

## Superiority of Levosimendan to Dobutamine in Postoperative Low Cardiac Output Syndrome: Is it Due to Previous Beta-Blocker Treatment?

### To the Editor:

We have read with interest the article of Levin et al<sup>1</sup> in which the authors present a randomized comparison between levosimendan (LS) and dobutamine (Db) in postoperative low cardiac output syndrome. They conclude that LS is superior to Db in terms of morbidity, mortality, and length of hospital stay.

A key aspect is the fact that, of the 68 patients randomized to Db, 45 (85.3%) had received preoperative treatment with beta-blockers. As expressed in the clinical practice guidelines concerning acute heart failure,<sup>2</sup> patients who receive treatment with beta-blockers require higher doses of Db to restore its inotropic effect. Likewise, the LIDO study,<sup>3</sup> which demonstrates that LS brings about a greater improvement in the hemodynamic parameters in patients with severe left ventricular dysfunction than Db, concludes that treatment with beta-blockers attenuates the action of Db, but not that of LS. The statistically significant differences between LS and Db in terms of hemodynamic parameters encountered in the study of Levin et al could be due to the lower chronotropic and inotropic activity of Db, as the majority of the patients had previously received treatment with beta-blockers. These hemodynamic differences at such a crucial time as when early postoperative low cardiac output develops (initiation of inotropy 3.5 hours after the surgical intervention) can ultimately have an impact on morbidity and mortality.

In short, we can conclude that the action of LS, in contrast to that of Db, is not attenuated by treatment with beta-blockers. This aspect is important, since LS can be considered a highly appropriate treatment in cases of severe left ventricular dysfunction and as a concomitant treatment with previous beta-blockers.

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## REFERENCES

1. Levin RL, Degrange MA, Porcile R, Salvagio F, Blanco N, Botbol AL, et al. Superioridad del sensibilizante al calcio levosimendán comparado con dobutamina en el síndrome de bajo gasto cardiaco postoperatorio. *Rev Esp Cardiol*. 2008;61:471-9.
2. Nieminen MS, Böhm M, Cowie MR, Drexler H, Filippatos GS, Jondeau G, et al. Guías de práctica clínica sobre el diagnóstico y tratamiento de la insuficiencia cardiaca aguda. *Rev Esp Cardiol*. 2005;58:389-429.
3. Follath F, Cleland JG, Just H, Papp JG, Scholz H, Peuhkurinen K, et al. Efficacy and safety of intravenous levosimendan compared with dobutamine in severe low-output heart failure (the LIDO study): a randomised double-blind trial. *Lancet*. 2002;360:196-202.

## Response

### To the Editor:

The authors wish to thank Dr Homs and Dr González-Costello for their interest in our article. They express their doubts concerning the effect of pretreatment with beta-blockers in patients with postoperative low cardiac output syndrome (LCOS) randomized to dobutamine, supporting their arguments with the practice guidelines for the treatment of acute heart failure and the LIDO study.<sup>1-3</sup>

We consider their doubts to be logical and valid; we have discussed this point over the last 2 years, and have obtained certain conclusions to the contrary.

First, we should correct an error: of the 68 patients assigned to dobutamine, 23 had not been taking beta blockers preoperatively; that is, one third of our patient population, a number that can not be considered small.

Second, we compared the mortality of the patients randomized to levosimendan (6/69) with that of those treated with dobutamine who had not received preoperative beta-blocker therapy (7/23), and a trend toward significance was observed ( $P=.1$ ), that was insufficient due to the smaller number of patients considered at that time.

With respect to possible differences in the chronotropic effect, Figure 5 of our study shows that, in contrast to the finding indicated in the letter, the group randomized to dobutamine had a slightly higher cardiac output.

Another argument that should be considered would be the initial dose of dobutamine employed (5 µg/kg body weight), which is twice as high as the initial dose we usually administer, and the rapid rate at which it was increased (every 15 minutes); after 45 minutes, the nonresponders were receiving 12.5 µg/kg.

With all due respect, both the guidelines and the LIDO study only marginally consider patients who are in the postoperative period following heart surgery. Thus, it is difficult not to evaluate situations, such as the use of cardiopulmonary bypass and its consequences, systemic

inflammatory response, coagulopathy, the use of general anesthesia and positive pressure mechanical ventilation, catecholamine discharge (which partly counteracts the effect of preoperative beta-blockers), all of which make postoperative LCOS a very particular form of acute heart failure.

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## REFERENCES

1. Levin RL, Degrange MA, Porcile R, Salvagio F, Blanco N, Botbol AL, et al. Superioridad del sensibilizante al calcio levosimendán comparado con dobutamina en el síndrome de bajo gasto cardíaco postoperatorio. *Rev Esp Cardiol*. 2008;61:471-9.
2. Nieminen MS, Bohm M, Cowie MR, Drexler H, Filippatos GS, Jouneau G, et al. Guías de Práctica Clínica sobre el diagnóstico y tratamiento de la insuficiencia cardíaca aguda. *Rev Esp Cardiol*. 2005;58:389-429.
3. Follath F, Cleland JG, Just H, Papp JG, Scholz H, Peuhkurinen K, et al. Efficacy and safety of intravenous levosimendan compared with dobutamine in severe low-output heart failure (the LIDO study); a randomized double-blind trial. *Lancet*. 2002;360:196-202.