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Evaluation of fluid volume status with a glucose challenge test in a patient with acute adrenal insufficiency

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Introduction

Evaluation of fluid volume status in critically ill patients is important in medical and surgical management. However, commonly monitored variables, including pulmonary artery wedge pressure, do not always reflect fluid status adequately [1,2]. ^{14}C-labeled glucose has been used as an indicator to measure the extracellular water content [3]. We demonstrated that the initial distribution volume of glucose (IDVG) reflects plasma volume rather than glucose metabolism [4,5]. Recently, we had a patient who developed severe hypotension shortly after aortic surgery. We could not convincingly rule out the presence of hypovolemia in this patient. Consequently, we performed a glucose challenge test and calculated the IDVG so as to evaluate fluid volume status in the body, and the result showed that obvious hypovolemia was not present. In retrospect, the patient was found to have developed acute adrenal insufficiency at that time. Thus we consider this case instructive.

Case report

A 67-year-old man weighing 51.5 kg was admitted to the intensive care unit (ICU) immediately after emergency operative repair of a ruptured abdominal aortic aneurysm. The patient was hypothermic. Two hours later, when normal body temperature had been restored with the aid of Bear Hugger (Augustine Medical, Inc., Eden Prairie, MN, USA), the patient became hypotensive: arterial blood pressure (ABP) of 78/40 mmHg associated with mean central venous pressure (CVP) of 0 mmHg and heart rate of 120 bpm (Table 1). These parameters were corrected by infusions of 1000 ml of blood and 560 ml of a colloid solution over 2 h. However, at 6 h after ICU admission, ABP again started to decrease gradually, and at 10 h, it fell to 82/52 mmHg associated with CVP of 4 mmHg and heart rate of 112 bpm. During this 10-h period the patient was agitated and frequently complained of abdominal and back pain. A total of 0.6 mg of buprenorphine was administered. Bloody drainage continued consistently at a rate of approximately 30 g·h^{-1}. Postoperative hemorrhage was strongly suspected to be the major cause of the hypotension, and a further 400 ml of blood and 500 ml of lactated Ringer's solution were administered rapidly, associated with a postoperative routine crystalloid infusion (90 ml·h^{-1}). However, at 11 h after ICU admission, the hypotension had deteriorated even more, although radial pulsation was easily palpable and the peripheral skin was warm. Analysis of arterial blood gases with Fio_2 0.4 by face mask had revealed a pH of 7.41, $Paco_2$ 30 mmHg, Pao_2 67 mmHg, and base excess −4.0 mEq·l^{-1}. Laboratory values included white blood cell count 10.0 per cubic millimeter, hemoglobin 10.0 g·100 ml^{-1}, serum sodium 127 mEq·l^{-1}, serum potassium 4.8 mEq·l^{-1}, serum chloride 105 mEq·l^{-1}, serum lactate 5.5 mmol·l^{-1}, and blood urea nitrogen (BUN) 35 mg·100 ml^{-1}. We then decided to estimate the IDVG derived from a glucose challenge test [6] so as to evaluate fluid volume status in the body.

An infusion of 25 ml glucose, at 20% (5g), was administered over 30 s, and arterial blood samples were drawn before the infusion and at 3, 4, 5, and 7 min post infusion. Plasma was separated immediately. Plasma glucose concentrations were measured in the ICU

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Table 1. Sequential changes in hemodynamic parameters after admission to the ICU

Time (h)	0	2	4	6	8	10	11
ABP (mmHg)	125/68	78/40	106/60	110/66	90/48	82/52	55/30
CVP (mmHg)	2	0	7	3	4	4	7
HR (bpm)	122	120	106	110	112	112	122
BE ($mEq \cdot l^{-1}$)	−7.4	—	−1.6	−1.0	—	−4.0	−5.0
Hb ($g \cdot 100 ml^{-1}$)	7.8	—	8.5	9.5	—	9.5	10.0
UV ($ml \cdot h^{-1}$)	34	32	100	150	12	12	0
BT (°C)	34.4	36.3	37.7	37.7	37.9	38.2	38.0
Rapid administration							
Blood (ml)			1000				400
Colloid (ml)			560				—
Lactated Ringer's solution (ml)			—				500

ICU, intensive care unit; ABP, arterial blood pressure; CVP, central venous pressure; HR, heart rate; BE, base excess; Hb, hemoglobin; UV, urine volume; BT, body temperature.

laboratory and the IDVG was calculated as described in a previous study [6]. The turnaround time of five plasma glucose determinations was 7 min. The plasma glucose concentration was $76 mg \cdot 100 ml^{-1}$ before the challenge, and 130, 123, 119, and $113 mg \cdot 100 ml^{-1}$ at 3, 4, 5, and 7 min post infusion, respectively. The computed IDVG [6] was 7.221 ($140 ml \cdot kg^{-1}$), which indicated that the IDVG was within the normal range ($130–160 ml \cdot kg^{-1}$ [7,8]). In addition, abdominal ultrasonography did not reveal any hemorrhage. Thus we believed that cardiovascular collapse in the absence of hypovolemia had developed in this patient. At that time neither a total of 40 mg of i.v. ephedrine nor an infusion of dobutamine up to $15 \mu g \cdot kg^{-1} \cdot min^{-1}$ improved the situation.

