute intestinal obstruction. *Indian J Gastroenterol* 2005;24:86.
- [19] Wu SH, Liao PY, Chen XQ, et al. Add-on therapy with montelukast in the treatment of Henoch-Schönlein purpura. *Pediatr Int* 2014;56: 315–22.
- [20] He GF. Clinical efficacy of montelukast sodium in the treatment of recurrent allergic purpura in children. *J Math Med* 2019;32:1192–4.
- [21] Wang XH. Clinical efficacy of montelukast sodium in the treatment of recurrent allergic purpura in children. *Chin Commun Phys* 2019;35:68.
- [22] Wang L. Therapeutic effect of montelukast sodium and desloratadine on children with allergic purpura. *Chin J Integr Trad West Cardiol* 2019;7:181.
- [23] Su HZ. Clinical efficacy of montelukast sodium in the treatment of children with allergic purpura. *Heilongjiang Med* 2019;32:319–20.
- [24] Yu ZL. The efficacy of montelukast sodium combined with loratadine in the treatment of children with allergic purpura. *Chin Prescr Drug* 2019;17:80–1.
- [25] Zhang YT, Wei PP. Efficacy evaluation of montelukast sodium combined with Yupingfeng granule in the treatment of allergic purpura in children. *Chin Commun Phys* 2019;35:111–3.
- [26] Zhu AH. Analysis of clinical efficacy of montelukast sodium in the treatment of recurrent allergic purpura in children. *Chin Pract Med* 2019;14:77–8.
- [27] Chen TX, Xu Y, Xie MH, et al. Clinical efficacy of montelukast sodium in the treatment of recurrent allergic purpura in children. *J Clin Ration Drug Use* 2019;12:86–7.
- [28] Wu MM. The efficacy of montelukast sodium in the treatment of children with allergic purpura. *World Latest Med Inform Dig* 2018;18:87.
- [29] Hui J. Clinical observation of the efficacy of montelukast sodium in the treatment of recurrent allergic purpura in children. *North Med* 2018;15:61–2.
- [30] Hou YF. Effect of montelukast sodium on recurrence rate of recurrent allergic purpura in children. *Clin Res* 2018;26:83–5.
- [31] Wang HL, Chen JL. Effect and safety of montelukast sodium on recurrent allergic purpura in children. *Clin Med Res Pract* 2018;3:75–6.
- [32] Li X. Clinical efficacy of montelukast sodium in the treatment of recurrent allergic purpura in children. *Contemp Med* 2018;24:103–5.
- [33] Zheng GH. The efficacy of montelukast sodium in the treatment of recurrent allergic purpura in children. *J Clin Ration Med* 2018;11:72–3.
- [34] Higgins JPT, Green S. *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available at: <http://www.cochrane-handbook.org>. Accessed August 1, 2019.
- [35] Egger M, Davey Smith G, Schneider M, et al. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;315:629–34.