

Reply from the authors

Editor—We thank Drs Banerjee and Saghal for their interest in our meta-analysis addressing the efficacy of perioperative pregabalin in acute postoperative pain.¹

Our literature search produced only 11 valid randomized controlled trials meeting the criteria for analysis. We refrained from performing a subgroup analysis based on different types of surgery because the number of included studies would be too small. It is also possible that patients who had received preoperative pregabalin would show a reduced intraoperative analgesic requirement. However, our meta-analysis was not designed to analyse intraoperative analgesic consumption. Furthermore, some studies in our review used pregabalin after operation.

It is true that there are differences in dosing frequencies of pregabalin, but we chose to look at ‘pregabalin’ vs ‘no pregabalin’ in our study. With regard to the variable analgesic strategies in the different studies, we also refrained from subgroup analysis because of the small number of studies. This point was highlighted in our discussion as a limitation of our meta-analysis. We had considered the influence of ondansetron, droperidol, and dexamethasone on postoperative nausea and vomiting in the analysis. These drugs were used both in the control and study groups in the studies. Therefore, the influence of pregabalin can still be compared.

Conflict of interest

None declared.

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1 Zhang J, Ho K-Y, Wang Y. Efficacy of pregabalin in acute postoperative pain: a meta-analysis. *Br J Anaesth* 2011; **106**: 454–62

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A further case of rocuronium-induced anaphylaxis treated with sugammadex

Editor—We write in support of the recent descriptions of sugammadex in the management of rocuronium-induced anaphylaxis.^{1,2} We describe a remarkably similar case of anaphylaxis and cardiovascular collapse in a peripheral hospital rapidly reversed by the use of sugammadex affording the stability to transfer the patient to the nearest intensive care unit (ICU).

A fit 47-yr-old lady was undergoing laparoscopic cholecystectomy for recurrent right upper quadrant pain. This 78 kg, non-smoker, had no significant medical co-morbidities and had experienced two previous Caesarean sections under general anaesthesia more than 12 yr ago, receiving first atracurium and second vecuronium, without complications. She

described a pre-existing allergy to cotrimoxazole manifesting as a peripheral rash and swelling. Anaesthesia for surgery was induced with a combination of ondansetron 4 mg, fentanyl 100 µg, morphine 10 mg, and propofol 200 mg. The patient was easy to hand ventilate and rocuronium 50 mg was given. After this ventilation quickly became difficult necessitating tracheal intubation, correct positioning was confirmed by capnography. End-tidal CO₂ was noted to be low at 2.3 kPa, the SpO₂ trace disappeared, and florid erythema was seen all over the abdomen and chest. The systolic arterial pressure was measured as 63 mm Hg, while heart rate increased to 150 beats min⁻¹. A diagnosis of anaphylaxis was made and vasopressor therapy commenced.

I.V. epinephrine boluses and crystalloid were used before commencement of an epinephrine infusion at 0.17 µg kg⁻¹ min⁻¹. Hydrocortisone 200 mg and chlorpheniramine 10 mg were given i.v. The necessary airway pressures remained high.

At this point, plans for ICU transfer were finalized and the use of sugammadex was suggested. One hour after the onset of anaphylaxis, 400 mg of sugammadex was administered. Within 2.5 min, the patient awoke and resumed spontaneous respiration, airway pressures improved, and it was possible to half the epinephrine infusion to 0.09 µg kg⁻¹ min⁻¹ while maintaining normotension and returning the heart rate to 84 beats min⁻¹. Shortly afterwards, transfer to an off-site ICU was commenced. The patient was sedated but allowed to breath spontaneously during the 25 min journey. Arterial pressure climbed and on arrival in the ICU, the epinephrine infusion was stopped, the patient was allowed to wake and was extubated shortly afterwards.

Subsequent tryptase levels were consistent with a type 1 hypersensitivity reaction (182 µg litre⁻¹ peak level, 3 h after cardiovascular collapse; normal <15 µg litre⁻¹), later confirmed by skin prick testing. Hydrocortisone and anti-histamine treatment continued for 24 h at which point the patient was discharged to the ward and then home within 48 h, with appropriate follow-up.

This patient demonstrated clinical and immunochemical evidence of anaphylaxis shortly after administration of rocuronium, notably without antibiotic administration. Sensitization to the non-depolarizing neuromuscular blocking agent, quaternary ammonium group is likely to have been triggered by previous exposure to neuromuscular blocking agents.³ The startling improvement in clinical parameters after sugammadex administration could be argued to be coincidental, but we were convinced by the timing and extent of the recovery in relation to the administration that this is unlikely. As authors, we have been persuaded that sugammadex played a pivotal role in stabilizing our patient at a time when, despite controversy, many feel rocuronium represents one of our most allergenic anaesthetic drugs.⁴

In summary, we believe that this is a further case of rocuronium-induced anaphylaxis with clinical improvement triggered by sugammadex and adds to the small body of evidence that this novel relaxant reversal has a role in the specific management of rocuronium-associated anaphylaxis.