Subsequently, an infusion of epinephrine was started at $0.1 \mu g \cdot kg^{-1} \cdot min^{-1}$ and increased up to $0.7 \mu g \cdot kg^{-1} \cdot min^{-1}$, resulting in ABP of 80/55 mmHg without a significant heart rate change. In the meantime, investigation of this patient's medical history revealed he had been taking 5 mg prednisone daily for 15 years due to polymyositis. Acute adrenal insufficiency was immediately suspected, and an i.v. bolus of 1 g methylprednisolone was given. Immediately after the injection, ABP gradually increased to 138/62 mmHg associated with resolution of the patient's agitated mental status. Consequently, the infusion of epinephrine was tapered off and discontinued on the 1st postoperative day. Thereafter, the patient had a relatively uneventful postoperative course, received glucocorticoid coverage, and required no further rapid blood or fluid infusions during his ICU stay. He was discharged from the ICU on the 4th postoperative day. However, the patient suddenly died of unknown causes on the 16th postoperative day. Autopsy revealed marked bilateral atrophy of the adrenal glands.

In retrospect, the plasma cortisol level immediately before the methylprednisolone injection was $20.5 \mu g \cdot 100 ml^{-1}$, which indicated that the hypothalamic-pituitary adrenal axis could not adequately respond to acute stress in this patient (normal range: more than $22 \mu g \cdot 100 ml^{-1}$ during acute stress [9]).

Discussion

Although true acute adrenal insufficiency is an uncommon event in post-operative intensive care, it does occur in a number of glucocorticoid-treated patients undergoing major surgery without perioperative glucocorticoid coverage [10]. Diagnosis of acute adrenal insufficiency during the early postoperative period is rather difficult when a patients has undergone emergency surgery lacking a comprehensive evaluation, and the clinical picture may be indistinguishable from hypovolemic shock [11] or septic shock [12,13].

In retrospect, as observed in a previous report [12], the patient probably had a hyperdynamic cardiac output associated with low vascular resistance, judging by his consistently palpable radial pulses and warm peripheral skin temperature even during severe hypotension. This patient also had signs and symptoms of acute adrenal insufficiency including hyponatremia, sustained abdominal pain, and agitated mental status [14]. Although a large dose of epinephrine by infusion could have reversed the severe hypotension, the patient rapidly and dramatically responded to additional glucocorticoids with resolution of hemodynamic instability, abdominal pain, and agitated mental status as described in a previous report [15]. Glucocorticoids have also been shown to have an alternative effect on adrenergic receptors, presumably by increasing the density of new β-receptors and coupling the receptor to the agonist [16]. The plasma cortisol level before methylprednisolone injection was relatively low, since the plasma cortisol level in acute stress normally requires at least $22 \mu g \cdot 100 ml^{-1}$ to respond to stress adequately [9], and the average

plasma cortisol level in severe stress has been demonstrated to be $50\mu g \cdot 100 ml^{-1}$ [14]. These findings as well as the results of the autopsy permit us to conclude that acute adrenal insufficiency developed in this patient, even though left ventricular dysfunction secondary to polymyositis [17] may have also played a role.

A small amount of glucose (5g) can be administered safely and repeatedly even in critically ill patients unless they have excessive hyperglycemia or there is a risk of ischemia of the central nervous system. In addition, the IDVG can be approximately predicted by only two plasma glucose determinations ($r = 0.94$, $P < 0.001$): immediately before glucose is given and 3min after the challenge [6]. The IDVG in this patient derived from two plasma samples was 7.451 ($145 ml \cdot kg^{-1}$), and the IDVG derived from four plasma samples within 7min was 7.221 ($140 ml \cdot kg^{-1}$), both of which indicated that the IDVG was within normal limits ($130–160 ml \cdot kg^{-1}$ [7,8]). Recently, the IDVG was found to reflect plasma volume [4,5] and to be approximately the same as the extracellular fluid volume of highly perfused tissues, including plasma volume measured by the sucrose dilution method in normo- and hypovolemic dogs [18], even though the IDVG does not directly indicate plasma volume.

In normal subjects, exogenous glucose loading inhibits hepatic glucose output and promotes insulin release from the pancreas. However, this does not hold true when patients have sepsis or stress associated with surgery; in such patients, the extracellular fluid volume of highly perfused tissues, including the plasma volume, is more likely to be measured.

In conclusion, we report herein on a patient who developed acute adrenal insufficiency shortly after emergency operative repair for a ruptured abdominal aortic aneurysm. The clinical picture was indistinguishable from shock due to loss of intravascular fluid volume. We conclude that the IDVG may have the potential to evaluate a patient's fluid volume status even during severe hypotension. However, further investigation will be necessary before the IDVG can be adapted to clinical use.

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