Levosimendan Following Coronary Artery Bypass Grafting in a Patient with End-Stage Renal Failure: A Case Report

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ABSTRACT

Levosimendan is a novel inotropic agent indicated for patients with decompensated heart failure. It has well recognised mechanisms of action. Its use however, has not been described in patients with end-stage renal failure.

This report describes the use of levosimendan in a post-operative coronary artery bypass graft patient with decompensated heart failure and end-stage renal failure previously receiving dialysis six days per week. Levosimendan proved to be a safe and useful agent when used as a continuous intravenous infusion initially at 0.05 μg/kg/min then increasing up to 0.2 μg/kg/min for a total of 42 hours. (**Critical Care and Resuscitation 2004; 6: 109-112**)

Key words: Levosimendan, coronary artery bypass graft, chronic renal failure

Levosimendan is a novel inotropic agent indicated for patients with decompensated heart failure. It has two main mechanisms of action. At therapeutic levels, it acts as a myocardial calcium sensitiser, enhancing cardiac contractility (with no increase in oxygen consumption),[1,2] and causes activation of K_{ATP} channels in smooth muscle producing venous, arterial and coronary vasodilatation.[3-7]

Fifty-four percent of the drug dose is excreted in urine and 44% in faeces,[8] with adverse effects being dose-related.[9] On review of the literature at the time of writing this report, apart from a single study evaluating the clearance of unchanged drug in mild to moderate renal failure,[9] there were no case reports or trials evaluating its use in patients with end-stage renal failure (ESRF).

This case report is presented which recounts the use of levosimendan in a patient who was preoperatively dialysis dependent, with a creatinine clearance (C_{cr}) of 0 mL/min. The intention was to infuse the agent carefully and monitor the patient's clinical response as there was no facility to measure levosimendan or its metabolites in blood or dialysate fluid.

CASE REPORT

A 59-year-old male presented to the emergency department (ED) complaining of chest pain. He had ST segment elevation in the anterior chest leads on electrocardiography. His past medical history included ischaemic heart disease for which he had undergone coronary artery bypass graft (CABG) ten years previously, type II diabetes mellitus and ESRF. He was anuric (i.e. C_{cr} 0 mL/min) and received haemodialysis six times per week. The plasma biochemical measurements on admission revealed a urea of 20.6 mmol/L and creatinine of 769 μmol/L.

Initially he required variable rates of dopamine to maintain a systolic blood pressure of 100 mmHg while he underwent coronary artery angiography. Following this, he was prepared for CABG with an intraaortic balloon pump (IABP) which was inserted a day prior to his surgery.

The CABG was performed without complication. Cardiopulmonary bypass time was 2 hours 38 minutes

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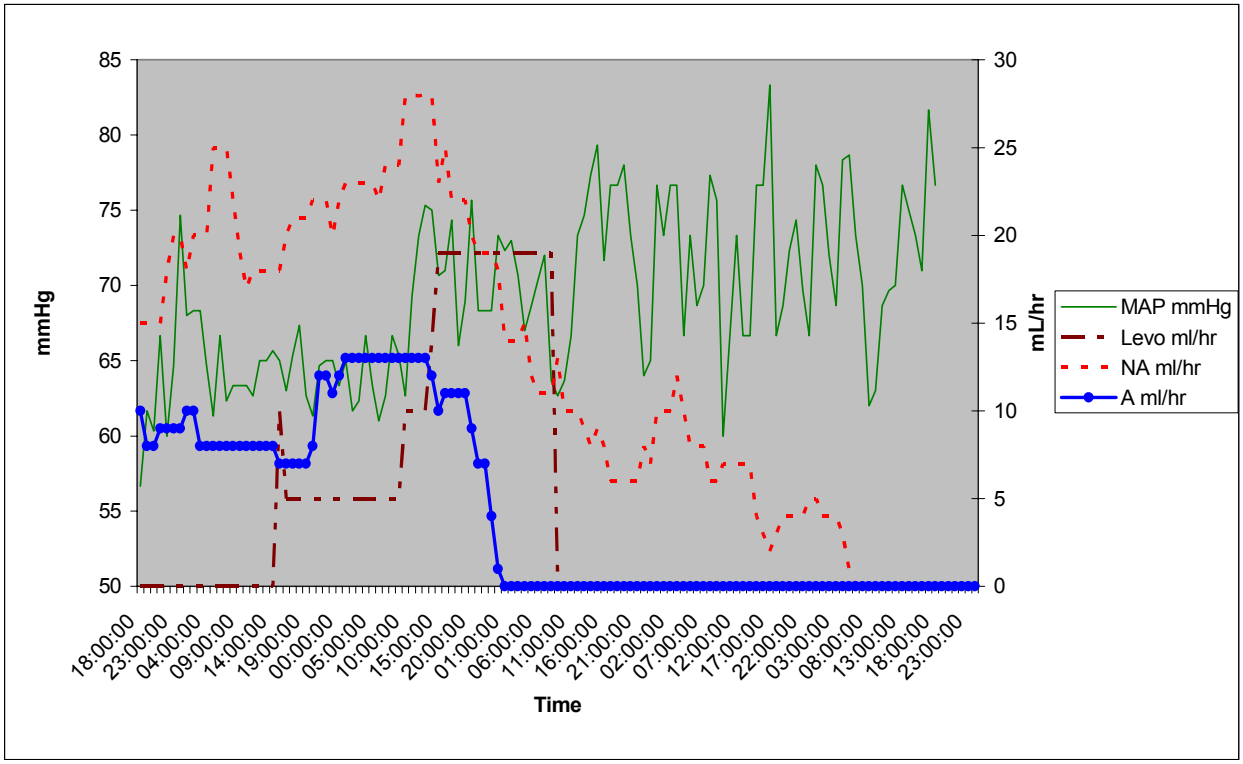
and the aortic cross-clamp time was 1 hour 47 minutes. He was admitted to the intensive care unit (ICU) for postoperative care.

