

Intermittent Intravenous Nitroglycerin Boluses for Acute Pulmonary Edema

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INTRODUCTION

Cardiogenic pulmonary edema (CPE) occurs when the pulmonary capillary pressure exceeds the forces that maintain fluid within the vascular space. Initial treatment includes maintenance of a patent airway, administration of 100% oxygen, and securing intravenous (IV) access. Pharmacologic treatment is often instituted with vasodilator therapy.¹⁻³ Paramedical staff will typically administer IV furosemide, IV morphine sulphate, and oral, sublingual or topical nitrates.

Furosemide IV has a direct venodilating effect with an onset of vascular effect within five minutes.² Effects of morphine are, in part, produced by decreased arterial resistance and pressure secondary to a reduction of centrally mediated sympathetic neural tone.¹ Nitrates have a profound venodilating effect that even at low doses result in an increase in vascular capacitance, thus lowering preload and pulmonary capillary pressure. Evidence also supports that nitrates have a relaxing effect on collateral vascular channels, particularly coronary collateral vessels,¹ making these agents the therapy of choice if CPE occurs as a result of myocardial ischemia.³

If the above measures fail, continuous infusion of nitroglycerin has been advocated for the treatment of acute CPE.¹ However, little information is available regarding the use of IV bolus nitroglycerin therapy. We report a case in which intermittent nitroglycerin boluses were used to treat acute CPE.

CASE

A 74 year-old, 52 kg, female developed sudden onset of shortness of breath at rest and was brought into the emergency department by the paramedical services. En route to hospital she received 60 mg furosemide IV, morphine 2.5 mg IV, and five doses of sublingual nitroglycerin 0.6 mg. Her medications at home prior to admission were isosorbide dinitrate 30 mg PO tid, furosemide 20 mg PO daily, and hydralazine 50 mg PO tid. Her past medical history included congestive heart failure, mild aortic stenosis, hypertension, and a silent anteroseptal myocardial infarction.

On admission, she had a pulse of 121 beats per minute, a respiratory rate of 32/min, and a blood pressure of 200/90 mmHg. She could only speak in short sentences. Oxygen by face mask was started at 10 L/min. She received nitroglycerin 2 mg IV bolus. This dose was repeated after five minutes and a third dose was given two minutes later. At this point her vital signs were not substantially changed. She received an additional IV bolus dose of 1 mg nitroglycerin. Her chest x-ray showed cardiomegaly, small bilateral pleural effusions and widespread pulmonary edema. After 30 minutes of observation her vital signs improved to a heart rate of 86 beats per minute, a respiratory rate of 22/min, and a blood pressure 165/67 mmHg. Dyspnea was improved and she was admitted to CCU with a diagnosis of CPE. A subsequent coronary angiogram showed normal large coronary arteries. A nuclear ventriculogram showed a dilated left ventricle, hypokinesis of the anterolateral wall, and a left ventricular ejection fraction of 41%. Her furosemide dose was increased and she was discharged home five days later.

DISCUSSION

Nitroglycerin IV is considered part of standard therapy of CPE.³ However, delivery by IV bolus (over one minute or less) has not been widely discussed.^{1,2} Although postulated as a possible mode of administration in a review published approximately 15 years ago, little additional information is available.⁴ Continuous infusions are generally begun at 5 mcg/min and then increased in increments of 5 mcg/min every three to five minutes

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until the desired clinical response is achieved or adverse effects occur.³

A review of the literature (MEDLINE 1961-1996) identified only two reports of bolus doses of nitroglycerin for CPE, both open trials.^{5,6} Bosc et al, used 3 mg bolus doses to treat CPE in 35 patients.⁵ Twenty-seven patients (71%) showed a marked improvement within five minutes of a single dose. Five patients (13%) experienced hypotension (SBP \leq 90 mmHg). One of these was a patient who weighed 35 kg, another was a 91 year-old man, and a third patient received 5 mg in error. None of the hypotensive episodes required treatment with inotropes or vasopressors. One patient developed hypotension and bradycardia, and required atropine.

In the report by Nashed et al, patients were treated with IV nitroglycerin boluses of 0.05 to 0.4 mg depending on the patient's systolic blood pressure as shown in Table I.⁶ This was followed by an infusion of nitroglycerin with additional nitroglycerin boluses repeated every five minutes as required. Twenty of the 24 cases (83%) responded within 30 minutes and in none of the cases did hypotension occur. One patient developed symptomatic bradycardia without hypotension, which resolved spontaneously after 10 minutes. A second patient experienced supraventricular tachycardia which responded to verapamil.

We believe that the benefit of a bolus technique, as suggested by Nashed et al,⁶ is that more drug is delivered early in treatment with more rapid resolution of

symptoms. However, in contrast to this group, we use a larger bolus dose and do not always start an infusion at the same time.

Currently, there is no standardized protocol in our emergency department for the treatment of CPE and the initial dose of nitroglycerin employed varies among clinicians. If additional doses of IV nitroglycerin are required, these are repeated at five to ten minute intervals and if multiple, repeat bolus doses are required a continuous infusion should be considered.


In conclusion, it appears from our experience and other limited reports^{5,6} that nitroglycerin IV bolus is a safe and effective method of treating acute CPE especially in patients with significant hypertension. Further study is needed to determine the optimal dose and whether such therapy is superior to other regimens. 

Table I. Nitroglyceria Dosing Regimens

Systolic BP	Bolus dose	Maintenance rate
BP \geq 180	0.4 mg	17 μ g/min
140 \leq BP < 180	0.3 mg	10 μ g/min
110 \leq BP < 140	0.15 mg	6.7 μ g/min
95 \leq BP < 110	0.05 mg	3.3 μ g/min

Adapted from Nashed et al,⁶ and reproduced with permission.

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