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Daily Rapid Aspirin Desensitization Protocol in a Patient with Coronary Artery Disease

Koroner Arter Hastalığı Olan Hastada Günübirlik Hızlı Aspirin Duyarsızlaştırma Protokolü

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ABSTRACT Aspirin/acetylsalicylic acid (ASA) is one of the best known, most widely used and oldest drugs in the world. Patients with atherosclerotic cardiovascular disease often need to use this drug for life. ASA hypersensitivity is a challenging situation for both patient and clinician in patients with acute coronary syndrome who urgently need ASA for antiplatelet therapy. Although current guidelines recommend alternative treatment options (P2Y12 inhibitors) if there is aspirin intolerance in people who need antiplatelet therapy, aspirin desensitization seems to be an option for people who need dual antiplatelet therapy. ASA desensitization has been successfully applied in recent years, especially in the patient group that needs to use this valuable drug, by shortening the procedure time required for desensitization. In this case report, our aim is to describe our protocol, which allows desensitization in a short time, similar to other protocols, after sharing the literature on this subject.

Keywords: Acute coronary syndrome; desensitization; aspirin; drug hypersensitivity

ÖZET Aspirin/asetilsalisilik asit (ASA) dünyada en çok bilinen, en yaygın kullanılan ve en eski ilaçlardan biridir. Aterosklerotik kardiyovasküler hastalığı olan hastaların sıklıkla ömür boyu bu ilacı kullanması gerekmektedir. ASA aşırı duyarlılığı, antiplatelet tedavi için acilen ASA'ya ihtiyaç duyan akut koroner sendromlu hastalarda hem hasta hem de klinisyen için zorlu bir durumdur. Mevcut kılavuzlar, antiplatelet tedaviye ihtiyaç duyan kişilerde aspirin intoleransı varsa alternatif tedavi seçeneklerini (P2Y12 inhibitörleri) önerse de, ikili antiplatelet tedaviye ihtiyaç duyan kişiler için aspirin desensitizasyonu bir seçenek gibi görünmektedir. ASA desensitizasyonu, desensitizasyon için gereken işlem süresini kısaltarak, özellikle son yıllarda bu değerli ilacı kullanması gereken hasta grubunda başarıyla uygulanmaktadır. Bu olgu sunumunda amacımız, diğer protokollere benzer şekilde kısa sürede desensitizasyona olanak sağlayan protokolümüzü bu konudaki literatürü paylaştıktan sonra anlatmaktır.

Anahtar Kelimeler: Akut koroner sendrom; desensitizasyon; aspirin; ilaç aşırı duyarlığı

Aspirin hypersensitivity is a clinical challenge in acute coronary syndrome (ACS) which urgently requires antiplatelet therapy with aspirin. Especially after percutaneous coronary intervention (PCI), dual antiplatelet therapy with aspirin and clopidogrel is recommended.[1] However, aspirin intolerance occurs in 6% to 20% of the general population with "true" aspirin hypersensitivity occurring in between 0.6% and 2.4%.[2] While aspirin intolerance is characterized with severe indigestion, aspirin hypersensitivity reactions have either a pharmacological basis involving cyclooxygenase-1 (COX-1) pathway or an immunological basis involving drug-specific immunoglobulin E production. Hypersensitivity to aspirin can be further divided to 3 clinical types; aspirin-exacerbated respi-

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ratory disease (AERD), cutaneous reactions and systemic reactions.[3] AERD and cutaneous reactions result from COX-1 inhibition which leads to activation and dysregulation of mainly mast cell function that causes histamine and cysteinyl leukotrienes release.[4]

Aspirin desensitization has been reported to have successful outcomes among patients requiring secondary prevention for cardiovascular diseases. Many desensitization protocols take a long time and are not practical at the time of acute presentation.[5,6] In this case report, we describe a successful short Aspirin/acetylsalicylic acid (ASA) desensitization protocol in a patient with a history of aspirin hypersensitivity reaction who underwent stent implantation for ACS.