On arrival, he required adrenaline at 0.13 μg/kg/min and noradrenaline at 0.19 μg/kg/min to maintain a systolic BP > 90 mmHg. His heart had an underlying nodal rate of 55 bpm so he was paced in the AAI mode at a rate of 90 bpm. A pulmonary artery catheter was also inserted. The IABP was set at 1:1 with 80% augmentation.

Over the next 24 hr, the patient's inotropic requirements remained high. Due to his recent coronary artery surgery, underlying heart disease and the possibility of myocardial stunning, an infusion of levosimendan (Simdax™, Mfd. Under license by Orion Corp., Espoo, Finland for Abbott Laboratories, U.S.A) was initiated empirically. To avoid the possibility of additional hypotension, the infusion began at 0.1 μg/kg/min with no initiating bolus dose. Despite this, significant hypotension developed, so the infusion was reduced to 0.05 μg/kg/min with a view to increasing the dose later as tolerated (Figure 1).

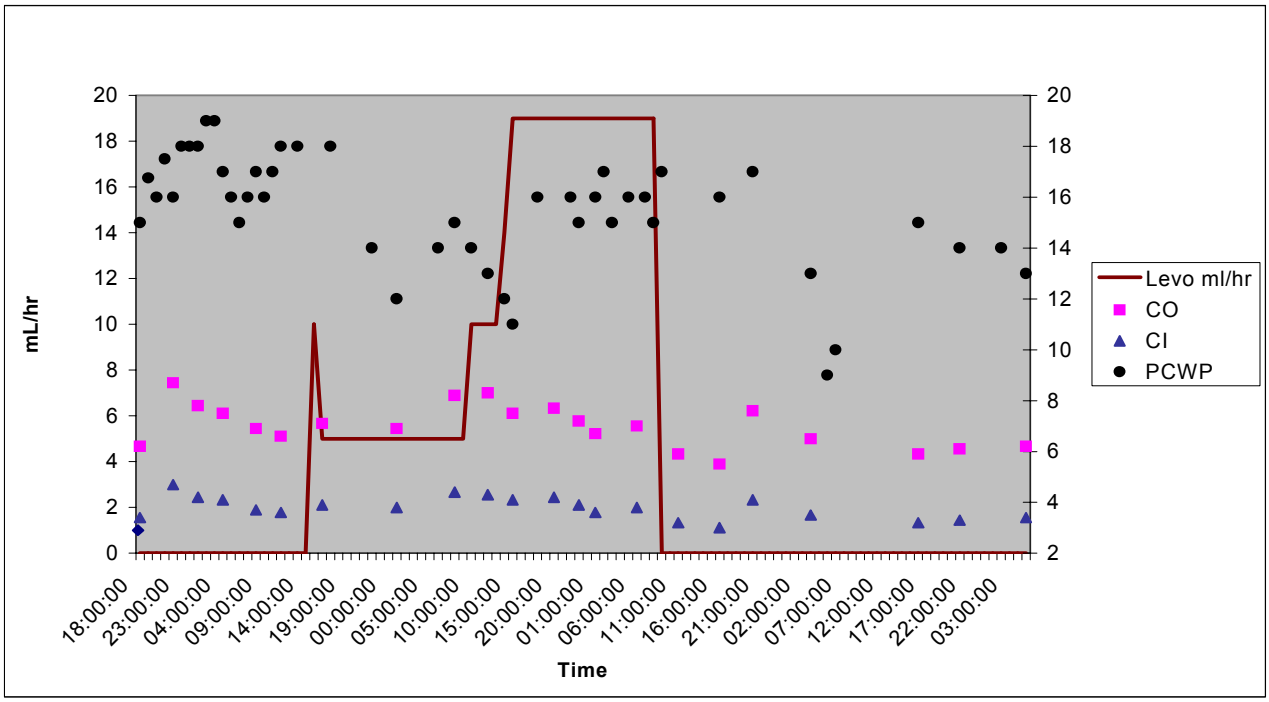
During the second 24 hr in the ICU, the levosimendan infusion was increased to 0.2 μg/kg/min with an initial increase in noradrenaline to counteract hypotensive effects. However, within two hours of the infusion reaching the therapeutic rate, the adrenaline and noradrenaline were able to be weaned to maintain an average mean arterial pressure of 70 mmHg. Adrenaline was discontinued 15 hr after the levosimendan infusion had reached a therapeutic rate (> 0.1 μg/kg/min) and noradrenaline was ceased 53 hr later. Changes in the cardiac index, cardiac output and pulmonary capillary wedge pressures during the levosimendan infusion are shown in figure 2. The IABP was removed after 71 hr and he was extubated 103 hr after his admission to the ICU. The levosimendan infusion lasted 42 hrs. Throughout the stay in the ICU the patient received renal replacement therapy with continuos veno-veno haemodiafiltration. He was discharged to the ward six days after his initial bypass surgery.

One day after discharge from the ICU, the patient underwent a one hour period of ultrafiltration with removal of two litres of fluid. However, during this process he became hypotensive and developed atrial fibrillation. He then developed ventricular fibrillation and required a 200 J direct current shock to return to a stable haemodynamic state. A dual chamber automatic



MAP = mean arterial pressure, Levo = levosimendan infusion (0.05 mg/mL), NA = noradrenaline (0.06 mg/mL), A = adrenaline (0.06 mg/mL)

