Case Report

Hyperlactatemia caused by intra-venous administration of glycerol: A case study

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Abstract

Glyceol® is an intracranial pressure reducing agent composed of 5% fructose and concentrated glycerol. Although rapid administration of fructose is known to cause lactic acidosis, little is known about hyperlactatemia caused by Glyceol® administration itself in adults. We observed an adult case of hyperlactatemia occurred after administration of 200 mL of Glyceol® over a period of 30 minutes. Since there was no evidence of an underlying liver disease or metabolic abnormality, and no findings of sepsis or impaired tissue perfusion, the cause of this condition was deemed to be the rapid loading of fructose contained as a constituent of Glyceol®. We then performed a retrospective chart review and found other 9 cases admitted to Jichi Medical University Hospital ICU and administered Glyceol® during the past year. Their lactate levels increased in general, peaked approximately 45 minutes after Glyceol® administration and returned to pre-administration levels around 3 hours after. Although hyperlactatemia is an important indicator of sepsis and impaired tissue perfusion, caution is required when performing such an assessment in patients being administered Glyceol®.

Keywords: Glycerol, hyperlactatemia, pyruvic acid

Access this article online

Website: www.ijccm.org

DOI: 10.4103/0972-5229.106514

Quick Response Code:

Introduction

Glyceol® is an intracranial pressure reducing agent composed of 5% fructose and concentrated glycerol. Although children with some congenital metabolic diseases experience hyperlactatemia, there are seldom, if ever, the case in adults.

Case Report

A 53-year-old woman with a medical history of the craniotomy for meningioma removal 10 years ago, was again scheduled the operation for her regrown tumor removal. She also had hypothyroidism for the past 10 years, which was treated with oral prednisolone at 20 mg/day and levothyroxine sodium at 50 μg/day.

Table 1 shows the results of blood chemistry tests performed at the time of admission to the hospital.

The patient was admitted to our ICU after the initial attempt of tumor removal, which resulted in failure because of severe hemorrhage prior to tumor handling. Surgery was then performed 3 months after ICU discharge, and the patient was once again admitted to the ICU after surgery. During both stays in the ICU the patient was administered 200 mL of Glyceol® over a period of 30 minutes, every 6 hours from 0:00 am. Despite her stable general condition, routine arterial blood gas analysis (Diagnostics 860, Chiron, CA, US) at around 6:30 every morning indicated reappeared hyperlactatemia. The fact that repeated measurements of her lactate levels were normal at other time points, made us to consider Glyceol® administration as the cause of her transient hyperlactatemia.

To exclude the possibility of impaired tissue perfusion caused by rapid infusion of hypertonic solutions as another cause of this transient hyperlactatemia, the

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patient was alternately administered Glyceol® and 20% mannitol solutions. The lactate levels increased gradually and peaked 45 minutes after Glyceol® administration, while no significant change was observed in case of mannitol. Blood glucose level increased slightly after Glyceol® administration but the increase was not significant [Figure 1]. This transient hyperlactatemia was reproducible by administration of Glyceol®.

Metabolic abnormality was also considered another possible cause of her transient hyperlactatemia; however her amino acid analysis, urinary organic acid analysis and serum acyl carnitine analysis all showed normal results, and hyperammonemia, hypoglycemia, or ketonuria were not observed. In addition, impaired perfusion, infection and convulsive seizure were not observed during patient admission. Liver diseases including hepatitis, congenital metabolic diseases, glycerol metabolism abnormality, any diseases similar to Reye's syndrome, mitochondrial disorders and other conditions were all considered as differential diagnoses but were all unlikely because of her laboratory finfings. Moreover, Glyceol® administration produced hyperlactatemia even after correcting her hemoglobin concentrations in order to improve oxygen transport, while increased urinary excretion of lactic and pyruvic acids was found [Table 2].

Since mannitol and Glyceol® administration resulted in different levels of lactate concentration, transient hyperlactatemia was unlikely to be triggered by impaired tissue perfusion caused by rapid infusion of hypertonic solutions.

We then performed a retrospective chart review and found other nine patients admitted to Jichi Medical University Hospital ICU after intracranial surgery and administered Glyceol® during the past year. All nine cases were confirmed to be without notable dehydration, infection or convulsive seizure before or after the administration of Glyceol®. We found that their lactate levels increased in general, peaked approximately 45 minutes after Glyceol® administration and returned to preadministration levels around 3 hours after [Figure 2]. No significant change in blood glucose was seen during Glyceol® administration.

