Case Report

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Epinephrine induced lactic acidosis during the management of anaphylactic shock: a case report

Running title: epinephrine induced lactic acidosis in anaphylactic shock

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ABSTRACT

In a case of contrast media-induced anaphylactic shock managed with epinephrine, a 57-year-old male developed lactic acidosis without cardiogenic shock or global hypoperfusion, highlighting epinephrine’s potential to trigger lactic acidosis. Despite previous management of similar reactions with antihistamines and corticosteroids, this case required intensive care unit admission and emergency intervention, with lactate levels peaking alarmingly. The rapid resolution of acidosis following epinephrine discontinuation underscores the need for careful monitoring and the consideration of alternative vasopressor strategies in severe anaphylaxis, illustrating the complex relationship between epinephrine’s metabolic effects and anaphylaxis-induced tissue hypoperfusion.

Keywords: anaphylaxis; epinephrine; lactic acidosis; critical care

CAPSULE SUMMARY

What is already known: Anaphylaxis is a severe systemic hypersensitivity reaction managed with epinephrine in ICU settings, but the complexities of associated conditions like lactic acidosis are not fully understood.

What is new in the current study: This case study reveals a direct correlation between epinephrine use in anaphylaxis and significant reversible lactic acidosis, underscoring the need for alternative management strategies in severe cases.
INTRODUCTION

Anaphylaxis is characterized as a systemic, immediate hypersensitivity reaction primarily mediated by IgE, leading to the release of mediators from mast cells and basophils. [1, 2] Anaphylaxis, a critical and potentially fatal manifestation of this hypersensitivity, demands prompt medical intervention to mitigate life-threatening consequences. Patients with such severe reactions often require management in an intensive care unit (ICU) setting.

Epinephrine stands as the primary, first-line treatment for anaphylaxis, its adrenergic agonistic properties promoting bronchodilation and vasoconstriction, thereby reversing the symptoms of anaphylaxis. [2] Although additional therapeutic agents may be considered after post-epinephrine administration and upon initiation of supportive care, their efficacy lacks robust evidence that supports epinephrine use. [3]

Shock, emanating from the cardiovascular system’s failure to maintain adequate tissue perfusion, presents through a variety of clinical syndromes. Lactic acidosis, marked by an elevation in blood lactic acid, signals tissue hypoperfusion and a shift toward anaerobic metabolism. [4] However, raised lactic acid levels may not exclusively indicate tissue hypoxia but can also mirror an adaptive response to severe infections or therapeutic interventions. [5] The occurrence of lactic acidosis in the context of anaphylactic shock, especially after epinephrine administration, introduces a complex clinical dilemma, prompting a reassessment of our understanding of the interplay between adrenergic stimulation, tissue perfusion, and metabolic pathways during acute anaphylactic reactions. The study was approved by the institutional review board of Samsung Medical Center (approval No 2024-02-086).

Although case reports of epinephrine-induced lactic acidosis are relatively common, instances where it complicates clinical judgment during the treatment of anaphylaxis are rare. This case report aims to highlight a significant episode of lactic acidosis that developed during the management of anaphylactic shock with epinephrine.

CASE REPORT
We present the case of a 57-year-old male patient, previously diagnosed with distal common bile duct cancer following an abnormal liver function test during a health screening two years prior, who underwent a pylorus-preserving pancreaticoduodenectomy. At the time of the initial computed tomography (CT) scan with contrast, no anaphylactic reactions were reported. Post-surgery, he was regularly monitored every six months with contrast-enhanced abdominal CT scans. During these follow-up sessions, he experienced symptoms of anaphylaxis, including rash and dizziness, which were preemptively treated with antihistamines and hydrocortisone before proceeding with the CT scans.

During his most recent CT scan with contrast, despite pre-treatment, he developed a rash, itching, altered consciousness, and significant hypotension (53/46 mmHg), leading to an emergency transfer to the emergency room (ER) following an intramuscular injection into the anterolateral aspect of the thigh of 0.5 mg epinephrine on the CT suite. Upon ER arrival, his vital signs were recorded as: temperature 36.3°C, heart rate 98 beat per minute, blood pressure 83/46 mmHg, respiratory rate 24 breathes per minute, and oxygen saturation 99% on room air. Physical examination revealed a skin rash on his trunk and extremities. Arterial blood gas analysis showed an elevated lactate level of 3.6 mmol/L, and electrocardiogram displayed sinus tachycardia. He was administered a third dose of intramuscular epinephrine and H1 and H2 blockers in the ER, accompanied by 1.5L of intravenous fluids. Despite these interventions, his blood pressure remained low as 76/39 mmHg, leading to his admission to the intensive care unit (ICU) for norepinephrine and epinephrine infusion.