Figure 1. Changes in the noradrenaline and adrenaline infusion rates and mean arterial pressure associated with the levosimendan infusion.



CO = cardiac output, CI = cardiac index, PCWP = pulmonary capillary wedge pressure

Figure 2. Changes in the cardiac index, cardiac output and pulmonary capillary wedge pressures during the levosimendan infusion.

implantable cardiac defibrillator device was inserted and he was discharged from hospital 19 days after his initial admission to hospital.

DISCUSSION

Levosimendan is a new option for the treatment of decompensated heart failure. By the nature of this illness, other co-morbidities commonly exist in this patient population, especially renal impairment. It is known that levosimendan is completely metabolised, with minimal amounts of unchanged drug found in urine or faeces.[10, 11] It is primarily metabolised by conjugation to cyclic or N-acetylated cysteinylglycine and cysteine conjugates. These metabolites are also pharmacologically active. Fifty-four percent of the drug dose (i.e. active metabolites) is excreted in urine and 44% in faeces.[8]

Levosimendan has been shown to be a drug that is well tolerated, with the majority of adverse events being secondary to its vasodilator effects[12] and with adverse events being dose-related.[10] The implications of this in a patient with anuric ESRF are obvious. It has been used safely in patients with mild to moderate renal failure,[9] however there are no data on its use in patients with ESRF (i.e. C_{cr} <30 mL/min).

The patient described in my report had significant medical co-morbidities, including dialysis dependent, anuric renal failure requiring haemodialysis six days per week. He was successfully treated with levosimendan in the post-operative period, with favourable effects on haemodynamic parameters and inotrope requirements. Although, following initiation of therapy there was significant hypotension, this was successfully managed by a "starting low and increasing slow" approach as well as using cautious fluid replacement and other inotropic support during the initial period of hypotension.

Levosimendan has thus far proven to be a useful drug in patients with decompensated cardiac failure and I believe that it is also a useful and safe agent even in patients with ESRF.

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