Discussion

Majority of the intravenously administered fructose is taken up by the liver and converted by fructokinase into fructose-1-phosphate, which then enters the glycolytic or gluconeogenesis system and is metabolized into lactate, glucose or glycogen. Fructokinase activity remains unchanged under insulin deficiency, and since

Table 1: Laboratory findings on admission

Blood cell count		Blood biochemistry	
WBC	7100 mm^{-3}	Alb	3.7 $g.dl^{-1}$
Hb	13.3 $g.dl^{-1}$	AST	15 $U.l^{-1}$
Ht	40.3%	ALT	18 $U.l^{-1}$
Plt	37.3 × 10^4 mm^{-3}	LDH	261 $U.l^{-1}$
		Na	136 $mmol.l^{-1}$
		K	4.3 $mmol.l^{-1}$
		T-Bil	0.61 $mg.dl^{-1}$
		BUN	20 $mg.dl^{-1}$
		Creatinine	0.59 $mg.dl^{-1}$
		CRP	0.02 $mg.dl^{-1}$
		ChE	211 $U.ml^{-1}$

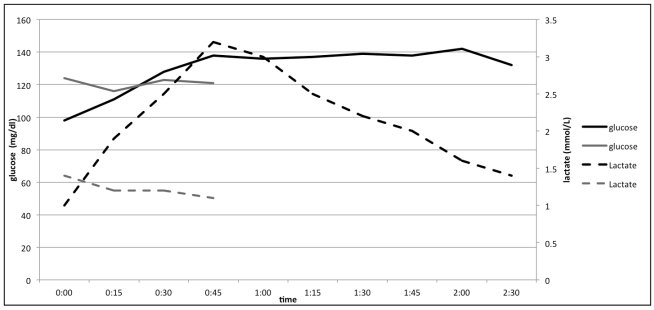

Figure 1: Serum lactate and glucose levels after administration of glycerol and mannitol. Gray line: 150 ml of 20% mannitol administered in 15 minutes. Black line: 200 ml of glycerol administered in 30 minutes

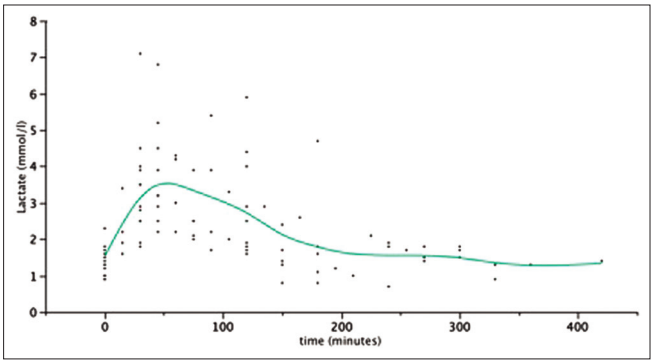

Figure 2: Serum lactate level after administration of glycerol 200 ml. This graph was described by spline curve

fructose metabolism does not involve glucokinase or phosphofructokinase, which activities are reduced under insulin deficiency, fructose is easily metabolized and causes the accumulation of pyruvate even in the conditions of reduced glucose tolerance. Metabolism of fructose into pyruvate in the liver is rapid enough to accumulate large amount of unmetabolised pyruvate by the TCA cycle, and hence cause hyperlactatemia. The ratio of administered fructose converted to glucose is reported to be about 30%.[1]

Lactate as an end-metabolite of fructose competes with renal uric acid excretion, and hence, accelerate nucleic acid turnover and increase uric acid production, and

Table 2: Urinary organic acid profiles 1 hour after the administration of glycerol

