Non-steroidal anti-inflammatory drugs exacerbated respiratory disease – a condition overlooked by anesthesiologist

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Abstract:

NSAID-exacerbated respiratory disease (N-ERD) is a chronic eosinophilic, inflammatory disorder of the respiratory tract occurring in patients with asthma and/or chronic rhinosinusitis with nasal polyps (CRNwNP), symptoms of which are exacerbated by NSAIDs, including acetylsalicylic acid (ASA). The clinical reaction to NSAID develops within 30-180 min and it is manifested by upper and/or lower airway symptoms. The majority of N-ERD patients suffer from moderate to severe asthma. A diagnosis of N-ERD is fundamentally based on the patient's history. N-ERD is suspected in patients having a history of upper/lower respiratory reactions after ingestion of ASA/NSAIDs or suffering from asthma along with chronic rhinosinusitis and nasal polyps. In this paper 57 years old women with history of well controlled asthma, allergic rhinitis and allergy to ASA is presented. After surgical procedure of total knee arthroplasty, during intensive care unit (ICU) stay, ketoprofen was administrated. Soon after, the patient develops symptoms such as dyspnea with decreased oxygen saturation (SpO2) and heaviness in stomach followed by appearance of swelling and itching of elbows and feet. After administrated therapy patient's condition was improved. NSAIDs are frequently used analgesics and antipyretics that should be used with caution in patients who suffer from asthma.

Keywords: Acetylsalicylic acid, Asthma, Chronic rhinosinusitis with nasal polyps, Non steroidal anti-inflammatory drugs exacerbated respiratory disease

Sažetak:

Respiratorna bolest uzrokovana nesteroidnim protuupalnim lijekovima – često previđeno stanje

Respiratorna bolest uzrokovana nesteroidnim protuupalnim lijekovima (engl. N-ERD) je kronični eozinofilni upalni poremećaj dišnog puta koji se pojavljuje kod bolesnika s astmom i/ili kroničnim rinosinusitisom s nosnom polipozom (engl.CRNwNP), a čiji se simpotmi pogoršavaju primjenom nesteroidnih protuupalnih lijekova (engl. NSAID), uključujući acetilsalicilnu kiselinu (engl. ASA). Klinička reakcija uzrokovana primjenom nesteroidnih protuuplanih lijekova razvija se unutar 30-180 minuta i uobičajeno se očituje simptomima od strane gornjegi/ili donjeg dišnog puta. Većina bolesnika koji imaju od N-ERD boluje od umjerenog do teškog oblika astme. Dijagoza N-ERDa temelji se uglavnom na pacijentovoj povijesti bolesti. Na N-ERD treba posumnjati kod bolesnika koji imaju anamnezu reakcije gornje/donjeg dišnog puta nakon primjene ASA-e/NSAID-a ili boluju od astme s kroničnim rinosinusitisom i nosnim polipima. U ovom radu prezentirana je 57-godišnja bolesnica s anamnezom dobro kontrolirane astme, alergijskim rinitisom i alergijom na ASA-u. Nakon kirurškog zahvata totalne endoproteze koljena, a tokom boravka u jedinici intenzivnog liječenja (engl ICU), primjenjen je ketoprofen. Ubrzo nakon toga bolesnica je razvila simptome kao što su dispneja sa smanjenjenom saturacijom krvi kisikom (SpO2) i težinom u želucu nakon kojih se pojavilo oticanje i

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svrbež laktova i stopala. Nakon primjenjene terapije stanje bolesnice se poboljšalo. Može se zaključiti das u NSAID-I često korišteni analgetici i antipiretici koji trebaju biti primjenjivani s oprezom kod bolesnika koji imaju astmu.

Ključne riječi: Acetilsalicilna kiselina, Kronični rinosinusitis s nosnom polipozom, Nesteroidni protuupalni lijekovi, Respiratorna bolest uzrokovana nesteroidnim protuupalnim lijekovima

Introduction

Although acetylsalicilyc acid (ASA) intolerance is well known for more than hundred years, fifty years later Samter at al. were first who described non-steroidal anti- inflammatory drugs - exacerbated respiratory disease (N-ERD), clinical syndrome that typically includes hypersensitivity to aspirin and other non-steroidal anti- inflammatory drugs (NSAIDs).[1]

N-ERD is a chronic eosinophilic, inflammatory disorder of the respiratory tract occurring in patients with asthma and/ or chronic rhinosinusitis with nasal polyps (CRNwNP), symptoms of which are exacerbated by NSAIDs, i ASA.[2,3] The prevalence of N-ERD in general population is unknown, respiratory symptoms following NSAID intake have been reported by 1,8% of the European population.[2,4] The incidence of N-ERD varies from 5.5%- 12.4% in adult asthmatic and increase to 14.9% in patients with more severe asthma.[2,5] This syndrome remains a diagnostic and therapeutic challenge. Despite the morbidity and relatively high prevalence of this syndrome, the initial cause and the underlying mechanism remain incompletely explained.

