Editorial
Allergy Asthma Immunol Res. 2016 July;8(4):279-281.
http://dx.doi.org/10.4168/aair.2016.8.4.279
pISSN 2092-7355 • eISSN 2092-7363

AAIR
Allergy, Asthma & Immunology Research

Is Montelukast Benefical in Children With Atopic Dermatitis?

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Atopic dermatitis (AD) has a wide range of clinical symptoms with a tendency toward chronic relapse. Patients with mild AD can be managed with use of emollients after bathing and use of topical corticosteroids or calcineurin inhibitors. On the other hand, those with moderate to severe AD often require systemic treatment, which could induce adverse effects and demand careful monitoring, particularly in long-term use. In fact, systemic steroids are recommended for limited cases of acute flare-up as a short therapeutic course due to an overall unfavorable risk-benefit profile. According to meta-analysis evaluating the efficacy and safety of systemic treatment in moderate-to-severe AD, cyclosporin A is recommended as a first-line treatment for short-term use, and azathioprine and methotrexate are also recommended as a second- or a third-line treatment.[1] However, long-term use of cyclosporine A was not recommended due to a lack of long-term safety data. In addition, there are patients who show a lack of response to these drugs. Therefore, approaches to develop and/or evaluate systemic treatment modalities based on appropriate assessment of efficacy and safety should be continued.

A thorough understanding of the etiology and pathogenesis of AD is crucial to the appropriate management of AD. Based on emerging evidences that skin barrier dysfunction predisposes to AD development, approaches have been directed toward correction of the primary abnormality in barrier function. However, additional factors are necessary for AD development, and a role of immune dysregulation has been strongly supported.[2,3] In fact, cyclosporine A, a gold standard of systemic therapy in AD, is a representative drug for immunomodulation. For immune dysregulation, Th1/Th2-cell dysregulation, IgE production, dendritic cell signaling, and mast cell hyperactivity have been considered largely attributed to the pathogenesis of AD.[2] Leukotrienes are arachidonic acid metabolites generated from many cells, including mast cells and lymphocytes.[4] Based on important biological effects of cysteinyl leukotrienes, such as potent bronchoconstriction and proinflammatory mediators, in asthma development,[5] their antagonists have been introduced as antiasthmatic medications in the late 1990s. Leukotriene receptor antagonists have also been successfully used in other conditions, particularly in allergic rhinitis. Although the exact mechanism of leukotriene receptor antagonists in AD is uncertain, evidence of enhanced leukotriene production in the pathogenesis of AD provide a theoretical rationale for the use of leukotriene receptor antagonists in AD patients.

Montelukast is a cysteinyl-leukotriene-1 receptor antagonist, which is the most commonly prescribed leukotriene receptor antagonist worldwide with zfirlukast.[7] However, montelukast is not possibly recommended as systemic treatment for AD due to its limited evidence.[1] In order to ensure the efficacy and safety profiles of montelukast in AD management, study results, which are evaluated under a well-designed study, such as a randomized, double-blind, placebo-controlled trial, are warranted. Considering that AD occurs more commonly in children, data tested on children could be more desirable. Encouragingly, montelukast could be a representative drug for systemic treatment as long as the safety is concerned. The absence of major adverse effects allows montelukast to grant a license for children aged 6 years or older.[8] The study to be published in this issue assessed,[11] efficacy and safety of montelukast in children with AD in a randomized double-blind placebo-controlled method, although there have been a few studies reported in the literature.[9,10] They recruited considerable portion of children less than 6 years of age.[10,11] In this study, no significant safety problems were noted in 2- to 6-year-old children,[11] which will encourage further trials of leukotriene receptor antagonists in children with AD.

Eight randomized, double-blind, placebo-controlled trials

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Received: April 5, 2016; Accepted: April 7, 2016.
• There are no financial or other issues that might lead to conflict of interest.