CASE REPORT

A 65-year-old retired soldier underwent coronary angiography with suspicion of ACS 10 days prior to admission. Acetylsalicylic acid 100 mg/day, clopidogrel 75 mg/day, metoprolol 50 mg/day and atorvastatin 40 mg/day were prescribed. Since he had a history of anaphylaxis with aspirin approximately 45 years ago, he was referred to our department for aspirin desensitization. He had not received any medication at the time of admission. We adapted the rapid desensitizing protocol developed by Lee et al. where the final dose is 80 mg, but the number of escalation doses in ours was different.[7] For premedication, Montelukast (10 mg, po), Ranitidine (50 mg, po), pheniramine hydrogen maleate (22.7 mg, intravenous) and methylprednisolone (40 mg, intravenous) were administered on start of the procedure. Hard gelatin capsules (No:0, Capsugel, France) containing 1, 3, 5, 7, 10, 20, 40 and 80 mg ASA were prepared from commercially available enteric coated ASA tablets. Placebo and ASA capsules were administered in escalating divided doses every 30 minutes while measuring arterial blood pressure, oxygen saturation, pulse and peak expiratory flow (Table 1). If mucocutaneous, respiratory or systemic reactions were to occur, desensitization protocol was planned to be stopped. After 240 minutes, the final dose was increased to 80 mg, followed by close vital monitoring for 1.5 hours. Since no reaction developed during the follow-up, the patient was taken to the acute care unit and kept under observation for 1 day (Table 1). 24 hours after completion of desensitization, a single dose of 80 mg ASA was administered and no complications were observed. At the 6-month follow-up after desensitization, the patient used 80 mg/day aspirin without any problems.

TABLE 1: Aspirin desensitization protocol.

Time (minutes)	Dose (milligram)	Cumulative dose (milligram)
0	Placebo	0
30	1	1
60	3	4
90	5	9
120	7	16
150	10	26
180	20	46
210	40	86
240	80	166

Informed consent was obtained from the patient.

DISCUSSION

Hereby, we present a rapid and safe aspirin desensitization protocol for ACS patients. To the best of our knowledge, a fixed interval (30 min), rapid (4 hr) and low-dose (80 mg) desensitization protocol has not been reported previously in patients with a history of anaphylactic reaction against aspirin. There is no standardized desensitization protocol or an expert consensus on initial dose, dose increments and dosing intervals for aspirin rechallenge in different types of aspirin hypersensitivity. In a meta-analysis, the success rate of protocols with >6 dose-escalation was shown to be higher.[8] Wong et al. described a series of 11 patients with cutaneous hypersensitivity, 9 of whom had stable coronary artery disease (CAD), administered graded oral aspirin every 20 minutes at the following doses; 0.1 mg, 0.3 mg, 1 mg, 3 mg, 10 mg, 30 mg, 40 mg, 81

mg, 162 mg and 325 mg.[9] During follow-up, 9 patients tolerated 325 mg aspirin, but 2 patients continued to use antihistamines. Aspirin Desensitization in Patients with Coronary Artery Disease (ADAPTED) registry, the largest evidence base currently, enrolled 330 patients including those with mucocutaneous (74.5%), respiratory (19.7%), and anaphylactoid (5.8%) aspirin hypersensitivity reactions, and those with unstable coronary disease including non-ST-elevation myocardial infarction (33.6%) and ST-elevation myocardial infarction (STEMIs) (23.6%).[10] As in this study, patients with STEMI underwent desensitization following their procedure and were treated with glycoprotein inhibitors periprocedural at the operator's discretion. Using a rapid desensitization protocol (1 mg at 0 hour, 5 mg at 30 minutes, 10 mg at 60 minutes, 20 mg at 90 minutes, 40 mg at 210 minutes, and 100 mg at 330 minutes), successful desensitization was achieved in 95.4% of patients including those with anaphylactoid reactions and 71% underwent PCI. In the present case, a lower total dose was administered compared to the ADAPTED registry (166 mg vs 176 mg). In our opinion rapid ASA desensitization can be performed safely in an outpatient or day unit setting. The success of aspirin desensitization has been established in several case series and meta-analyses. This case report showed the safety and efficacy of a short protocol for patients with history of aspirin hypersensitivity and CAD. Successful aspirin desensitization permits patients with CAD to pursue long-term use of aspirin.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Denis Çetin, Zehra Tuba Karaman;* ***Design:*** *Denis Çetin, Zehra Tuba Karaman, Nihal Mete Gökmen;* ***Control/Supervision:*** *Nihal Mete Gökmen;* ***Data Collection and/or Processing:*** *Denis Çetin, Zehra Tuba Karaman;* ***Analysis and/or Interpretation:*** *Denis Çetin, Nihal Mete Gökmen;* ***Literature Review:*** *Denis Çetin, Zehra Tuba Karaman;* ***Writing the Article:*** *Denis Çetin, Zehra Tuba Karaman, Nihal Mete Gökmen;* ***Critical Review:*** *Nihal Mete Gökmen;* ***References and Fundings:*** *Denis Çetin, Zehra Tuba Karaman;* ***Materials:****Denis Çetin, Zehra Tuba Karaman, Nihal Mete Gökmen.*

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