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ARTIKEL LAPORAN KASUS

MONTELUKAST AND DESLORATADINE COMBINATION THERAPY IN ACUTE URTICARIA PATIENT UNRESPONSIVE TO SYSTEMIC ANTIHISTAMINE AND CORTICOSTEROID

TERAPI KOMBINASI MONTELUKAST DAN DESLORATADIN PADA PASIEN URTIKARIA AKUT YANG TIDAK RESPONSIF DENGAN ANTIHISTAMIN DAN KORTIKOSTEROID

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ABSTRAK
Pendahuluan: Urtikaria adalah penyakit kulit yang umum ditemukan, ditandai adanya edema setempat yang timbul mendadak dan menghilang dalam 24 jam. Antihitamin-H1 adalah obat pilihan untuk urtikaria yang kadang-kadang dikombinasikan dengan kortikosteroid sistemik. Penggunaan montelukast pada kasus urtikaria masih jarang dilaporkan.
Laporan Kasus: Seorang perempuan berusia 21 tahun datang dengan keluhan bentol-bentol gatal di seluruh tubuhnya dengan sensasi terbakar yang dominan sejak 5 hari yang lalu. Keluhan tetap tidak berkurang bahkan setelah pemberian desloratadine sampai empat kali dosis dan kombinasi metilprednisolon 16 mg. Keluhan akhirnya membaik setelah pasien diberi montelukast 10 mg perhari dikombinasikan dengan desloratadine 5 mg dua kali sehari.
Diskusi: Leukotrien adalah mediator lipid yang dapat meningkatkan vasopermeabilitas dan vasodilatasi pada kulit. Perbaikan gejala yang terjadi setelah pemberian terapi kombinasi montelukast dan desloratadine membuktikan keterlibatan leukotriene pada patogenesis kasus urtikaria akut pasien ini.
Simpulan: Terapi kombinasi montelukast dan desloratadine dapat bermanfaat pada beberapa kasus urtikaria akut. Studi lebih lanjut dengan kontrol yang cukup dapat dilakukan untuk menentukan efektivitas montelukast yang dikombinasikan dengan antihistamin untuk kasus urtikaria akut.
Kata Kunci: urtikaria akut, antihistamin, antileukotrien, montelukast

ABSTRACT
Introduction: *Urticaria is a common skin disease, characterized by localized edema that appears suddenly and disappears within 24 hours. Antihitamin-H1 is the drug of choice for urticaria which is sometimes combined with systemic corticosteroids. The use of montelukast in cases of urticaria is still rarely reported.*
Case Report: *A 21-year-old woman came with complaint of itchy bumps all over her body with a dominant burning sensation since 5 days ago. Complaint remained unchanged even after administering up to four doses of desloratadine and a combination of 16 mg methylprednisolone. The complaint finally improved after the patient was given montelukast 10 mg per day combined with desloratadine 5 mg twice a day.*
Discussion: *Leukotriene is a lipid mediator that can increase vasopermeability and vasodilation in the skin. The improvement in symptoms that occurred after the combination therapy of montelukast and desloratadine proved the involvement of leukotrienes in the pathogenesis of this patient's case of acute urticaria.*
Conclusion: *Combination therapy with montelukast and desloratadine may be useful in some cases of acute urticaria. Further studies with sufficient control may be conducted to determine the effectiveness of montelukast in combination with antihistamines for cases of acute urticaria.*
Key Words: *acute urticaria, antihistamine, antileukotriene, montelukast*

INTRODUCTION

Urticaria is a common skin disorder, and a manifestation of a heterogenous group of diseases, characterized by wheals that appear suddenly and disappear within 24 hours, accompanied by itching or burning sensation.[1–3] External triggers or idiopathic causes can lead to inflammatory process involving upper layer of the dermal skin. Acute urticaria is defined if it lasts less than 6 weeks. Most acute episodes of urticaria are caused by food allergy or to viral illnesses, especially in children. Urticaria occurs in approximately 15 to 20% of the general population at least once in their lifetime.[4]

H1 antihistamines are the drug of choice for urticaria, which are sometimes combined with systemic corticosteroids.[1,2] Although, histamine is an important key in mediating mast cell degranulation, leukotrienes also play a role as a potent proinflammatory mediators. Leukotrienes derived from arachidonic acid through the 5-lipoxygenase pathway and its activity can be blocked by leukotriene receptor antagonist (LTRA).[5]

Montelukast is a LTRA that is often used to treat chronic bronchial asthma and relieve allergic symptoms with marked selectivity and affinity to cysteinyl leukotriene receptor type 1.[6] The use of LTRA has been suggested in patients with antihistamines-resistant urticaria. Montelukast has been used to treat various form of urticaria, including urticaria related to food and chronic urticaria, as monotherapy and combination therapy with antihistamines.[7]

The use of montelukast in some cases of chronic urticaria has been reported with varied therapeutic responses, but its use in acute urticaria cases is still rare.[8] We report montelukast therapy in an acute urticaria patient with a predominant symptom of burning sensation on the skin that is unresponsive to the administration of a combination of antihistamines and systemic corticosteroids.

