Preoperative optimization with levosimendan in heart failure patient undergoing thoracic surgery

Moana Rossella Nespoli (MD,Dr) a,⁎, Marco Rispoli (MD,Dr) a, Dario Maria Mattiacci (MD,Dr) a, Marianna Esposito (MD,Dr) a, Antonio Corcione (Prof) b, Carlo Curcio (MD,Dr) b, Salvatore Buono (MD,Dr) b

a Anesthesia and Intensive Care, AORN dei Colli Vincenzo Monaldi Hospital, Naples, Italy
b Thoracic Surgery, AORN dei Colli Vincenzo Monaldi Hospital, Naples, Italy

ARTICLE INFO
Article history:
Received 12 May 2016
Received in revised form 1 August 2016
Accepted 1 August 2016
Available online 4 August 2016

Keywords:
Preoperative optimization
Levosimendan
Heart failure patient
Thoracic surgery

ABSTRACT
INTRODUCTION: We present the case of a patient with dilatative cardiomyopathy waiting for heart transplantation with pleural effusion to be subjected to pleural biopsy, treated with preoperative infusion of levosimendan to improve heart performances.

PRESENTATION OF CASE: A 56-year-old man (BMI 22.49) with dilatative cardiomyopathy (EF 18%) presented right pleural effusion. The levosimendan treatment protocol consisted of 24 h continuous infusion (0.1 ug/kg/min), without bolus. The patient was under continuous hemodynamic monitoring prior, during and after levosimendan administration. The surgery for pleural biopsy was performed with unipolar Video Assisted Thoracoscopic approach (VATS).

DISCUSSION: A significant increase of Cardiac Index (CI) and Stroke Volume Index (SVI) were observed at 4 h after infusion initiation and was sustained during the next 24 h after the end of infusion. Levosimendan administration was safe.

CONCLUSION: In this case the prophylactic preoperative levosimendan administration is safe and effective in cardiac failure patient undergoing thoracic surgery, but prophylactic preoperative levosimendan treatment in these patients merits further study.

© 2016 The Authors. Published by Elsevier Ltd on behalf of IJS Publishing Group Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction
Heart failure is an important risk factor for mortality and cardiovascular complications after non cardiac surgery [1,2]. Levosimendan, in contrast to other positive inotropic agents, has the advantage to improve cardiac performance and hemodynamics in CHF patients without increasing myocardial oxygen consumption or showing any proarhythmic effects [3].

The use of levosimendan for perioperative optimization of patients undergoing cardiac surgery has been reported in several studies [4,5], however it has not been thoroughly evaluated in cardiac failure patients undergoing non cardiac surgery.

We present the case of a patient with dilatative cardiomyopathy waiting for heart transplantation with pleural effusion to be subjected to VATS for pleural biopsy, treated with preoperative infusion of levosimendan to improve heart performance. Consent was obtained from the patient.

2. Presentation of Case
A 56-year-old man (height 170 cm, weight 65 kg, BMI 22.49) with dilatative cardiomyopathy (EF 18%) presented right pleural effusion. Cytological examination of pleural fluid was not diagnostic to exclude a malignancy therefore needed surgical pleural biopsies to get diagnosis in order to be put in list for transplantation.

The patient previously underwent surgery for aortic and mitral valve replacement and implanted a pacemaker (INCEPTA CRT-D P162).

The patient was admitted to our PACU the day before the surgery for levosimendan administration.

The levosimendan treatment protocol consisted of 24 h continuous infusion (0.1 ug/kg/min), without bolus. The patient was under continuous hemodynamic monitoring prior, during and after levosimendan administration.
The monitoring included continuous heart rate monitoring via electrocardiogram, arterial blood pressure via femoral artery catheter, urine output, pulse oximetry, PVC through venous catheter in internal jugular vein, cardiac output (CO), cardiac index (CI), stroke volume index (SVI), central venous oxygen saturation (ScvO2) and oxygen delivery (DO2) via EV1000 (Edwards Lifesciences). Blood tests were performed every 12 h and blood gas analysis every 4 h. Before levosimendan infusion CI was 1.9, SVI was 28, ScvO2 was 48%. The surgery was performed at the end of levosimendan treatment.

Intraoperative monitoring included continuous electrocardiogram, SpO2, blood pressure, bispectral index monitor (BIS), train of four watch (TOF), INVOS 5100C cerebral somatic oximeter (Medtronic, Dublin, Ireland) to assess the cerebral oxygenation, EV1000 to assess emodinamic parameters. Midazolam premedication (0.03 mg/kg) was administered i.v. 10 min before induction of anesthesia. General anesthesia was induced with a target controlled infusion of propofol/remifentanil and rocuronium bromide (0.6 mg/kg) and maintained with propofol/remifentanil and supplemental bolus of rocuronium accorded TOF values. A left DLT 39 Fr (Rusch, Durham, NC) was positioned and checked with FOB, the lungs were mechanically ventilated with an oxygen-air mixture (FiO2 50%), the OLV was performed with CMV-AF 5 ml/Kg, RR for EtCO2 <40 mmHg, PEEP 5.