Table. Summary for double-blind, randomized, placebo-controlled trials of montelukast used in AD patients

	Participants		Methods					Results	References		Remarks
	Age (year)	No	Run-in period (week)	Duration (week)	Cross-over	Wash-out period (week)	Clinical Assessment	Efficacy	Authors	Nationality	
Children	6-16	11	2	Total 8 (4+4)	O	2	Score for disease extent & severity	O	Pei et al. (2001)	Hong Kong	
	2-16	25	2	Total 8 (4+4)	O	2	SCORAD	O	Ehlayel et al. (2007)	Qatar	
	2-6	54		Total 16 (8+8)	O	2	SCORAD	No difference	Jeon et al. (2016)	Korea	The latest study
Adult	≥18	8		Total 8 (4+4)	O	2	6 clinical severity score	O	Yanase & David-Bajar (2001)	USA	
	18-28	20		6	X	X	SCORAD	O	Nettis et al. (2002)	Italy	
	16-70	47	2	4	X	X	EASI	No difference	Veien et al. (2005)	Denmark	2-center
		31					SCORAD	O	Rahman et al. (2006)	Bangladesh	Based on abstract
	16-60	54	2	8	X	X	SASSAD	No difference	Friedmann et al. (2007)	UK	2-center

No, number of patients who completed the study.

have reported the efficacy of montelukast not only in children with AD but also in adults with AD, in which the efficacy results were inconsistent regardless of participant age, children or adult (Table).[12-16] The results from 3 studies using a relatively large sample size compared to the other 5 studies, have demonstrated no significant difference in efficacy between the montelukast-treated and placebo-treated groups.[11,14,16] The duration of study[12] and the proportion of extrinsic subgroup of AD have been suggested as factors affected the difference in the result.[6] However, studies to date have not completely evaluated the efficacy of montelukast and the factor affecting its efficacy in AD treatment. Further studies designed with a well-organized system are necessary to determine the efficacy of montelukast.

ACKNOWLEDGMENTS

This work was supported by the National Research Foundation of Korea (NRF) grant, funded by the Korean government (MSIP) (No. NRF-2014R1A2A2A09051812).

REFERENCES

1. Roekevisch E, Spuls PI, Kuester D, Limpens J, Schmitt J. Efficacy and safety of systemic treatments for moderate-to-severe atopic dermatitis: a systematic review. J Allergy Clin Immunol 2014;133:429-38.
2. Elias PM, Steinhoff M. "Outside-to-inside" (and now back to "outside") pathogenic mechanisms in atopic dermatitis. J Invest Dermatol 2008;128:1067-70.
3. Boguniewicz M, Leung DY. Atopic dermatitis: a disease of altered skin barrier and immune dysregulation. Immunol Rev 2011;242:233-46.
4. Murphy RC, Hammarström S, Samuelsson B. Leukotriene C: a slow-reacting substance from murine mastocytoma cells. Proc Natl Acad Sci U S A 1979;76:4275-9.
5. Busse WW. Leukotrienes and inflammation. Am J Respir Crit Care Med 1998;157:S210-3.
6. Rackal JM, Vender RB. The treatment of atopic dermatitis and other dermatoses with leukotriene antagonists. Skin Therapy Lett 2004;9:1-5.
7. Dempsey OJ. Leukotriene receptor antagonist therapy. Postgrad Med J 2000;76:767-73.
8. Price D. Tolerability of montelukast. Drugs 2000;59 Suppl 1:35-42.
9. Pei AY, Chan HH, Leung TF. Montelukast in the treatment of children with moderate-to-severe atopic dermatitis: a pilot study. Pediatr Allergy Immunol 2001;12:154-8.
10. Ehlayel MS, Bener A, Sabbah A. Montelukast treatment in children with moderately severe atopic dermatitis. Eur Ann Allergy Clin Immunol 2007;39:232-6.
11. Jeon YH, Min TK, Yang HJ, Pyun BY. A double-blind, randomized, crossover study to compare the effectiveness of montelukast on atopic dermatitis in Korean children. Allergy Asthma Immunol Res 2016;8:305-11.
12. Yanase DJ, David-Bajar K. The leukotriene antagonist montelukast as a therapeutic agent for atopic dermatitis. J Am Acad Dermatol 2001;44:89-93.
13. Nettis E, Pannofino A, Fanelli M, Ferrannini A, Tursi A. Efficacy and tolerability of montelukast as a therapeutic agent for severe atopic dermatitis in adults. Acta Derm Venereol 2002;82:297-8.
14. Veien NK, Busch-Sørensen M, Stausbøl-Grøn B. Montelukast treatment of moderate to severe atopic dermatitis in adults: a randomized, double-blind, placebo-controlled trial. J Am Acad Dermatol 2005;53:147-9.

15. Rahman ML, Choudhury AM, Islam MM. Effectiveness of montelukast in the treatment of atopic dermatitis. Mymensingh Med J 2006;15:85-8.

16. Friedmann PS, Palmer R, Tan E, Ogboli M, Barclay G, Hotchkiss K, et al. A double-blind, placebo-controlled trial of montelukast in adult atopic eczema. Clin Exp Allergy 2007;37:1536-40.