No abnormalities were found in the chest X-ray and electrocardiogram at ICU admission. Throughout the ICU stay, even though his blood pressure recovered to 101/45 mmHg, his lactate levels continued to climb, reaching a peak of 13.5 mmol/L (Table 1). Utilizing point-of-care ultrasound evaluation at the bedside, it was possible to exclude the presence of cardiogenic shock. Additionally, the capillary refill time was observed to be within 2 seconds. After excluding other possible causes for the lactate elevation, epinephrine-induced lactic acidosis was suspected. Consequently, epinephrine administration was halted, decreasing lactate levels to 2.5 mmol/L. The patient’s condition eventually stabilized, allowing for the discontinuation of the concurrent norepinephrine and his subsequent discharge from the ICU.
DISCUSSION

This case reports highlights the rare yet critical incidence of significant lactic acidosis following the administration of epinephrine in treating anaphylaxis. The treatment involved multiple doses of epinephrine, fluid resuscitation, and vasopressor support in the ICU, reflecting the complex management of severe anaphylaxis. The observed severe lactic acidosis, which markedly improved upon the cessation of epinephrine, suggests that epinephrine may directly impact the development of this complication.

Anaphylaxis is a critical, life-threatening systemic hypersensitivity reaction characterized by rapid symptom onset across multiple organ systems. The immediate administration of epinephrine is essential, aiming to prevent potentially fatal delays. [6-8] Epinephrine activated adrenergic receptors, promoting vasoconstriction, improved cardiac output, and bronchodilation. [9]

In cases of severe anaphylaxis with persistent hypotension, continuous epinephrine infusion may be necessary. [10] However, this can induce lactic acidosis through mechanisms such as increased glycolysis, Na-K-ATPase activation, excessive vasoconstriction, and increased metabolic demand, elevating lactate production and causing tissue hypoxia. [11, 12]

Lactic acidosis, characterized by lactate levels >5mmol/L and pH <7.35, is categorized into type A or B. [13] Type A occurs in response to hypoxia or hypoperfusion, inhibiting pyruvate dehydrogenase, which prevents pyruvate conversion to acetyl-CoA, forcing anaerobic metabolism into lactate. Type B occurs in the absence of hypoxia or hypoperfusion, where pyruvate converts to lactate via aerobic glycolysis, commonly caused by diseases, drugs, or metabolic errors. [14] The patient in this case, who had not received other drugs known to cause lactic acidosis and had normal liver and kidney functions without evidence of global hypoxia or hypoperfusion, experienced lactic acidosis resolution spontaneously hours after stopping the epinephrine infusion.

Managing lactic acidosis in anaphylaxis contexts requires balancing the treatment of hypersensitivity reaction and mitigating acidosis effects. Persistent epinephrine-induced lactic acidosis,
despite clinical recovery, may necessitate reducing or stopping the infusion and considering alternative vasopressors. [6] The decision to continue or discontinue epinephrine depends on the shock status. With clinical improvement but worsening lactic acidosis, discontinuing epinephrine should be considered.

CONCLUSION

This case underlines the importance of vigilance concerning lactic acidosis during anaphylaxis treatment with epinephrine, especially in scenarios requiring prolonged infusions. The interrelation between anaphylaxis-induced tissue hypoperfusion and the metabolic effects of epinephrine necessitates meticulous monitoring and strategic management, including the potential needs for alternative treatments in the face of persistent, severe lactic acidosis.
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Conflicts of interest
None.

Author contributions
Conception and design: R-E Ko and H-S Oh; data analysis and interpretation: R-E Ko and H-S Oh; drafting the manuscript for intellectual content: R-E Ko and H-S Oh; revision of the manuscript: CR Chung, C-M Park, and GY Suh. All authors have read and approved the final manuscript.

Ethical approval and consent to participate
The study was approved by the institutional review board of Samsung Medical Center (approval no. 2024-02-086)
REFERENCES


Figure 1. At intensive care unit admission

Panel (A) shows a chest X-ray of a patient with normal lung fields, cardiac silhouette, and clear costophrenic angles. Panel (B) presents a standard 12-lead electrocardiogram, demonstrating normal sinus rhythm with no electrical or structural abnormalities.
Figure 2. Dynamics of lactate and epinephrine administration over time

This figure illustrates the changes in lactate levels and epinephrine dosages over time. The X-axis represents time in hours from a reference point labeled as Time 0. The left Y-axis shows lactate levels measured in millimoles per liter (mmol/L), while the right Y-axis presents epinephrine dosages in micrograms per kilogram per minute (mcg/kg/min). Lactate levels are marked with red circles and epinephrine dosages with blue squares.
Table 1. Hemodynamics and laboratory data

<table>
<thead>
<tr>
<th>Time</th>
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<th>53 m</th>
<th>2h 7m</th>
<th>4h 14m</th>
<th>8h 13m</th>
<th>9h 51m</th>
<th>11h 42m</th>
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<td>92</td>
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<td>97</td>
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<td>50</td>
<td>48</td>
<td>46</td>
<td>55</td>
<td>57</td>
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<td>PO₂, mmHg</td>
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<td>0.1</td>
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BE = base excess, DBP = Diastolic blood pressure, HR = heart rate, RR = respiratory rate.