The surgery for pleural biopsy was performed with uniporal Video Assisted Thoracoscopic (VATS) approach at V intercostal space. The time of intervention was 70 min. One thoracic drainage was placed at the end of surgery. Patient awake comfort full.

No complications occurred during anesthesia and hemodynamic and respiratory parameters were stables during surgery.

The monitoring was continued postoperatively in the PACU until 24 h post infusion. An evident increase of CI and SVI were observed at 4 h after infusion initiation and was sustained during the next 24 h after the end of infusion (Fig. 1 and Fig. 2). Additionally, ScvO2 was increased at 4 h after infusion initiation and kept increasing during the 24 post infusion hours. (Fig. 3). Levosimendan showed no harmfull effect on HR, SAP, DAP or MAP, administration was safe, no adverse drug reaction or complication occurred during follow up.

Pleural biopsies reported histological evidence of chronic pleurisy.

3. Discussion

A decreased preoperative EF has been associated with increased postoperative morbidity and mortality, while perioperative left ventricular dysfunction is one of the major predictors of postoperative cardiac complication [6].

During the last years an increasing number of patients with high perioperative risk and decreased left ventricular function are referred to cardiac and non cardiac surgery; heart failure is the major cause of perioperative morbidity and mortality.

The effect of levosimendan as an inodilator are based on a triple mechanism of action that provides positive inotropy equal or even superior to any of the other commercially available inotropic agents with a neutral effect on oxygen consumption and with preconditioning, cardioprotective, antistunning and antischemic effects [7–13].

Levosimendan produces significant dose-dependent increases in stroke volume and cardiac output and decreases in pulmonary capillary wedge pressure, mean blood pressure, mean pulmonary artery pressure, mean right atrial pressure ant total peripheral resistance [14].

Clinical studies show that levosimendan effectively improves general and pulmonary haemodynamics in patients undergoing cardiac surgery, thereby reducing the need for inotropic agents and mechanical circulatory support and additionally optimising renal and hepatic function.

The unique inotropic and cardioprotective properties of levosimendan can provide sustained effects for several days and can thus help to reduce complications in the postoperative period [4].

Tritapepe and colleagues reported that short infusion of levosimendan before the initiation of CABG results in higher postoperative cardiac index and lower troponina concentration, in significant reductions in tracheal intubation time, length of ICU stay and number of patients requiring inotropic support [15].
In a randomized trial vs placebo, Levin and colleagues evaluated the effects of 23 h infusion preoperative levosimendan in high risk patients with severe left ventricular dysfunction undergoing CABG with cardiopulmonary bypass (EF < 25%). Levosimendan group had a lower incidence of complicated weaning from CPB, decreased mortality and lower incidence of LCOS, lower requirement for inotropes and intra-aortic balloon pumps [16].

Taking into account these multiple but complementary mechanisms, levosimendan appears to be a suitable agent for preoperative optimization of cardiac functions in heart failure patients undergoing major elective surgery [17,18], but has not been thoroughly evaluated in CF patients undergoing thoracic surgery.

We evaluated the effects of prophylactic preoperative levosimendan administration in a CF patient undergoing thoracic surgery in unipolar VATS in general anesthesia.

Considering that in case like this it is not unusual to have unilateral effusion especially since the left chest/pleura was transversed through previous operation and therefore adhesion formation in the space would limit a visible effusion on the left, pleural biopsy could seem an overtreatment, but the transplant list required us to have the assurance about not being a malignant lesion, regardless of clinical probability.

The high risk related to general anesthesia in not negligible, but pleuroscopy or thoracoscopy in local anesthesia allow surgeons to take samples in the more favorable area of the pleura with random biopsies. In our case we need to get that specific effusion, in the dorsal apex area of the lung, so lung collapse was needed.

Hemodynamic monitoring was performed with EV 1000 (Edwards Lifesciences).

The EV1000 clinical platform presents the physiologic status of the patient in an intuitive and meaningful way and offers you scalability and adaptability for both the OR and ICU.

With EV 1000 we have monitored hemodynamic optimization. Cardiac output, CI, SVI measured continuously can be used (in combination with SaO2 and hemoglobin) to monitor and optimize DO2 with fluid and inotropic agents [19,20].

In our CF patient levosimendan increases CI, SVI and ScvO2. Levosimendan administration in a 24 h continuous infusion resulted in beneficial improvement of patient’s hemodynamics and cardiac performance, effects that were sustained for at least another 24 h and, in the case of EF, 7 days. No difference was noted between CI, SVI, Do2 values at the end of levosimendan infusion and the postoperative values. The finding that this optimization was sustained constantly throughout the intra and postoperative period, when the surgical stress is greater.

4. Conclusion

In conclusion, in our experience the prophylactic preoperative levosimendan administration is safe and effective in cardiac failure patient undergoing thoracic surgery. Levosimendan could be safely administered to CF patients undergoing thoracic surgery, but prophylactic preoperative levosimendan treatment in these patients merits further study.

Ethical approval

In our case report was not made no experimentation, you just described our clinical practice.

Consent

In our case report was not made no experimentation, you just described our clinical practice, written informed consent for procedures was obtained from the patient.

