

G-CSF in acute myocardial infarction - Experimental and clinical findings/ G-CSF in acute myocardial infarction: a word of caution

*Akut miyokard infarktüsünde G-CSF- Deneysel ve klinik bulgular/
Akut miyokard infarktüsünde G-CSF: Uyarı*

Dear Editor

We read with interest a recent review article by Ince et al. who have analyzed the clinical and experimental data regarding G-CSF in acute myocardial infarction (AMI) (1). The authors should be congratulated for their contribution to the evolution of cellular therapeutic strategies. Over the last decade the scientists made an exceptional progress in cellular therapy methods under regenerative medicine (2). We have, however, several concerns about the treatment by G-CSF after reperfusion of infarcted myocardium for myocardial regeneration. The investigators already pointed to the fact that G-CSF treatment before percutaneous coronary intervention (PCI) in patients with AMI resulted in unacceptable rates of in-stent restenosis (MAGIC-trial) (3).

In the article by Ince et al. the investigators conclude: "Treatment by G-CSF after reperfusion of infarcted myocardium could offer a pragmatic concept of potential myocardial regeneration". Inhibition of adverse remodeling following AMI and myocardial regeneration are two different scenarios. The recent experimental study by Li et al. (4) demonstrated that G-CSF treatment in rats prevented cardiac remodeling and improved cardiac function after AMI by preserving the number of cardiomyocytes in the infarction area. However, most bone marrow-derived (BMD) cells in the infarcted area were CD68-positive macrophages or α 1A4 positive (vascular smooth muscle cells, myofibroblasts, or bone marrow stromal cells). The authors were unable to clearly demonstrate BMD cardiomyocytes in the infarcted area and concluded that inhibition of adverse remodeling was the result of direct protective effect of G-CSF against cardiomyocytes death.

Although various clinical studies confirmed the safety and feasibility of G-CSF in AMI as the authors suggested, sporadic cases of AMI were reported in cancer patients, in healthy subjects and in patients with severe coronary artery disease receiving G-CSF (5).

In a recent report from our university we demonstrated a subclinical but significant alteration in haemostatic parameters of healthy voluntary stem cell donors leading to a prothrombotic state, who received G-CSF for stem cell mobilization (6). The tissue factor pathway is affected by G-CSF and the use of G-CSF in coronary syndromes is still under intensive investigation by coagulation specialists (7).

Thus, the overall safety profile of G-CSF in patients with coronary artery disease is still of concern and its efficacy is questionable (5). In conclusion, the use of a growth factor is a hard task, and physicians should await the evidence-based data and the safety profiles before launching growth factor based protocols.

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Author's reply

We thank the authors for the thoughtful contribution in their letter. They indeed confirm and underline the potential mechanism of G-CSF induced inhibition of apoptosis and prevention of adverse remodeling as described in our review (1).

Moreover, the study of Li et al (2) is again confirmation of earlier findings by Harada et al (3), as quote in our paper entitled "Prevention of left ventricular remodeling with G-CSF after acute myocardial infarction ..." (4).

In the setting of acute myocardial infarction with additional glycoprotein IIb/IIIa inhibition no such clinical prothrombotic state was observed. Finally, as suggested by the authors, we are providing data and safety profiles of growth factor protocols to enrich the scientific body of evidence.

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