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CASE REPORT

Cardiology

Ultra-high dose intravenous nitroglycerin in an ESRD patient with acutely decompensated heart failure

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Abstract

Acute cardiogenic pulmonary edema is a highly unstable and potentially lethal condition that is most commonly associated with markedly elevated blood pressure (BP). Use of nitrates, diuretics, and non-invasive positive pressure ventilatory support are the mainstays of early intervention and stabilization. Use of high-dose bolus intravenous nitroglycerin, which causes both preload and afterload reduction, has shown significant promise in studies to date, reducing the need for endotracheal intubation (ETI) and intensive care unit admission. To date, the highest recorded total dose of nitroglycerin used during the initial stabilization of acute pulmonary edema has been 20 mg. Here, we describe a patient with end-stage renal disease who developed acute cardiogenic pulmonary edema and received a total of 59 mg nitroglycerin (56 mg push dose intravenous + 3 mg intravenous drip) over 41 minutes leading to successful stabilization and avoidance of ETI, facilitating rapid initiation of emergent hemodialysis.

1 | INTRODUCTION

Mainstay therapy for acute heart failure (AHF) consists of vasodilators and diuretics. Vasodilators, such as nitroglycerin (NTG), provide both preload and afterload reduction, which is beneficial in AHF, especially for those who present with markedly elevated blood pressure (BP).[1] The mortality rate for severe AHF may be as high as 15% during the initial treatment period and 35% by 1 year.[2] Unfortunately, standard vasodilatory therapy does not reduce mortality or hospital readmission in these patients.[3] However, recent studies have found that the use of high-dose intravenous NTG in this setting may provide significant advantages over traditional treatment dosages.[4] Higher dose nitrates have been shown to lower rates of mechanical ventilation and endotracheal intubation (ETI), improve BP, and reduce myocardial injury.[4,5] This approach has also been shown to shorten hospital length of stay and decrease intensive care unit admissions.[4] When given sublingually and transdermally, nitrate doses up to 121 mg have been given over 48 hours and shown to be helpful and safe.[6] Existing data suggest a substantial improvement in symptoms and better in-hospital outcomes for patients with AHF, with minimal adverse effects.

1.1 | Narrative

A 72-year-old African-American man with a history of chronic obstructive pulmonary disease (COPD), heart failure with reduced ejection

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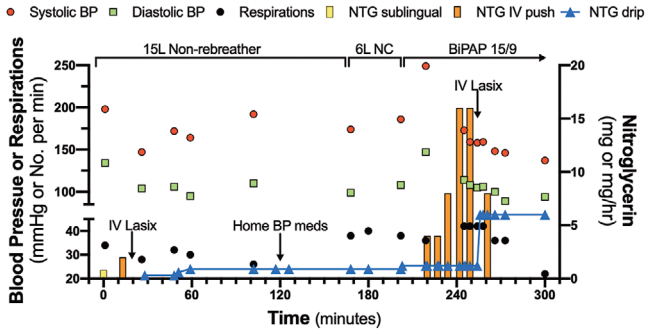

FIGURE 1 Overview of patient vital signs (left axis) and nitroglycerin dosing (right axis) during his ED course. Also shown are the delivery of oxygen and provision of other medications. Note: BiPAP, bilevel positive airway pressure; BP, blood pressure; IV, intravenous; NC, nasal canula; NTG, nitroglycerin

fraction, and end stage renal disease (ESRD) on hemodialysis Monday, Wednesday, and Friday, presented to the emergency department (ED) by ambulance with acute worsening of chronic dyspnea over the past day. He arrived to the ED in respiratory distress with a BP of 220/180 mm Hg and oxygen saturation in the low 80s on room air. On examination, he was tachycardic and tachypneic with a respiratory rate of 34 breaths per minutes. He had elevated jugular venous pressure and audible crackles halfway up the lungs bilaterally. There was no obvious evidence of lower extremity edema or ascites. He was initially placed on a non-rebreather at 15L. An electrogram showed sinus tachycardia at a rate of 127 beats per minutes with a prolonged QTc at 540 ms. There was no sign of acute ischemia, including in the inferior leads. After receiving an initial dose of 0.8 mg sublingual and 2 mg intravenous bolus NTG, the patient improved and crackles were diminished. A subsequent chest x-ray showed no acute cardiopulmonary process. Initial workup was significant for a serum creatinine of 6.89 mg/dL and a blood urea nitrogen of 46 mg/dL (estimated [glomerular filtration rate] GFR = 10 mL/min/1.73 m^2). A venous blood gas revealed hypoxic hypercapnic respiratory acidosis (pH = 7.31, PCO_2 = 54, pO_2 = 28, HCO_3 = 27) and a high sensitivity cardiac specific troponin (hs-cTnI) of 113 ng/L (Beckman Coulter assay; reference range: 3 ng/L detection limit and ≥18 ng/L suggestive of myocardial injury). A coronavirus swab was negative.

