CASE REPORT – OPEN ACCESS

International Journal of Surgery Case Reports 6 (2015) 285–288

Contents lists available at ScienceDirect

International Journal of Surgery Case Reports

journal homepage: www.casereports.com

Temporary hyperlactataemia during partial hepatectomy: Report of two cases

Yi Zou [1], Jitong Liu [1], Yongqiong Liao, Wanmin Pei, Gaoyin Kong*

Department of Anesthesiology, Hunan Provincial People's Hospital, Jiefang West Road No. 61, Changsha City, Hunan Province, PR China

ARTICLE INFO

Article history:
Received 16 August 2014
Received in revised form
15 September 2014
Accepted 18 September 2014
Available online 11 December 2014

Keywords:
Lactic acidosis
Hepatectomy
Hepatic vascular occlusion

ABSTRACT

Lactic acidosis (LA) is characterized by accumulation of lactate in the body, and it may detrimentally affect homeostasis. Perioperative LA is rarely seen, here we presented 2 cases of patients suffered with temporary hyperlactataemia during partial hepatectomy, intended to emphasize that prolonged hypovolemia condition caused by controlled low central venous pressure, and overused hepatic vascular occlusion technique during parenchymal resection of hepatic surgery may seriously impact on the internal environment of patients. And we also discussed how to well manage long-time hepatectomy to prevent LA from occurring and to treat it appropriately.

1. Introduction

Lactic acidosis (LA) is defined as metabolic acidosis caused by accumulation of lactate in the body, and is characterized by hyperlactataemia with a plasma lactate concentration of above 5 mmol/L.[1] It is mostly found in patients with shock, sepsis, liver disease and respiratory failure, and is of low survival rate.[2] However, it is not known how common it is for temporary hyperlactataemia to occur during liver resection. Here we presented 2 cases of temporary hyperlactataemia which occurred during partial hepatectomy, and considered that prolonged hypovolemia caused by controlled low central venous pressure (CLCVP), and overused hepatic vascular occlusion (HVO) during parenchymal transection may seriously impact the internal environment of patients. However, this complication may fully recover within a short time with no serious consequence if properly treated.

2. Case presentation

2.1. Case 1

A 64-year-old Chinese woman diagnosed with hilar cholangiocarcinoma, but with no history of cardiovascular or respiratory disease, diabetes mellitus, blood transfusion or allergy, was scheduled for liver segments I, V, VI, VII and VIII resection. Her laboratory examinations were unremarkable.

Rapid sequence introduction (RSI) followed by intratracheal intubation were achieved. Anesthesia was maintained by continuous propofol infusion and sevoflurane inhalation. A central venous line via the right internal jugular vein and a radial arterial cannula were then placed for measurement of central venous pressure (CVP) and arterial blood pressure (ABP), respectively at the start of the operation. $2^1/_2$ h into the operation, the patient had totally received colloid 1750 ml, Inverl Sugar Injection (ISI) 100 ml, and the ABP was 80–90/40–50 mmHg, CVP 3 cm H_2O. Then colloid 250 ml and ISI 400 ml were dripped continuously at a low rate. $3^1/_2$ h into the operation, the 1st blood gas analysis revealed pH 7.27, lac 2 mmol/L, BE −8.8 mmol/L, Glu 12.2 mmol/L (Table 1).

5 h into the operation, because of rapid bleeding from the operating field (about 50 ml bleeding in 5 min), the surgeons requested a CLCVP. The CVP was lowered to 2 cm H_2O by restricting fluid transfusion. As the ABP was 80–85/45–50 mmHg, epinephrine infusion in 0.1 mg/h was used to maintain the mean arterial pressure (MAP) at 50–60 mmHg. $6^1/_3$ h into the operation, parenchymal transection started under CLCVP. 35 min later, the 2nd blood gas analysis revealed pH 7.29, lac 5.4 mmol/L, BE −8.1 mmol/L, Glu 17.1 mmol/L. 5% $NaCO_3$ 250 ml were immediately administered for acidosis therapy. During this period, complete HVO of less than 15 min each was implemented twice. $11^1/_2$ h into the operation, parenchymal transection finished. The total blood loss was 1700 ml. Because of the unstable circulation, epinephrine 0.1–0.4 mg/h was continuously infused to maintain the ABP at 80–85/45–50 mmHg. Meanwhile, the 3rd blood gas analysis revealed pH 7.01, Lac 15 mmol/L, BE −20.3 mmol/L, and Glu 21.3 mmol/L, another 150 ml of 5% $NaCO_3$

* Corresponding author. Tel.: +86 13908476981.
E-mail address: 1193135376@qq.com (G. Kong).
[1] These 2 authors are of equal contribution to this work.

http://dx.doi.org/10.1016/j.ijscr.2014.09.026

Table 1
Blood gas analysis of the 1st patient.

