#### SOPHIO GAMKRELIDZE, NINO JOJUA, MAIA SHENGELIA

# THE ROLE OF MONTELUKAST IN MANAGEMENT OF CHILDREN WITH COVID-19 INFECTION

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სოფიო გამყრელიძე, ნინო ჯოჯუა, მაია შენგელია მონტელუკასტის როლი პოსტკოვიდ-19 რესპირაციული სიმპტომების მქონე ბავშვების მენეჯმენტში

ა. წერეთლის სახელმწიფო უნივერსიტეტი, მედიცინის ფაკულტეტი; ქუთაისის უნივერსიტეტი; შპს N3 ბავშვთა პოლილინიკა; ქუთაისი, საქართველო

## რეზიუმე

პოსტკოვიდური სიმპტომების მენეჯმენტი მუდმივი განახლების პროცესშია. ახალი კორონავირუსის გავრცელებული რესპირაციული სიმპტომებიდან აღსანიშნავია მშრალი შემაწუხებელი ხველა. სამედიცინო ლიტერატურაში ძნელია მოიპოვო ინთორმაცია მონტელუკასტის ეფექტურობის შესახებ პოსტკოვიდური რესპირაციული სიმპტომების მქონე ბავშვებში. გემოალნიშნულმა გამოიწვია ჩვენი დაინტერესებაც და ქ. ქუთაისის შპს ბავშვთა N3პოლიკლინიკის ბაზაზე ჩავატარეთ კვლევა პაციენტებში კოვიდ და პოსტკოვიდური პერიოდის მშრალი , შემაწუხებელი ხველის ჩივილებით. კვლევაში მონაწილე 76 (2 დან 18 წლის ასაკის, 43 გოგო და 33 ბიჭი) პაციენტს ხველის ჩივილებით, დაენიშნა გლუკოკორტიკოსტეროიდის ადგილობრივი საინპალიაციო ფორმა-ბუდესონიდი ჯენერიული აქტიური ნივთიერებით და/ან ლეიკოტრიენების რეცეპტორების ანტაგონისტი და/ან ანტიჰისტამინური მედიკამენტები. დაკვირვებამ ცხადყო, რომ მშრალი ხველის კლინიკური ეფექტი უდავოდ გამოვლინდა უფრო მეტად იმ პაციენტებში, რომლებიც ანტიალერგიულ მედიკამენტებს იღებდნენ კომბინაციაში, კორტიკოსტეროიდები, ივულისხმება საინპალიაციო ლეიკოტრიენების რეცეპტორების ანტაგონისტი და/ან ანტიჰისტამინური მედიკამენტები ერთად. კვლევით მიღებული შედეგების ანალიზმა ასევე ცხადყო, რომ განსაკუთრებული კლინიკური ეფექტი დადასტურებულად გამოვლინდა იმ ბავშვებში, რომლებიც იღებდნენ მონტელუკასტს ასაკობრივი დოზირების გათვალისწინებით, მონო თუ კომპლექსურ თერაპიაში ვიდრე პაციენტები, რომელთა მკურნალობის კურსი არ მოიცავდა მონტელუკასტს. კვლევის მონიტორინგმა ნამდვილად დაადასტურა მონტელუკასტის კლინიკური ეფექტი კოვიდ დადებით ბავშვებში გახანგრძლივებული მშრალი ხველით. COVID-19-ის მკურნალობის შედეგების რეესტრი დაგვეხმარება გადავჭრათ კლინიკური გამოწვევა, სადაც დღემდე უფრო მეტი კითხვა გვაქვს, ვიდრე პასუხი.

The pandemic, emerged with the new coronavirus 2019 (COVID-19), has not yet been brought under control, despite serious measures taken all over the world and efforts to control and treat the disease. Up till now, a specific treatment for COVID-19 infection is not available. Management of coronavirus infection especially in children is a continuous process of constant updating. The treatment approach of COVID-19 infection may include montelukast, cysteinyl leukotriene (CysLT) receptor antagonist, and the possibility of decrease severe COVID-19 progression will be mentioned [1,3].

Common symptoms of the novel coronavirus, not only in adult in children too, is dry and lingering cough. The cough is caused by increased bradykinin and its bronchoconstrictor effect, and montelukast, a selective LTD4 antagonist, has an inhibitory effect on bradykinin-induced airway hypersensitivity [2,4]. Montelukast is a potent cysteinyl leukotriene (CysLT) receptor antagonist with anti-inflammatory effects and has been proven to significantly suppress oxidative stress. In addition, the use of montelukast is known to have a decreasing effect on the frequency and severity of wheezing in patients with clinical episodic wheezing (wheezing after an upper respiratory tract infection caused by adenovirus, influenza, metapneumovirus, coronavirus). In these patients, montelukast does not prevent these viral infections, but seems to limit the upper respiratory tract [2,4].

It is difficult find the date about effect of montelukast in children with covid-19 infection. According of this, the aim of the present article was to review the role of montelukast that could be beneficial in management of children with covid-19 infection. Based on gathered theoretical evidence, montelukast should be further tested to prevent and treat COVID-19 outcomes.

