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Case Report

# Hyperinsulinemic Euglycemia Therapy for Acute Nitroglycerin Poisoning: Case Report

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## ABSTRACT

Nitroglycerin, a vasodilator, is commonly administered to treat ischemic heart disease. Adverse effects after toxicity are light-headedness, nausea, blurry vision, and syncope due to low systolic blood pressure as well as methemoglobinemia. A 19-year-old female was admitted to our toxicology department after suicidal ingestion of 320 mg extended-release nitroglycerin about 45 minutes before the admission. She was conscious, and her initial blood pressure was 98/65 mm Hg, which was decreased to 77 mmHg within 1.5 hours despite administration of 1 liter of normal saline. Due to severe hypotension, norepinephrine infusion was started for systolic blood pressure maintenance above 80mm Hg; however, she started complaining of palpitation and chest pain. So, the dose of norepinephrine was reduced, and glucose, insulin, and potassium protocol were started. After 3 hours of therapy, her hemodynamic condition stabilized with systolic blood pressure above 90mm Hg; hence norepinephrine was discontinued. She was discharged on the 3rd day after the psychiatric consultation, with regular clinical and paraclinical examinations.

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## 1. Introduction

Nitroglycerin, a vasodilator, is commonly administered to treat ischemic heart disease. Its effect is considered included in cardiac preload reduction and decrease of myocardial wall stress [1]. To our knowledge, human poisoning due to nitroglycerin medication is a scarce condition. Our data are limited to some narrative case reports published in the 20th century. Manifestations, however, could be exaggerated forms of known effects of the drug. Serious adverse effects are light-headedness, nausea, blurry vision, and syncope due to low systolic blood pressure.

Venous pooling and vasodilatation in the cranium can cause severe headaches [2]. Methemoglobinemia has previously been reported as a considerable manifestation of intoxication [3]. There is no effective antidote for nitroglycerin poisoning, and its management is supportive care [2]. This report describes the successful management of a case of severe hypotension and metabolic acidosis due to suicidal ingestion of extended-release nitroglycerin.

## 2. Case Presentation

A 19-year-old female was admitted to the clinical toxicology department of our hospital in 2021 after suicidal ingestion of 50 tablets (320 mg) of extended-release nitroglycerin about 45 minutes before the admission. On arrival, she was symptom-free. She was conscious, and her vital signs at presentation were: blood pressure, 98/65 mm Hg; heart rate, 91 beats/min; respiratory rate, 18 beats/min; and oxygen saturation was 98% on room air. Respiratory examinations and heart auscultation were normal.

The patient was previously healthy and used no medication. In the first Arterial Blood Gas (ABG) sampling pH, HCO3-, Base Excess (BE), and PCO2 were 7.32, 20.1 mmol/L, -6 mmol/L, and 32 mmHg, respectively. A summary of the preliminary medical test results is shown in Table 1. Due to admission within the first hour of ingestion, activated charcoal was given. The systolic blood pressure and oxygen saturation with a fingertip pulse oximeter were checked every 30 minutes. Supportive care was started, including normal intravenous saline for systolic blood pressure maintenance above 80mm Hg and norepinephrine in the case of insignificant response. During 1.5 hours after admission, 1 liter of normal saline was administered, but the systolic blood pressure decreased to 77 mmHg. Norepinephrine was started at 0.5 mcg/kg/min and increased to 5 mcg/kg/min. After 15 minutes, her Systolic Blood Pressure (SBP) rose to 101 mm Hg, but she started complaining of palpitation and chest pain. An electrocardiogram (ECG) was requested, and Venous Blood Gas (VBG) analysis was performed. The ECG showed diffuse T wave inversions.

VBG values are listed in Table 2, hour 3. Due to the significant drop in BE, despite the improvement in SBP, along with symptoms of chest pain and ECG changes, the dose of norepinephrine was reduced to 2 mcg/kg/min. glucose, insulin, potassium (GIK) protocol was started with 50 grams of glucose, 50 units of regular insulin, and 30mEq of potassium in 1 liter of normal saline for injection over an hour; followed by 25 grams of glucose, 25 units of regular insulin and 15mEq of potassium in 500 ml of normal saline for hourly injection. She remains hemodynamically stable with SBP≥90 mmHg. The subsequent VBG examination was performed about 3 hours afterward (Table 2, hour 6). Norepinephrine was discontinued regarding acceptable values in SBP and VBG. Her urine output was 100 ml/hour despite a large-volume normal saline infusion. Fortunately, respiratory auscultation and heart echocardiogram were normal, with an ejection fraction of 55%. Six hours later, another VBG examination was performed (Table 2, hour 12), and treatment with GIK and normal saline was also discontinued. For the following hours, she received only maintenance fluid therapy. She remained clinically stable.

The subsequent VBG analysis showed mild metabolic acidosis and good blood pressure (Table 2, hour 18), which returned to normal the next day (Table 2, hour 36). The liquid diet started, and the regular diet was ordered after tolerating it. She was discharged on the 3rd day after the psychiatric consultation, with normal clinical and paraclinical examinations. The patient agreed to publish this report.

## 3. Discussion

Herein we report a case of nitroglycerin poisoning with severe hypotension and metabolic acidosis. The mechanism of cardiovascular compromise in nitroglycerin poisoning is its breakdown and the release of nitric oxide in vascular smooth muscle cells [4]. Proper action of the vasculature results from the balance between nitric oxide-dependent vasodilatory effect and endothelin-1-dependent vasoconstriction effect of insulin [5]. Moreover, a high concentration of nitric oxide is associated with a decrease in ATP production in pancreatic β-cells, which leads to lower insulin production; however, it is vice versa at lower concentrations [6].