Author contribution

Nespoli Moana Rossella: study design, writing the paper.
Marco Rispoli: study design.
Dario Maria Mattiacci: data collection.
Esposito Marianna: data collection.
Antonio Corcione: data analysis.
Carlo Lucio: data interpretation.
Salvatore Buono: data analysis and interpretation.

Guarantor

Nespoli Moana Rossella.

References

[1] W.G. Toller, H. Metzler, Acute perioperative heart failure, Curr. Opin. Anaesthesiol. 18 (2005) 129–135.
[2] A.F. Hernandez, D.J. Wheelan, S. Stroud, J.L. Sun, C.M. O’Connor, J.G. Jollis, Outcomes in heart failure patients after major non cardiac surgery, J. Am. Coll. Cardiol. 44 (2004) 1446–1453.
[3] T.M. Ng, Levosimendan a new calcium-sensitizing inotrope for heart failure, Pharmacotherapy 24 (2004) 1366–1384.
[4] W. Toller, et al., Preoperative and perioperative use of levosimendan in cardiac surgery; European expert opinion, Int. J. Cardiol. 184 (2015) 323–336.
[5] G.C. De Hert, S. Lorsombradee, S. Cromheecke, P.J. Van der Linden, The effects of levosimendan in cardiac surgery patients with poor left ventricular function, Anesth. Analg. 104 (2007) 766–773.
[6] L. Romero, C. de Virgilio, Preoperative cardiac risk assessment: an updated approach, Arch. Surg. 136 (2001) 1370–1376.
[7] A. Rognoni, A. Lupi, A. Cavallino, A. Veia, S. Bacchini, R. Rosso, G.G. Secco, A.S. Bongo, Levosimendan preoperative, Curr. Pharm. Des. 19 (22) (2013) 3976–3978.
[8] Z. Papp, J. Edes, S. Frubwald, et al., Levosimendan: molecular mechanism and clinical implications: consensus of experts on the mechanisms of action of levosimendan, Int. J. Cardiol. 159 (2012) 82–87.
[9] O. Ericsson, P. Pollesello, H. Haikala, Effect of levosimendan on balance between ATP production and consumption in isolated perfused guinea-pig heart before ischemia or after reperfusion, J. Cardiovasc. Pharmacol. 44 (2004) 316–321.
[10] I. Lepran, P. Pollesello, S. Vajda, A. Varco, J.G. Papp, Preconditioning effects of levosimendan in a rabbit cardiac ischemia reperfusion model, J. Cardiovasc. Pharmacol. 48 (2006) 148–152.
[11] E.F. Du Toit, A. Gens, L.H. Opie, P. Pollasello, A. Lochper, A role of the RISK pathway and KATP channels in pre and postconditioning induced by levosimendan in the isolated guinea-pig heart, Br. J. Pharmacol. 154 (2008) 41–50.
[12] L.N. Jamali, J.R. Kersten, P.S. Page, D.A. Hettrick, D.C. Wartier, Intracoronary levosimendan enhances contractile function of stunned myocardium, Anesth. Analg. 85 (1997) 23–29.
[13] J. Levojoki, P. Pollesello, P. Kaheinen, H. Haikala, Improved survival with simandren after experimental myocardial infarction in rats, Eur. J. Pharmacol. 419 (2001) 243–248.
[14] M.S. Nieminen, S. Fruhwald, L.M. Heunics, et al., Levosimendan: current data, clinical use and future development, Heart Lung Vessel 5 (2013) 227–245.
[15] L. Tripati, V. De Santis, D. Vitale, et al., Levosimendan pre-treatment improves outcomes in patients undergoing coronary artery bypass graft surgery, Br. J. Anaesth. 102 (2009) 198–204.
[16] R. Levin, M. Degrange, C. del Mazo, E. Tanus, R. Porcie, Preoperative levosimendan decreases mortality and the development of low cardiac output in high-risk patients with severe left ventricular dysfunction undergoing coronary artery bypass grafting with cardiopulmonary bypass, Exp. Clin Cardiol. 17 (3) (2012) 125–130.
[17] A. Morelli, C. Ertmer, P. Pietropaoli, M. Westphal, Reducing the risk of major elective non-cardiac surgery: is there a role for levosimendan in the
preoperative optimization of cardiac function? Curr. Drug Targets 10 (September (9)) (2009) 863–871.

[18] S. Katsargakis, A. Kapralou, P. Dimitrousis, H. Markogiannakis, A. Larentzakis, G. Kofinas, P. Misthos, K. Filis, D. Theodorou, Prophylactic preoperative levosimendan administration in heart failure patients undergoing elective non cardiac surgery: a preliminary report, Hellenic J. Cardiol. 50 (2009) 185–192.

[19] K. Reinhart, et al., Continuous central venous and pulmonary artery oxygen saturation monitoring in the critically ill, Intensive Care Med. 30 (8) (2004) 1572–1578.

[20] J. Wilson, I. Woods, J. Fawcett, et al., Reducing the risk of major elective surgery: randomised controlled trial of preoperative optimisation of oxygen delivery, BMJ 318 (1999) 1099–1103.