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Review

Acetylsalicylic acid desensitization in the new era of percutaneous coronary intervention☆

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ABSTRACT

Dual antiplatelet therapy is essential in patients undergoing percutaneous coronary intervention with stent implantation. Hypersensitivity to acetylsalicylic acid (ASA) limits treatment options. Desensitization to ASA has classically been studied in patients with respiratory tract disease. Over the last years, many protocols have been described about ASA desensitization in patients with ischaemic heart disease, including acute coronary syndrome and the need for coronary stent implantation. It is important to know the efficacy and safety of ASA desensitization in these patients.

Desensibilización al ácido acetil salicílico en la nueva era del intervencionismo coronario percutáneo

Palabras clave:
Hipersensibilidad al ácido acetil salicílico
Desensibilización al ácido acetil salicílico
Cardiopatía isquémica
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RESUMEN

El tratamiento con doble antiagregación plaquetaria es imprescindible en los pacientes que van a ser sometidos a un intervencionismo coronario percutáneo con implante de *stent*. La hipersensibilidad al ácido acetil salicílico (AAS) limita las posibilidades terapéuticas. La desensibilización al AAS ha sido clásicamente estudiada en pacientes con enfermedad del tracto respiratorio. En los últimos años se han descrito varios protocolos de desensibilización en pacientes con cardiopatía isquémica, incluyendo el síndrome coronario agudo y la necesidad de implante de *stent* coronario. Es importante conocer la eficacia y seguridad de la desensibilización al AAS en estos pacientes.

Introduction

Inhibitors of platelet activation represent the mainstay of treatment of patients with ischaemic cardiomyopathy, whether they are stable or have acute coronary syndrome (ACS), especially in those who undergo percutaneous coronary intervention (PCI).[1–3] Dual antiplatelet-aggregation treatment (acetylsalicylic acid [ASA] and adenosine diphosphate receptor inhibitors) has been demonstrated to reduce adverse cardiovascular events in patients with ACS and after PCI with stent implantation.[4–7] It is considered to be necessary to prevent stent thrombosis, and the required duration of treatment is more prolonged with drug-eluting stents.[8,9] Hypersensitivity to ASA limits the therapeutic options in PCI, and may influence whether or not a stent is used; the type of stent used, if any; and the short-term prognosis. Some published studies report therapeutic alternatives to ASA without any increase in the rate of major cardiac episodes.[10] However, these studies are few in number and not randomized, and it seems that ASA remains the best option. Desensitization to ASA in certain types of hypersensitivity to Aspirin® and other non-steroidal anti-inflammatory drugs (NSAIDs) seems to offer encouraging results. Even so, the potential serious adverse effects in a group of unstable patients who undergo PCI have meant that its use is still not very widespread. We conducted a review of the available medical literature regarding the outcomes achieved with different ASA desensitization protocols

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in patients with ischaemic cardiomyopathy who were to undergo cardiac catheterization with potential PCI.

Hypersensitivity to acetylsalicylic acid

ASA, the active substance in Aspirin®, is an NSAID that irreversibly inhibits cyclooxygenase-1 and -2 (COX-1 and COX-2). Its main activity is to decrease production of thromboxane A2, which is a potent stimulator of platelet aggregation, through inhibition of COX-1.[11,12] By means of inhibition of COX-2, it acts as an anti-inflammatory drug, reducing the synthesis of prostaglandins, which are precursors of vascular inflammation in atherosclerotic plaques.[13]

ASA and other NSAIDs are responsible for a significant number of adverse reactions whose 2 most common forms of clinical presentation are respiratory and cutaneous symptoms.[14,15] The prevalence of intolerance to ASA in patients with asthma is up to 10%, and 30–40% in those with asthma and nasal polyps (ASA triad). In patients with chronic idiopathic urticaria, it may be as high as 20–30%.[16–18]

Classification of types of hypersensitivity reactions to acetylsalicylic acid and other non-steroidal anti-inflammatory drugs[19]

Non-immune-mediated hypersensitivity reactions (with cross-reactivity)

- NSAID-exacerbated respiratory disease: this manifests with respiratory tract symptoms such as nasal discharge, laryngospasm and bronchospasm. Patients with a prior history of asthma, nasal polyps and rhinosinusitis have an elevated risk of having it.
- NSAID-exacerbated cutaneous disease: this manifests as exacerbated urticaria and/or angio-oedema in patients with a history of chronic idiopathic urticaria.
- NSAID-induced urticaria or angio-oedema: this manifests with urticaria and/or angio-oedema in patients without a history of chronic idiopathic urticaria.

