Letters to the Editor

doi:10.1093/eurheartj/ehl487

Online publish-ahead-of-print 5 February 2007

Levosimendan: Perpetuum mobile?

We read with great interest the well-written review about levosimendan by De Luca et al. Levosimendan is certainly an interesting drug that appears to deliver favourable effects in patients with acute heart failure. Numerous studies have demonstrated the positive inotropic action of levosimendan. In 1998, Lillegard et al. published in this journal an interesting article, which is quoted very often in articles dealing with levosimendan. These authors reported that levosimendan increases cardiac output and stroke volume in patients after coronary bypass surgery, neither increasing myocardial oxygen consumption nor changing myocardial substrate utilization. This observation has been accepted as a fact and has not been challenged.

Cardiac excitation–contraction coupling (EC coupling) is an energy-consuming process. Changes in cardiac contractile force can be effected at each of three distinct levels: (i) the modulation of intracellular calcium; (ii) the alteration of the contractile protein response to intracellular calcium; and (iii) changes in loading conditions. Of note, regardless at which level of EC coupling levosimendan exerts its action, it will always act at the expense of energy substrate.

Based on these considerations we do believe that a drug which increases myocardial contractility certainly also increases energy consumption, otherwise levosimendan is the driving force of a cardiac ‘perpetuum mobile’.

References

4. Stefan Agewall Division of Cardiology Aker University Hospital and Faculty of Medicine University of Oslo 0514 Oslo Norway Tel: +47 22 89 46 55 Fax: +47 22 89 42 59 E-mail address: stefan.agewall@medisin.uio.no

Online publish-ahead-of-print 8 February 2007

Variability in response to clopidogrel: where is the threshold for ‘low response’?

We read with great interest the recent trial of Geiser et al. investigating the influence of low response to clopidogrel on the 3-month composite endpoint in 379 patients after coronary stent implantation. The authors identified ‘low-responders’ to clopidogrel therapy with a single measurement of optical aggregometry and found that these patients had significantly more major cardiovascular (CV) events within 3 months than those with adequate response. Regarding the outcome, the rate of adverse CV events appears to be unexpectedly high, reaching 8.0% with all-cause death, stroke, and myocardial infarction vs. 0–3% in similar studies. This is mainly driven by the particularly high mortality rate (all-cause, 2.5%; cardiac, 3.9%) in 3-month time. As the main difference between low- and adequate-responders was registered as divergence in mortality, this might be of substantial importance. Furthermore, there were significantly more acute coronary syndrome patients among the low-responders (43.1 vs. 81.8%, P < 0.001), that itself, may have resulted in higher mortality of this group. Statins (88.3 vs. 72.7%, P = 0.06) and beta-blockers (94.4 vs. 81.8%, P = 0.05) were also less frequently administered to these patients. These uncontrolled factors may have biased the statistical analysis. Apart from the above-mentioned facts, the results of the study are in line with recent observations. We have recently presented our data of the link between efficacy of thienopyridine therapy and need for repeat revascularization after coronary stent implantation, while Hochholzer et al. confirmed in 802 patients that the level of platelet aggregation immediately before PCI correlates with the 30-day adverse outcome. In conclusion, the presented observations all support that low response to clopidogrel interferes with the clinical outcome. However, efficacy of clopidogrel shows normal distribution, and according to the findings of the two latter trials, all patients above the median have a greater risk to major adverse cardiac events. Thus, as cut-off limit for low-responders among patients after coronary stent implantation, the median value might give more appropriate estimation of both short- and long-term risk than 70% of maximal residual aggregation value.

References


Aradi Dániel
Department of Interventional Cardiology
Heart Institute, Medical Faculty
University of Pécs
13 Ifjúság útja
Pécs, H-7624
Hungary

Tünde Pintér
Department of Interventional Cardiology
Heart Institute, Medical Faculty
University of Pécs
13 Ifjúság útja
Pécs, H-7624
Hungary

Iván G Horváth
Department of Interventional Cardiology
Heart Institute, Medical Faculty
University of Pécs
13 Ifjúság útja
Pécs, H-7624
Hungary

© The European Society of Cardiology 2007. All rights reserved. For Permissions, please e-mail: journals.permissions@oxfordjournals.org