

Antiplatelet therapy with clopidogrel or ticlopidine reduces intimal hyperplasia in an animal model of experimental arterial injury

Klopidogrel veya tiklopidin antiplatelet tedavisi deneysel hayvan model arteriyel hasarlarında intimal hiperplaziyi azaltır

Atherosclerotic disease is the most common cause of cardiovascular disorders, which is the leading cause of death in adults in the Western world. Atherosclerosis is a multifactorial ongoing process starting in the early twenties leading to unstable atherosclerotic plaques, ischemia, infarction, and eventually death. Treatment options are available include drug therapy which influences hypercholesterolemia, diabetes, hypertension and prevent thrombus formation. Interventions with percutaneous revascularization techniques or more invasively with bypass grafting of arteries are also available. End-stage atherosclerotic disease leading to permanent organ damage as seen after massive myocardial infarction may require organ transplantation.

The long-term results of these interventions are compromised by renewed narrowing of the dilated lesion after percutaneous angioplasty (restenosis), venous bypass graft (graft failure) or the smaller arteries in transplanted organs (transplantation arteriosclerosis). The common etiology in these different modalities is intimal hyperplasia leading to restenosis, graft failure and transplantation arteriosclerosis.

In this issue of the Anatolian Journal of Cardiology, Göncü et al., demonstrate antiplatelet therapy with clopidogrel or ticlopidine to be equally effective in reducing intimal hyperplasia in an experimental arterial injury animal model (1). This confirms previous studies by Waksman et al. demonstrating that clopidogrel reduces inflammation and neointima formation in balloon-denuded rabbit iliac arteries (2). Herbert et al. (3) showed diminished myointimal thickening of air-dried injured rabbit carotid arteries when animals were treated with clopidogrel or ticlopidine. The authors suggest an indirect mechanism for the witnessed decreased intimal hyperplasia as result of semi-quantified lower basic fibroblast growth factor (bFGF) and platelet derived growth factor beta (PDGFβ) expression. They however do not provide proof of an inhibitory effect of clopidogrel or ticlopidine on smooth muscle cell proliferation. This could be more adequately confirmed by means of 5-bromo^{2'}-deoxy-uridine (BrdU) or Ki67 proliferation staining in their animal model. The authors do not address inward or outward remodeling, nor do they compare percentage of stenosis and vessel wall thickness between the different subgroups. This compromises the presentation and interpretation of their results.

Clopidogrel and ticlopidine have been clinically proved to be effective in preventing cardiovascular events in patients with unstable angina, risk of ischemic stroke, myocardial infarction, peripheral artery disease and after percutaneous coronary intervention (4). Their attributive role in improving clinical outcome after artery bypass grafting is however not

established (5). The authors' recommendation of ADP-selective platelet inhibitors usage in clinical settings of vascular reconstructive interventions should be taken with caution until further experimental and clinical proof of their concept is available. The emerging clopidogrel resistance among patients may also warrant detection of genetic polymorphisms in susceptible populations or platelet function assays before including them in clinical studies investigating a possible role for ADP-selective platelet inhibitors in preventing bypass graft failure (6).

In conclusion, the authors contribute to the accumulating evidence for the role of clopidogrel and ticlopidine in preventing intimal hyperplasia after arterial endothelial denudation as seen after angioplasty. Translation to the clinical setting, especially that of arterial bypass grafting, requires further investigation.

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