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## Novel therapy for cardiogenic shock

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Cardiogenic shock, hypotension, L-NMMA, therapy

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## Comments

Cardiogenic shock complicates acute myocardial infarction (AMI) and carries a high mortality rate despite therapy. Conventional therapy includes coronary revascularisation, afterload reduction, inotropes and mechanical adjuncts including ventilation and intra-aortic balloon pump (IABP). Nitric oxide (NO) is involved in vasodilation. In this uncontrolled trial, N<sup>G</sup>-monomethyl-L-arginine (L-NMMA), a nonspecific nitric oxide synthetase inhibitor, was administered to promote vasoconstriction in order to augment blood pressure (BP). There were no untoward effects or deaths directly attributable to the drug, and 10 of the 11 patients showed improvement. As the authors themselves point out, this is a preliminary report of a drug showing promise which needs to be studied further.

## Introduction

A study to assess the safety and efficacy of L-NMMA in the treatment of cardiogenic shock.

## Methods

- . Eleven consecutive patients with extensive AMI complicated by cardiogenic shock
- . All mechanically ventilated/IABP
- . Coronary angiography + primary percutaneous transluminal coronary angioplasty when feasible
- . All commenced on dopamine/dobutamine/frusemide infusions

. Cardiogenic shock defined as persistent unaugmented systolic BP < 100 mm Hg, accompanied by pulmonary congestion (on chest X-ray), cardiac index (CI) < 2.5 L/min/m<sup>2</sup> and wedge pressure > 15 mm Hg despite therapy.

. Patients with tachyarrhythmia/bradyarrhythmia, mechanical complication, fever > 38<sup>o</sup> C, creatinine > 200 μmol/mL

. L-NMMA was administered intravenously, initially as bolus of 1 mg/kg then as an infusion of 1 mg/kg/h for 5 h.

## Results

Within 10 min mean arterial pressure (MAP) increased from 76 ± 9 to 109 ± 22 mm Hg. CI initially fell from 2.0 ± 0.5 to 1.7 ± 0.4 L/min/m<sup>2</sup>; however, after discontinuation it rose to 1.85 ± 0.4 L/min/m<sup>2</sup>. Urine output (UO) increased by 148%. The positive changes in MAP and UO persisted after 24 h. Ten of the eleven patients were weaned off ventilation and IABP; eight were discharged from the coronary care unit and seven were alive at the 1 month follow-up.

## Additional information

Trials of L-NMMA in septic shock have been disappointing, and interestingly there was an alarming amount of electrocardiographic evidence of myocardial ischaemia. (*Mayr et al Crit Care Med* 1996, **24**:1930-1930 and *Grover et al, Crit Care Med* 1999, **27**:913-922). The 1999 Nobel prize in medicine was awarded to Drs [Robert%20Furchgott](#), [Louis%20Ignarro](#), and [Ferid%20Murad](#) for their discoveries that vascular endothelial cells make NO and that NO stimulates cyclic-guanosine monophosphate synthesis in the smooth muscle cells, causing relaxation. This is controlled by endothelial NO synthetase.

## References

1. Cotter G, Kaluski E, Blatt A, Milovanov O, Moshkovitz Y, Zaidenstein R, Salah A, Alon D, Michovitz Y, Metzger M, Vered Z, Golik A: L-NMMA (a nitric oxide synthetase inhibitor) is effective in the treatment of cardiogenic shock. *Circulation*. 2000, 101: 1358-1361.