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Intracoronary levosimendan prevents myocardial ischemic damages and activates survival signalling through ATP-sensitive potassium channel and nitric oxide

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Objective: Levosimendan has been reported to exert cardioprotection. In this study, we have examined the cardiac effects of different doses of intracoronary levosimendan on ischemia/reperfusion injuries, and the involvement of K(ATP) channels and nitric oxide (NO).

Methods: The experiments were performed in a total of 56 anesthetized pigs. In 21 pigs, 1.5, 5 and 12 μg/min levosimendan was infused over 15 min into the coronary artery at the onset of 1 h reperfusion following 2-h ischemia and the effects on cardiac function, infarcted area, and on apoptosis/autophagy were examined. In addition, the activation of Akt and extracellular receptor kinase (ERK) was analyzed. The findings were compared with those obtained in a further 14 pigs where the highest dose levosimendan was infused after glibenclamide and l-nitro-arginine methyl ester (l-NAME).

Results: Intracoronary 1.5, 5 and 12 μg/min levosimendan caused an increase of segmental shortening, dP/dtmax and cardiac output of 7.8%, 22.6%, and 31.6%; 7.6%, 16.9%, and 21.6%; 2.8%, 5.9%, and 6.2%, respectively, from values measured at the end of ischemia. The beneficial effects elicited by levosimendan were still evident at the end of reperfusion when the increase of segmental shortening, dP/dtmax and cardiac output caused by the three doses of levosimendan amounted to 3.7%, 13.3%, and 16.5%; 1.5%, 9.4%, and 11%; 1.4%, 2.7%, and 3.9%, respectively. When doses of 5 and 12 μg/min levosimendan were used, a reduction of infarcted area to about 69% and 67% of area at risk was observed, and was significantly different from that of about 79% measured in control animals. In addition, after intracoronary levosimendan, the inhibition of apoptosis and activation of autophagy and a dose-related increase of the level of phosphorylation of ERK and Akt were observed. These responses were completely prevented by glibenclamide and significantly reduced by l-NAME.

Conclusions: The results of this study show that intracoronary levosimendan reduces cell death induced by ischemia/reperfusion in a dose-dependent manner and activates survival signaling through K(ATP) channel opening and NO. These findings support interesting implications for cardioprotection in interventional cardiology and cardiac surgery.

Biography

Elena Grossini got the degree in Medicine at University of Turin in 1995 and Ph.D. in Molecular Medicine at University East Piedmont, Novara, in 2000. She has been working as Assistant Professor in Physiology at University East Piedmont since 2002. She has published more than 60 papers in international journals and has been recruited as expert reviewers for main journals in Physiological, Pharmacological, Cardiovascular and Endocrine fields.

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