Although its pathogenic mechanisms have not been well elucidated, it has been postulated that this type of hypersensitivity reaction could be mediated by increased production of leukotrienes by 5-lipoxygenase (5-LO), which causes mast cells to release histamines and cytokines. 5-LO activity is inhibited by prostaglandin E2 (PGE2), which is synthesized by COX-1. When COX-1 is inhibited by ASA or other NSAIDs, the effect of PGE2 is lost, causing a rapid production of leukotrienes that triggers the hypersensitivity reaction (Fig. 1).

All drugs that inhibit COX-1 could trigger this type of reaction after the first dose administered. Selective COX-2 inhibitors are generally well tolerated.[20]

Immune-mediated hypersensitivity reactions (without cross-reactivity)

- Urticaria, angio-oedema or anaphylaxis induced by a single NSAID: this manifests immediately with urticaria and/or angio-oedema or anaphylaxis induced by a single NSAID or NSAIDs belonging to the same chemical group.
- Delayed hypersensitivity reaction induced by a single NSAID: this normally manifests 24–48 h after administration of the drug as a skin reaction (skin rash or more serious forms) or other symptoms

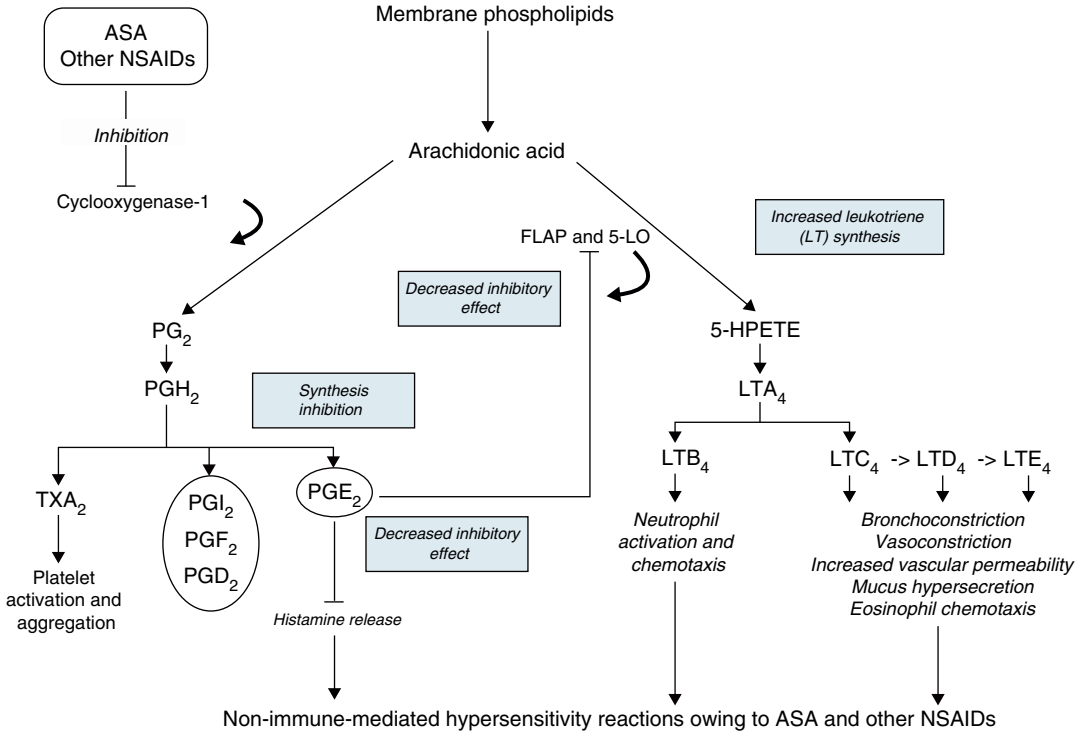

Fig. 1. Arachidonic acid is the precursor of prostaglandins (PGs) and thromboxane A2 (TXA2). Acetylsalicylic acid (ASA) and other non-steroidal anti-inflammatory drugs (NSAIDs) inhibit cyclooxygenase-1 (COX-1), resulting in inhibited synthesis of PGs, including prostaglandin E2 (PGE2). In the absence of the inhibitory effect of PGE2 on 5-lipoxygenase-activating protein (FLAP) and 5-lipoxygenase (5-LO), increased leukotriene (LT) synthesis occurs through 5-hydroperoxyeicosatetraenoic acid (5-HPETE); in addition, there is increased histamine release. These pro-inflammatory substances are responsible for non-immune-mediate cutaneous and respiratory hypersensitivity reactions.
Source: Adapted from Gollapudi et al.[35]