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Can we use adenosine diphosphate (ADP) to study "aspirin resistance"? The Janus faces of ADP-triggered platelet aggregation

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Abstract:
There is a growing number of contradictory reports indicating that adenosine diphosphate (ADP) can be a useful agonist in monitoring of the antiplatelet action of acetylsalicylic acid (ASA) in humans and animals. In the current study, we aimed to determine the conditions for using ADP to trigger platelet aggregation in order to detect ASA-mediated inhibition of rat platelet reactivity.
Initially, we examined the usefulness of different ADP concentrations (0.25, 0.5, 1, 5 and 10 μM) in detecting the *in vitro* ASA-mediated platelet inhibition using whole blood aggregometry, as well as we monitored the role of ADP in generation of thromboxane A_2 (TXA_2). To study *ex vivo* ASA inhibitory potential on platelet aggregation induced by a range of ADP concentrations, animals were subjected to one or 10-day ASA administration at the dose of 50 mg/kg.
Our experiment shows that ADP in a concentration-dependent manner induces TXA_2 generation in the whole blood with hirudin as an anticoagulant. However, *in vitro* and e*x vivo* examination of ASA inhibitory potential on platelet aggregation revealed that irrespectively of administration regimen, ASA failed to block platelet aggregation induced by ADP at the concentrations higher than 0.5 μM.
Our findings suggest that the mechanism of ADP-induced platelet aggregation depends on agonist concentration. It appears that only low ADP concentrations (up to 0.5 μM) induce TXA_2-dependent rat platelet aggregation. Therefore, ADP could be considered a useful platelet agonist for monitoring of ASA-mediated platelet inhibition only if used at much lower concentrations than those commonly employed.

Key words:
platelet aggregation inhibitors, acetylsalicylic acid, rats, TXA_2 generation