Aspirin resistance

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Abstract:
Aspirin protects many though not all patients from acute cardiovascular events. It is generally accepted that such prophylactic effect depends mainly on the antithrombotic action involving inhibition of thromboxane $A_2$ production and platelet aggregation. In many patients aspirin failure to protect against cardiovascular event is obvious, as their symptoms simply cannot be controlled by the administration of a single drug. Others do not adhere properly to the treatment regimen. There is, however, a group of subjects, in which aspirin fails to inhibit platelet function (measured by various in vitro tests) and thromboxane $A_2$ (TxA$_2$) formation (measured either in whole blood or as urinary TXA$_2$ metabolite excretion). There is evidence that such impairment of biochemical aspirin effect may be of importance in predicting future cardiovascular events. Several factors can influence antiplatelet effectiveness of aspirin; among them: hypercholesterolemia, increased expression of the isoform 2 of cyclooxygenase, genetic factors (polymorphisms of integrin, and factor XIII A-subunit), use of other nonsteroidal anti-inflammatory use, and possibly others. Still, several questions remain unanswered. While biochemical aspirin resistance can predict major cardiovascular events we are still lacking a reliable test to predict such a risk in an individual patient. In addition, we do not know whether any alteration in therapy may improve clinical outcome in a subject identified as aspirin-resistant.

Key words:
aspirin, platelets, aggregation, cardiovascular disease

Introduction

Acetylsalicylic acid (aspirin, ASA) is the most widely prescribed drug all over the world with indications ranging from fever to clinical manifestations of arterial thrombosis.

Cyclooxygenase (COX)-1 and -2 are 72 kD luminal proteins of the endoplasmic reticulum and nuclear envelope, where they catalyze the conversion of arachidonic acid to prostanooids.

Aspirin inhibits COX-1, a constitutive enzyme, by acetylating a serine residue at position 529, which blocks the access of arachidonic acid to the catalytic site in the core of the enzyme molecule. Suppression of prostaglandin PGH$_2$ formation results in decreased production of PGD$_2$, PGE$_2$, PGF$_{2\alpha}$, prostacyclin and thromboxane A$_2$ (TXA$_2$). This latter compound acts as an platelet agonist, vasoconstrictor and vascular smooth muscle cell mitogen [21]. A capacity of the anucleate platelets for TXA$_2$ synthesis is restored only by newly released platelets. The effect of a single dose of aspirin disappears within 7–10 days. The COX-1 activity is present in most tissues, including the endothelium, that possess the capacity to generate the new enzyme molecules and recover their normal function within a few hours following aspirin administration. Therefore, a single dose of aspirin has only a transient systemic effect on COX-1 with the exception of the platelets [21].