Conflict of interest

None declared.

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- 1 McDonnell N, Pavy T, Green L, Platt P. Sugammadex in the management of rocuronium-induced anaphylaxis. *Br J Anaesth* 2011; **106**: 199–201
- 2 Wordsworth H, Raja Y, Harrison S. Sugammadex and rocuronium-induced anaphylaxis. *Br J Anaesth* 2011; **106**: 911–12
- 3 Rose M, Fisher M. Rocuronium: high risk for anaphylaxis? *Br J Anaesth* 2001; **86**: 678–82
- 4 Dewachter P, Mouton-Faivre C, Emala C. Anaphylaxis and anaesthesia. *Anesthesiology* 2009; **111**: 1141–50

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Is preoperative levosimendan indicated to treat normal left ventricular function and left ventricle outflow obstruction?

Editor—We read with great interest the article by Leppikangas and colleagues¹ evaluating the haemodynamic effects of preoperative levosimendan in patients undergoing high-risk cardiac surgery. The authors addressed the interesting issue of the high-risk cardiac surgical patient and the optimization of perioperative pharmacological heart support. However, based on our personal experience with levosimendan in cardiac surgery setting and on the evidence from the existing literature, we have several concerns with the study. First, the study was conducted in patients undergoing combined aortic valve replacement and coronary artery bypass graft as they were considered high risk. All the patients enrolled did not match criteria for inclusion in the study protocol [left ventricular ejection fraction (LVEF) <50% or wall thickness >12 mm] neither for inotropic pretreatment: the preoperative EF was normal. Secondly, all the patients had a serious contraindication to levosimendan; in fact, they suffered from severe aortic valve stenosis with high gradient that naturally increases after an inodilator administration. Moreover, the control group did not receive the standard inotropic treatment in use at the authors' centre, but only placebo, although considered high risk. Thirdly, the control group had no difference in terms of myocardial injury, mechanical ventilation, and intensive care unit (ICU) stay. Surprisingly, mortality was higher in the levosimendan group. Fourthly, quite a high-dose bolus was given to coronary artery disease (CAD) patients with ventricular outflow obstruction and myocardial hypertrophy, despite the danger of hypotension due to vasodilatation. At our institutions, we started using levosimendan in 2004. According to our policy, an inotrope is administered only if a need for

increased inotropy is demonstrated by echocardiography and clinical evaluation. Therefore, we usually give levosimendan perioperatively in patients with severely depressed ventricular function (EF<30%) starting just after induction of anaesthesia without bolus. When acute ventricular failure occurs at the time of weaning from cardiopulmonary bypass (CPB), we give a bolus of 6–12 µg followed by an infusion of 0.1–0.2 µg kg⁻¹ min⁻¹. However, in severe aortic valve stenosis with severely depressed LV function, we usually give levosimendan in bolus (24 µg) at the initiation of CPB followed by an infusion of 0.1 µg kg⁻¹ min⁻¹ for 24 h. By doing so, we observed a reduced ICU stay and a reduced perioperative intra-aortic balloon pump application over the years. Some considerations need to be added. It is agreed that levosimendan offers haemodynamic support^{2–4} and myocardial protection^{5,6} in the perioperative scenario. However, preoperative administration of the drug requires monitoring in a high-dependency setting. Therefore, besides the risks of giving it in aortic stenosis patients, we should take into consideration the logistic and financial implications of such a policy in an era of cost containment. The inodilator itself needs to be used appropriately due to the high cost if compared with other inotropic drugs. Finally, the preoperative use of levosimendan to optimize patients' cardiovascular function, either in cardiac or non-cardiac surgery, would be appropriate if patients meet some 'common sense' criteria, including depressed myocardial function (EF<40%) to increase CI, CAD patients unsuitable for revascularization at risk for ischaemia (cardiac protection, low anaerobic threshold in which it could be worth increasing the DO₂). In conclusion, levosimendan shows relevant advantages in high-risk patients undergoing cardiac surgery in terms of haemodynamic support and cardioprotection, but it is our opinion that an always cautious and cost-effective application should be advocated.

Conflict of interest

None declared.

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- 1 Leppikangas H, Jarvela K, Sisto T, et al. Preoperative levosimendan infusion in combined aortic valve and coronary bypass surgery. *Br J Anaesth* 2011; **106**: 298–304
- 2 De Hert SG, Lorscheider S, Cromheecke S, Van der Linden PJ. The effects of levosimendan in cardiac surgery patients with poor left ventricular function. *Anesth Analg* 2007; **104**: 766–73
- 3 Eriksson HI, Jalonen JR, Heikkinen LO, et al. Levosimendan facilitates weaning from cardiopulmonary bypass in patients undergoing coronary artery bypass grafting with impaired left ventricular function. *Ann Thorac Surg* 2009; **87**: 448–54
- 4 Tritapepe L, De Santis V, Vitale D, et al. Levosimendan pretreatment improves outcomes in patients undergoing coronary artery bypass graft surgery. *Br J Anaesth* 2009; **102**: 198–204