Time	pH	pCO_2 (mmHg)	pO_2 (mmHg)	K^+ (mmol/L)	Ca^{2+} (mmol/L)	Glu (mmol/L)	Lac (mmol/L)	Hct (%)	Hb (g/dL)	HCO_3^- (mmol/L)	BE (mmol/L)
19:06	7.27	38	543	5.2	1.08	12.2	2	27	8.4	17.4	−8.8
22:25	7.29	37	558	3	1.03	17.1	5.4	27	8.4	17.8	−8.1
0:24	7.01	40	520	3.5	0.9	21.3	15	26	8.1	10.1	−20.3
1:32	7.06	39	515	3.4	0.93	19.5	>15	26	8.1	11	−18
2:12	7.04	34	366	3.3	0.92	17	>15	26	8.1	9.2	−20
3:42	7.33	44	475	3.3	0.81	13.7	>15	31	9.6	23.2	−2.7
4:20	7.2	30	207	3.2	1.01	15.4	>15	37	13	11.7	−15
8:57	7.5	40	142	4.1	1.05	14.7	10.1	36	12.6	31.2	7.4

were administered. Hypertonic Sodium Chloride Hydroxyethyl Starch 40 Injection 400 ml, concentrated red blood cells (CRBC) 4u and fresh frozen plasma (FFP) 450 ml were given for fluid resuscitation. The ABP was elevated to 105–115/70–80 mmHg, but blood gas analysis revealed lactate concentration still remained above 15 mmol/L (Table 1). At the end of the operation, the patient was kept anesthetized and transferred to the intensive care unit (ICU) for postoperative management without removal of the tracheal tube.

Follow-up in the next day, the patient was conscious with no remarkable complications and was extubated in the afternoon. He was then transferred to the general ward with an uneventful recovery. The last blood sample taken in the morning revealed pH 7.50, Lac 10.1 mmol/L, BE 7.4 mmol/L, and Glu 14.7 mmol/L.

2.2. Case 2

A 57-year-old Chinese man with alcoholic liver disease and a large right liver hepatocellular carcinoma was scheduled for liver segments VI and VII resection. There was no history of cardiovascular or respiratory disease, diabetes mellitus or allergy. His laboratory examinations were unremarkable.

The patient's preoperative ABP was 154/73 mmHg. General anesthesia was induced by RSI, and was maintained with sevoflurane, propofol and dexmedetomidine. Folley catheter insertion, central venous catheterization via the right internal jugular vein and radial arterial cannulation were then inserted to measure the urine volume, CVP and ABP. At the start of the operation, the systolic blood pressure (SBP) and CVP were maintained at 120–130 mmHg and 6 cm H_2O, respectively, by crystalloid/colloid transfusion and anesthetics. 30 min into the operation, the 1st blood gas analysis revealed pH 7.29, Lac 1.7 mmol/L, BE −7.3 mmol/L and Glu 7.2 mmol/L (Table 2).

$1^2/_3$ h into the operation, hepatic parenchymal transection started and the recorded urine volume was 450 ml. To facilitate the surgical procedure, the CVP was maintained at 2–4cmH_2O, and SBP > 90 mmHg. 4 h into the operation, parenchymal transection was finished (tumor size 10 cm × 10 cm × 5 cm). During the transection, right-HVO was implemented for 8 times (mean occlusion time 13.4 min, mean interval time 6.7 min). The total colloid transfusion volume was 750 ml, Ringer's solution 500 ml, Plasmalyte-A 500 ml, blood loss was 600 ml and urine 250 ml. The 2nd blood gas analysis at this time revealed pH 7.19, Lac 7.2 mmol/L, BE −11.4 mmol/L, Glu 8 mmol/L. 5% $NaCO_3$ 100 ml were immediately administered, and massive transfusion of Plasmalyte-A combined with diuresis by furosemide for lactate discharge were initiated. 1 h later, blood gas analysis revealed pH 7.21, Lac 9.1 mmol/L, BE −8.2 mmol/L, Glu 7.7 mmol/L. 5% $NaCO_3$ 150 ml were given and Plasmalyte-A transfusion with diuresis were continued.

The patient's vital signs were stable till the operation was finished . He was extubated $1^1/_2$ h later and transferred into the ICU. During LA therapy, the patient had totally received colloid 500 ml, Plasmalyte-A 4500 ml and urinated 4800 ml, the blood lactate level raised to 11.4 mmol/L and then declined (Table 2).

Follow-up in the next day, the patient had been sent back to the general ward and was conscious with stable vital signs. Blood gas analysis in the morning revealed pH 7.38, BE 0.9 mmol/L, Glu 7.7 mmol/L, but lactate concentration was unknown because a different blood gas analyzer was used. Anion gap (AG) was calculated as 12 mmol/L (normal value 8–16 mmol/L). The patient also had an uneventful recovery and discharged two weeks later.