In patients with N-ERD, the clinical reaction to aspirin or other NSAID is manifested by upper and/ or lower airway symptoms, which develop within 30-180 min.[6,7] The reaction usually starts with nasal congestion and /or rhinorrhea, followed by wheezing, coughing, and shortness of breath. Symptoms may appear much faster, progressing rapidly to severe bronchospasm or even leading to death, especially in patients with unstable asthma.[8] A subgroup of N-ERD patients will develop pronouncing flushing, urticarial, and/ or gastrointestinal symptoms.[8,9]

The majority of N-ERD patients suffer from moderate to severe asthma, although some patients may present with a mild asthma phenotype.[10,11] Clinical presentation of upper airway disease in N-ERD patients are usually symptoms such as nasal blockage, nasal congestion or stiffness, facial pain or pressure and nasal discharge/ postnasal drip.[12,13] Partial loss of smell or anosmia occurs more frequently in N-ERD patients.[12,14] Recurrence of nasal polyps after surgery is more frequent in N-ERD than NSAIDs tolerant CRNwNP patients.[13]

A diagnosis of NERD is fundamentally based on the patient's history. N-ERD is suspected in patients having a history of upper/ lower respiratory reactions after ingestion of ASA/ NSAIDs or suffering from asthma along with chronic rhinosinusitis and nasal polipes.[15]Even though up to date there there is a lot of knowledge about diagnosis and treatment of N-ERD, there are still gaps that should be addressed in the future. In this paper the case of patient who developed N-ERD is presented.

Case report

A 57 year old women was admitted to the hospital for planned surgical procedure of total knee arthroplasty. The patient had a history of well controlled asthma, allergic rhinitis and allergy to ASA. Postoperatively, during Intensive care unit (ICU) stay, ketoprofen was administrated. Soon after administration of ketoprofen, dyspnoea with decreased oxygen saturation (SpO_2) and heaviness in stomach has occured. The therapy with dexamethasone and chlorpyramine intravenously (iv) and inhalations of salbutamol was immediately started. Two hours later, erythema, swelling and itching of elbows and feet appeard. After administration of 125 mg of methylprednisolone iv, the symptoms partially regressed. A CT angiography was performed and there were no signs of pulmonary thromboembolism. The CT has shown confluent zones of ground glass changes and bilatelar narrow zones of lung parenchyma consolidation. There was no significant pericardial or pleural effusion. In consultation with pulmonologist, further therapy was prescribed: oxygenation through Venturi mask and depending on results of repeated acid-base status analysis, it was suggested to take in consideration usage of non invasive ventilation (NIV). In addition to latter one, it was recommended to administer 40 mg of methylprednisolone once per day in duration of seven days, salmeterole/ fluticasone inhalation 3 times per day, bilastine 1-2 tablets once daily, cefepime 2 g iv twice daily, as well as radiological and laboratory control.

Discussion

N-ERD is a unique and often clinically severe disease affecting a subgroup of adults with asthma, chronic rhinosinusitis with nasal polyposis, and respiratory reactions with exposure to all cyclooxygenase 1 (COX-1) - inhibiting nonsteroidal anti-inflammatory drugs. It is heterogenous disorder with various clinical manifestations. Pathophysiology of N-ERD is complex. Two major patho-

genic mechanisms are: overproduction of cysteinyl leukotrienes with dysregulation of arachidonic acid metabolism and increased type 2 eosinophilic inflammation affected by genetic mechanisms.[15,16] According to the literature review in patients with N-ERD, the clinical reaction to ASA or other NSAIDs is developed within 30-180 min. It usually starts with nasal congestion and/or rhinorrhea, followed by wheezing, coughing, and shortness of breath. The majority of N-ERD patients suffer from moderate to severe asthma, although some patients may present with a mild asthma phenotype. In this case, patient with known history of asthma with allergic rhinitis and history of allergy to ASA was treated with ketoprofen. Symptoms appeared within 120 minutes after administration of ketoprofen. Patient presented with respiratory insufficiency, gastrointestinal symptoms and skin erythema, swelling and itching. After administrationon oxygen therapy, bronchodilatators, intravenous and inhaled corticosteroids, the patient's general condition has improved.

N-ERD may be optional diagnose when a clear history of multiple reactions develops within 1-2 hours after ingestion of NSAID, manifesting with respiratory symptoms in patient with adult-onset asthma and recurrent nasal polyposis. However, the reliance exclusively on a history may result in either under diagnosis or over diagnosis of NSAIDs hypersensitivity. In certain cases, a challenge test with ASA or culprit drug is necessary to establish the diagnosis.[2,3] Reliable *in* vitro biomarkers have yet not been identified.[15] The successful management of patient with N-ERD requires a collaboration among several specialist as well as pharmacological and non-pharmacological measures.

Conclusion

Ketoprofen and other NSAIDs are frequently used analgesics and antipyretics that should be used with caution in patients who suffer from asthma. A diagnosis of NERD is fundamentally based on the patient's history. The complete avoidance of culprit drugs is essential. Patients with N-ERD require comprehensive diagnostic and therapeutic approaches and pose a significant challenge for a physician.

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