After the initial sublingual and intravenous bolus NTG, the patient was given 40 mg of intravenous furosemide for diuresis. There was an initial improvement in the patient's BP to 160/100 mm Hg and respiratory rate to the low 20s. He was started on a 5 μg/minutes (0.3 mg/hours) continuous NTG infusion, which was gradually scaled up to 20 μg/minutes based on the patient's symptoms (see Figure 1 for a time course of vital signs and treatments). At this time, the patient was stable enough to be given his home anti-hypertensive medications orally (80 mg valsartan, 10 mg amlodipine, and 25 mg metoprolol) and was transitioned from 15 L/minutes nonrebreather to 6 L/minutes nasal cannula. However, shortly thereafter, he developed worsening tachypnea and BP increased substantially to 249/147 mm Hg. He was placed on bilevel positive airway pressure (BiPAP) and intravenous push doses of NTG were administered in rapid succession starting with 2 2-mg doses followed by a 4-mg dose and an 8-mg dose. Endotracheal intubation was considered as he was tachypneic to the 40 seconds. Two additional 16-mg intravenous push doses of NTG followed by another 8 mg were given, and he experienced significant improvement in his symptoms. He was given another dose of intravenous furosemide (40 mg) and the NTG drip was increased to 100 μg/minutes. At this stage, his BP had improved to the 140s/90s with a respiratory rate in the 20 seconds. He was admitted to the ICU for further management, including bronchodilators and emergent hemodialysis.

2 | DISCUSSION

It has previously been demonstrated that high-dose bolus intravenous NTG for acute, cardiogenic pulmonary edema is associated with lower rates of ICU admission and ETI[4] and shorter lengths of stay in the hospital. Based on published reports, most patients are rapidly stabilized on lower doses of (ie, 1–2 mg NTG)[5] with the highest reported total dose given over a short time period of 20 mg.[4] For the patient presented in this case report, these doses were not sufficient, and intravenous bolus doses were quickly escalated up to 16 mg at a time for a NTG total of 56 mg given over 41 minutes (not including the continuous infusion drip that provided another ~3 mg). In this case, use of high dose intravenous NTG was safe and successful in a patient with acute cardiogenic pulmonary edema and markedly elevated BP. This patient had a known history of ESRD with similar episodes due to poor compliance with his hemodialysis and chronic oral antihypertensive regimen. Although this patient initially had a clear chest x-ray, likely due to the rapid onset of symptoms and initial aggressive treatment, his initial physical examination findings on presentation were consistent with his condition.

Although high-dose bolus intravenous NTG has been shown to be better tolerated in some phenotypes (ie, ESRD patients, African-Americans), it has a relatively short half-life and remains an ideal choice for AHF patients with markedly elevated BP and severe cardiogenic pulmonary edema.[7] Current recommendations for high dose bolus intravenous NTG are to use 2-mg doses given every 3 to 5 minutes. Although such an approach may, in combination with titrated drips, have a higher rate of hypotension as a complication,[5] this is very rare, particularly in African-Americans with poor baseline BP control. Although our case highlights the safety and use of this approach in this one African-American patient, it also provides important insight into the potential for symptom rebound, particularly if BP control is not adequately maintained. For this reason, we advocate for concurrent administration of an intravenous NTG infusion with oral antihypertensive therapy, with down titration (and ultimate discontinuation) of the infusion once the BP has stabilized.

In summary, when it comes to use of bolus intravenous NTG for AHF with acute hypertensive cardiogenic pulmonary edema, our case shows that early aggressive dosing coupled with on-going maintenance of BP reduction was both safe and effective for this single patient.

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