Compound Name	MRA	Normal	Normal (low)	Normal (high)	Factor
Lactic-2	81.28	0.80	0.00	4.70	101.61
Glycolic-2	3.28	0.70	0.00	2.20	4.69
Glyoxylic-OX-2	1.73	1.20	0.00	6.10	1.44
3-OH-propionic-2	4.45	0.20	0.00	1.10	22.25
Pyruvic-OX-2	76.01	4.50	0.00	24.10	16.89
3-OH-butyric-2	2.78	0.70	0.00	3.70	3.97
3-OH-isobutyric-2	16.55	2.50	0.00	9.00	6.62
2-Keto-isovaleric-OX-2	3.27	0.00	0.00	0.10	?
Ethylhydracrylic-2	4.70	0.00	0.00	2.90	?
Urea-2	20.72	376.10	104.60	763.00	0.06
Benzoic-1	2.71	4.40	0.00	18.70	0.62
2-Keto-3-methylvaleric-OX-2	4.37	0.00	0.00	0.00	?
2-Methyl-3-OH-valeric-2(1)	155.20	0.00	0.00	0.00	?
Glycerol-3	1885.68	0.30	0.00	0.80	6285.60
2-Methyl-3-OH-valeric-2(2)	155.20	0.00	0.00	0.00	?
Ethylmalonic-2	2.28	0.90	0.00	6.20	2.53
2-Keto-isocaproic-OX-2	5.23	0.00	0.00	0.00	?
Succinic-2	8.90	32.70	6.50	65.80	0.27
Glyceric-3	17.18	0.20	1.60	1.60	85.92
Fumaric-2	7.89	2.00	0.00	7.30	3.94
3-Methylglutaconic-2	1.98	1.10	0.00	4.20	1.80
Malic-3	2.26	0.10	0.00	0.70	22.57
Adipic-2	1.45	3.00	0.50	5.00	0.48
7-OH-octanoic-2	1.48	0.00	0.00	0.00	?
5-OH-methyl-2-furoic-1	3.53	0.00	0.00	0.00	?
2-OH-glutaric-3	2.40	2.30	0.60	5.90	1.04
3-OH-glutaric-3	8.64	0.00	0.00	0.00	?
Phenyllactic-2	2.04	0.30	0.00	4.90	6.78
2-Ketoglutaric-OX-2(1)	31.60	26.10	3.00	102.90	1.21
4-OH-phenylacetic	14.81	27.10	8.60	73.20	0.55
Hexanoylglycine-1	2.09	0.00	0.00	0.00	?
Aconitic-3	35.21	64.70	15.10	86.10	0.54
Homovanillic-2(HVA)	4.60	16.30	5.80	24.90	0.28
Isocitric-4	8.53	22.90	8.30	29.00	0.37
Citric-4	115.55	441.10	31.40	572.30	0.26
Hippuric-1	7.09	30.10	6.20	284.10	0.24
Vanilmandelic-3(VMA)	41.43	46.60	11.70	84.60	0.89
Indole-3-acetic-2	11.58	27.60	0.00	78.70	0.42
3,6-Epoxydodecanedioic-2	9.15	1.60	0.00	5.20	5.72
Tetracosane(C24)	42.25	0.00	0.00	0.00	?
IS-2(tropic acid)	237.52	0.00	0.00	0.00	?

then induces hyperlactatemia.[2] Renal excretion of uric acid is known to be inhibited competitively by acidosis of most organic acids including lactate.[3] Because of the rapid metabolism of fructose, large quantities of ATP are consumed in the liver, thus affect the hepatic metabolism. Furthermore, along with decreased ATP, amount of inorganic phosphoric acid is also reduced and can cause hypophosphatemia. Although we did not measure phosphoric acid and uric acid levels in the case reported here, it is likely that phosphoric acid levels may differ from baseline levels immediately after Glyceol® administration.

The preferred rate of fructose administration is generally taken as not more than 0.3 g/kg/hour.[4] According to the report that investigated the optimum dosage of Glyceol® for intracranial pressure reduction, recommended dosage of Glyceol® administration in the case of 50 kg body weight would be 200 mL/40 minutes or 300 mL/hour and below. In our case described here and in nine cases investigated retrospectively, the rate of Glyceol® dosage all exceeded the above-mentioned recommended limit. Therefore, excessive fructose loading might be the cause of transient hyperlactatemia in our cases.

Hyperlactatemia is a sensitive indicator of impaired tissue metabolism, and associated with morbidity in circulatory shock patients.[5,6] In septic shock patients, hyperlactatemia is also reported to be associated with prognostic outcomes.[7] Lactate measuring within 3 hours of Glyceol® administration will not represent an accurate clinical status, critical care physicians must keep this rather unfamiliar phenomenon in mind when evaluate the lactate levels in patients with critically ill.

Conclusions

Since the cause of hyperlactatemia was deemed to be the rapid loading of fructose contained as a constituent of Glyceol®, clinicians must be cautious about the dosage of this hypertonic solution. Furthermore, lactate measurement should be done before Glyceol® administration, and as one possible cause of hyperlactatemia, physicians must keep this rather unfamiliar phenomenon in mind.

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How to cite this article: Katayama S, Nunomiya S, Wada M, Misawa K, Tanaka S, Koyama K, *et al*. Hyperlactatemia caused by intra-venous administration of glycerol: A case study. Indian J Crit Care Med 2012;16:241-4.

Source of Support: Nil, **Conflict of Interest:** None declared.