It is proposed that hyperinsulinemia will cause more uptakes of glucose by myocardial cells, increase cardiac con-

**Table 1.** Laboratory blood test results

| Test Item | | Values | Units |
|---|---|---|---|
| Blood biochemistry | AST | 52 | IU/l |
| | ALT | 46 | IU/l |
| | Na | 139 | mEq/l |
| | K | 3.5 | mEq/l |
| | Blood Glucose | 95 | mg/dl |
| | BUN | 12 | mg/dl |
| | Creatinine | 1 | mg/dl |
| | C-reactive protein | Negative | |
| Complete blood counts | WBC | 7.4 | *109 /l |
| | RBC | 4.37 | *1012 /l |
| | Hemoglobin | 13.2 | g/dl |
| | Hematocrit | 38.8 | % |
| | Platelets | 165 | *109 /l |
| Serological markers | HBsAg | Negative | |
| | Anti-HCV | Negative | |
| | Anti-HIV | Negative | |

AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; BUN: Blood urea nitrogen; WBC: White blood cell count; RBC: Red blood cell count.

tractility and increase peripheral vascular tone. The use of GIK is well described in the treatment of calcium channel antagonists and beta-blocker medications [7, 8]. However, there is no definitive strategy proposed for the use of GIK in the other antihypertensive drug toxicities. Reviewing the literature, we found some papers accentuating the role of NO-cGMP–mediated mechanisms on vasodilation with calcium channel blockers and beta-blockers [9, 10].

Our patient suffered severe hypotension despite receiving 1 liter of normal saline within the first hours of admission. Hence, norepinephrine, the second choice drug for treating persistent hypotension in vasodilator toxicity, was started [11]. But she started complaining of palpitation and chest pain associated with diffuse T wave inversions on ECG. Her VBG analysis revealed metabolic acidosis with a base excess of -10.3 mmol/L.

**Table 2.** Venous blood gas analysis, systolic blood pressure, and $O_2$Saturation on pulse oximetry during medical management

| Time After Admission (Hour) | pH | $HCO_3$ | BE | $PCO_2$ | SBP | O2Sat (Pulse Oximeter) |
|---|---|---|---|---|---|---|
| 3 | 7.38 | 14.8 | -10.3 | 25 | 103 | 98 |
| 6 | 7.25 | 18 | -9.2 | 41 | 101 | 96 |
| 12 | 7.30 | 19.2 | -7.2 | 39 | 96 | 97 |
| 18 | 7.31 | 18.1 | -8.4 | 36 | 95 | 97 |
| 36 | 7.36 | 23.2 | -2.2 | 41 | 125 | 98 |

As we know, BE is a valuable point to determine whether volume depletion is present and is a helpful guide to volume resuscitation [12]. Therefore, we assumed that she needed more volume resuscitation than a vasoconstrictor medication, and despite the acceptable response, the dose of norepinephrine was reduced.

Reviewing the literature and toxicology textbooks, we found no studies to prove the effectiveness of vasoconstrictors in nitroglycerin poisoning. Nevertheless, we thought that an ancillary medication could be helpful due to the anticipation of prolonged fluid therapy in the field of extended-release nitroglycerin use. Regarding its vasoconstrictor effect via endothelin-1- dependent pathway in vascular endothelial cells, we assumed that high dose insulin could alleviate the vasoconstrictor effect of nitroglycerin [5]. Reviewing the literature, we found only one report by Smith et al. presenting a case of an angiotensin II receptor antagonist, valsartan, and a calcium channel antagonist, amlodipine congestion, successfully managed by GIK administration [13]. Surprisingly, amlodipine can cause NO-dependent dilation of arteries in peripheral arteries [14]. Interestingly, Smith et al. showed as the insulin dose was increased, the need for epinephrine decreased [13].

In our case, GIK treatment was associated with a significantly lower need for norepinephrine administration. In the lack of evidence-based medical advice for using high-dose insulin in overdose with NO-mediated vasodilators, a possible mechanism (vasoconstrictor effect via endothelin-1- dependent pathway) and safety come from trials in patients undergoing cardiovascular surgery [15, 16], encouraged us to use this strategy. In addition to aggressive fluid therapy, GIK Helped her stay hemodynamically stable, and improvement in blood gas analysis was recorded.

For better patient cooperation and less harm, all blood gas sampling except the first one was performed via the venous system, but measuring O2 saturation with a pulse oximeter was performed to determine every need for additional observation of methemoglobinemia. Fortunately, our patient did not develop cyanosis, and her O2 saturation remained within the normal limit during our evaluation.

## 4. Conclusion

The primary treatment strategy for nitroglycerin poisoning is supportive care until the drug is metabolized. However, severe hypotension can make it more challenging to prevent cardiovascular collapse. In this article, for the first time, we report a case of extended-release nitroglycerin poisoning, which was successfully managed using excessive fluid therapy as well as administration of GIK for managing hypotension. We think that glucose, insulin, and potassium can be used to augment vascular tone in hypotension due to nitroglycerin, as well as other medications exert their therapeutic action through nitric oxide-induced vasodilation.

## Ethical Considerations

### Compliance with ethical guidelines

There were no ethical considerations to be considered in this work.

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### Authors' contributions

All authors equally contributed to this work.

### Conflict of interest

The authors declared no conflict of interest.

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