CASE ILLUSTRATION

A 21-year-old female college student came with a major complaint of itchy wheals on her body. Since 5 days ago, the wheals appeared after she drank a glass of chocolate milk and was exposed to ammonium sulfate vapor in a laboratory. Wheals appeared on the body and extremities, accompanied by a dominantly burning sensation, with no sign of angioedema. She had consumed one chlorpheniramine maleat tablet, and the symptoms were slightly improved, but reappeared with a larger size and quantity. We diagnosed the patient with acute urticaria, and gave her 5 mg of desloratadine. Soon after she took it, the wheals were reduced. A few hours later the patient felt a burning sensation in some areas of the skin, followed by the appearance of wheals in the site location. We then increased the desloratadine dose up to four times a day, and added one tablet of 16 mg methylprednisolone. The symptoms improved, but one hour later, more severe complaints reappeared along with shortness of breath. She went to the emergency room, and was injected with intravenous dexamethasone. The wheals were reduced, but a few hours later the wheals recurred.

Complete blood count was within normal limit with differential count of leukocytes of 0/0/0/82/12/6. IgE level was 3.4 IU/ml (N: <87). Patient was treated with 10 mg montelukast once a day and 5 mg desloratadine twice a day. A few hours later, she felt prompt improvement of the complaints which totally cleared after seven days of therapy.

Figure 1. The presentation of the wheals on patient's knee

DISCUSSION

Untreated urticaria is associated with high cost in health care facility.[9] The patients also suffer from impaired quality of life, due to diminishes physical function, emotional problems, limitation of sexual relationships and social interaction, also work-related environment. The burden of urticaria needs to be resolved with effective treatment. [9,10]

The principles of acute urticaria therapy according to guidelines from the Cochrane and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group consist of identifying and eliminating the causes of urticaria, avoiding precipitating factors, inducing tolerance, and pharmacological therapy to prevent the release of mediators from mast cells. The recommended pharmacological therapy is second generation antihistamine class 1 (AH1) which can be evaluated every 2-4 weeks, and the dose can be increased up to 4 times. If it is still not resolved, it is recommended to add omalizumab and cyclosporine in addition to giving AH1.[2]

Our patient suffered from acute urticaria that may be spontaneous, but may also be triggered by chocolate milk ingestion or ammonium sulfate exposure, both of which may induce Nonimmunologic Contact Urticaria (NICU). NICU is triggered by immediate contact and occurs without prior sensitization. Due to stimulation of a vasogenic mediator from the cells, especially granulocyte. Histamine will also be released, accompanied by leukotriene, prostaglandin,

substance A, and eicosanoid. Leukotriene is associated with the activation of leukocyte, chemotaxis and phagocytosis. The symptoms of NICU usually occur in the form of wheals accompanied by itching and burning sensation.[11–15] NICU is caused by a wide variety of agents. Its etiology can be classified into: animals, foods, fragrances and flavorings, preservatives, disinfectant, plant, and metal.[15,16] The clinical manifestation vary according to the concentration, site of exposure, mode of exposure, and the substance.[12]

Leukotriene is a lipid mediator derived from arachidonic acid and produced by eosinophils, basophils, and mast cells that is involved in urticarial reaction. It is known to contribute to the pathogenesis of inflammatory diseases of the respiratory tract and skin, such as atopic dermatitis and psoriasis. Cycteinyl leukotriene is also known to improve vasopermeability and vasodilation that can cause wheals and erythema lesions on the skin.[17] When injected to the dermal layer, leukotriene is able to produce a wheal and flare with 100-fold greater potency than histamine. Leukotriene also forms more severe itching sensation than histamine. There are two class of LTRA that have been developed. The first class is leukotriene D4 (LTD4) receptor antagonist, such as montelukast and zafirlukast. The second class blocks 5-lipoxygenase pathway that contributes to leukotriene synthesis, such as zileuton.[18] Montelukast is a novel LTRA that acts selectively, and it is shown to be effective in the therapy of urticaria.[19]

The use of antileukotriene for urticaria cases has been reported in some studies and case reports of chronic urticaria, and is effective as a combination therapy with antihistamines. H1 antihistamine is the key of pharmacotherapy and has been recommended as first-line therapy due to its efficacy and safety profile.[9,19–21] However, there has been no case report of acute urticaria treated with the combination of first class LTRA and H1 antihistamine.[9]

Our patient has tried to avoid things that might cause urticaria and was unresponsive to the combination therapy of antihistamine and corticosteroids, thus we suspected that histamine was not the only inflammatory mediator involved. After we added montelukast in addition to antihistamine therapy, the symptoms were significantly reduced, thus supporting the alleged involvement of leukotriene in the pathogenesis of acute urticaria in our patient.

CONCLUSION

Our patient did not respond well to the use of antihistamines as the first line therapy of acute urticaria. The combination of montelukast and desloratadine is effective in the treatment of acute urticaria in this patient. Further studies and clinical trials with adequate controls should be conducted to define the usefulness of montelukast in combination with antihistamine for acute urticaria.

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