The above-mentioned aroused interest and the study of the child patients, with the symptoms like a lingering cough was conducted on the basis of the N 3 Children clinic (Kutaisi, Georgia). 76 patients involved in the study (2 to 18 years of age, 43 girls, 33 boys) with the symptoms of dry and lingering cough were prescribed an inhaled form of local glucocorticosteroid – Budesonide with generic active substance and/or leukotriene receptor antagonist, and/or antihistamines. According to treatment design, the patients were divided into treatment groups. One part of the group – 18 patients (23%) was prescribed only inhalers, one part 20 (27%) – leukotriene receptor antagonists, one part -19 (25%) – antihistamines and the last one 19 patients (25%) – all three antihistamines simultaneously, respectively. The patients take montelukast for oral dosage form (chewable tablets): children 2 to 5 years of age - 4 mg once a day in the evening; children 6 to 14 years of age - 5 milligrams (mg) once a day in the evening. Duration of treatment was 14 days.

Follow-up showed that the clinical effect of dry cough was more pronounced in children administering montelukast only or in combination in comparison with the patients taking only local glucocorticosteroid and antihistamines, such as desloratedine or levocetirizine separately, on a selective basis. Relatively good clinical efficacy was revealed in children taking agents in combination, that is, the simultaneous administration of inhaled corticosteroids, leukotriene receptor antagonists, and/or antihistamines. Monitoring of clinical results showed reduction in dry cough as a symptom after using montelukast; in addition, XR monitoring has confirmed the rapid and more effective relief of inflammatory foci in children actively and systematically actively and systematically received montelukast, compared with those not taking the mentioned agents to relieve dry cough. It was also noted that the indicator of respiratory distress alleviation degree was not in correlation with treatment using the above medications.

Montelukast works as a cysteinyl leukotriene (CysLT) receptor antagonist. Leukotrienes are inflammatory mediators produced by the immune system. They promote bronchoconstriction, inflammation, microvascular permeability, and mucus secretion. Montelukast has an anti-inflammatory effect with bradykinin and leukotriene antagonist; It suggests that it may be effective to use it, possibly at high doses, in order to reduce its severity during the course of the disease or before the disease occurs fully in people at risk. The healing effects of montelukast on these damages can be seen.

Analysis of the obtained results revealed that 65 (85%) patients, who underwent the above treatment with montelukast, had sooth in cough as a symptom, however, the clinical effect was obtained nearly in 10 days after treatment, while 11 (15%) patients failed to achieve clinical efficacy applying this treatment regimen. The obtained results indicate the efficacy of montelukast, as symptomatic agents, for the treatment of Covid-19 patients with a dry and lingering cough. Research monitoring has also confirmed the ancillary effect of montelukast. The issue of COVID-19 infection management in children still remains open and research in this direction is still active around the world.

#### References:

- 1. Zhang J.J., Dong X., Cao Y.Y., Yuan Y.D., Yang Y.B., Yan Y.Q. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. *Allergy*. 2020 PubMed PMID: 32077115. Epub 2020/02/23.
- 2. Bisgaard H., Flores-Nunez A., Goh A., Azimi P., Halkas A., Malice M.P. Study of montelukast for the treatment of respiratory symptoms of post-respiratory syncytial virus bronchiolitis in children. *Am J Respir Critical Care Med.* 2008; 178(8):854–860. PubMed PMID: 18583576. Epub 2008/06/28. Eng.
- 3. Noor A., Najmi M.H., Bukhtiar S. Effect of Montelukast on bradykinin-induced contraction of isolated tracheal smooth muscle of guinea pig. *Indian J Pharmacol.* 2011;43(4):445–449. PubMed PMID: 21845003. PubMed Central PMCID: PMC3153711. Epub 2011/08/17. Eng.

4. Brodlie M., Gupta A., Rodriguez-Martinez C.E., Castro-Rodriguez J.A., Ducharme F.M., McKean M.C. Leukotriene receptor antagonists as maintenance and intermittent therapy for episodic viral wheeze in children. *Cochr Database Syst Rev.* 2015 CD008202. PubMed PMID: 26482324. Pubmed Central PMCID: PMC6986470. Epub 2015/10/21.

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#### **SUMMARY**

Management of coronavirus infection especially in children is a continuous process of constant updating. It is difficult find the date about effect of montelukast in children with Covid-19 infection. According of this, the aim of the present article was to review the role of montelukast that could be beneficial in management of children with covid-19 infection. 76 patients (2 to 18 years of age, 43 girls, 33 boys) with the symptoms of dry and lingering cough were involved in the study. According to treatment design, the patients were divided into treatment groups. One part of the group was prescribed only inhalers, one part – leukotriene receptor antagonists, one part – antihistamines and the last one – all three antihistamines simultaneously, respectively. Follow-up showed that the clinical effect of dry cough was more pronounced in patients administering montelukast only or in combination in comparison with the children taking only local glucocorticosteroid and antihistamines, such as desloratadine or levocetirizine separately, on a selective basis. The obtained results indicate the efficacy of montelukast, as symptomatic agents, for the treatment of Covid-19 patients with a dry and lingering cough. Research monitoring has also confirmed the ancillary effect of montelukast in children with Covid-19 infection.

Keywords: COVID-19, cough, montelukast, children