3. Discussion

Lactate is a byproduct of glycolysis from pyruvate metabolism in anaerobic conditions. It can be produced in any kind of tissue and is rapidly metabolized by the liver and kidneys. Hence, the blood lactate level is usually between 0.5 and 1.0 mmol/L.[3] LA is a kind of metabolic acidosis when lactate accumulates in the body. It is defined to happen with pH < 7.35, Lac >5 mmol/L, HCO_3^- < 15 mmol/L and increased AG. The clinical manifestations of LA are hyperventilation, tachycardia, hypotension, and circulatory instability,[1] mostly found in patients with shock, sepsis, liver disease, and respiratory failure, and is refractory to normal acidosis therapy with a mortality rate of nearly 80%.[4] It happens also in diabetic patients who are alcoholic or treated with metformin and in patients who are lack of vitamin B1 or with propofol infusion syndrome (PRIS).[4–9]

Kelliher and Fawcett[10] reported a case of LA in a diabetic patient treated with metformin who underwent hepatic resection, but the patient's ABP or CVP during the surgical procedure were not mentioned. The author emphasized the side-effect of metformin which inhibited hepatic and renal gluconeogenesis, resulting in lactate accumulation, and recommended to stop the drug 48 h before surgery. However, Cox and his colleagues[11] studied the prevalence of LA in diabetic ketoacidosis (DKA). They discovered that lactate

Table 2
Blood gas analysis of the 2nd patient.

Time	pH	pCO_2 (mmHg)	pO_2 (mmHg)	K^+ (mmol/L)	Ca^{2+} (mmol/L)	Glu (mmol/L)	Lac (mmol/L)	Hct (%)	Hb (g/dL)	HCO_3^- (mmol/L)	BE (mmol/L)
14:17	7.29	39	208	3.1	1.33	7.2	1.7	39	12.1	18.8	−7.3
18:04	7.19	43	256	3.8	1.2	8	7.2	40	12.4	16.4	−11.4
19:09	7.21	49	270	3.4	1.16	7.7	9.1	37	11.5	19.6	−8.2
20:21	7.24	54	247	3.2	0.99	7.9	10.8	41	12.7	23.1	−4.8
21:03	7.27	47	246	3.1	1.08	7.5	11.4	42	13	21.6	−5.3
21:27	7.19	59	126	3.1	1.04	7.4	11.1	43	13.3	22.5	−5.7
06:06	7.38	45	82	3.3	1.01	14.9	–	47	16.5	26.6	0.9

and glucose levels in DKA patients were correlated positively ($r = 0.34$; $P = 0.004$), and considered the causes of lactate accumulation were due to ischemia and hypoxia of tissues as a result of dehydration induced hypoperfusion and stress induced catecholamine release. Coincidently, patients in Kelliher's case and our 1st case both presented with a high glucose level (15 mmol/L and 12.2–21.3 mmol/L, respectively). Therefore, perioperative hyperglycemia is an important inducing factor of LA.

Although our 2nd patient did not present with a dramatically elevated glucose level (7.2–8 mmol/L), LA still occurred. Obviously, there are many common features between the two cases, such as prolonged periods of hypotension, CLCVP, HVO and propofol infusion.

PRIS induced LA is not common, but is potentially lethal, so adequate attention should be given. This disorder is usually triggered by propofol infusion faster than 5 mg/kg/h for more than 48 h. It is characterized by LA, heart failure and a disturbance in mitochondrial long chain fatty acid oxidation induced multiorgan failure and rhabdomyolysis.[6–9] Mijzen et al.[12] suggested that under normal conditions, reversal of T-waves on the electrocardiogram (ECG) may be an early warning sign of PRIS. Despite there is no evidence whether our patients presented with PRIS, anesthesiologists should pay attention to the emulsive property of propofol.

In normal conditions, the liver accounts for more than 50% of lactate clearance,[3] therefore, lactate metabolism will be disturbed in conditions of hepatic dysfunction or HVO. A study has shown that the blood lactate level was significantly elevated after occlusion of the liver hilus in hepatectomy,[13] thus, if the process of hepatic parenchyma transection is prolonged, and HVO is performed frequently or reperfusion period is short, lactate will undoubtedly accumulate. This indicated that extra lactate production and its diminished clearance should happen with HVO. In our cases, the 1st patient received complete HVO twice and hepatic parenchymal transection lasted 2h40 min, while in the other patient, right HVO was for 8 times, and transection was for 2h35 min. Despite the duration of major surgical procedure in Kelliher's case was not given, the total operative time was 6.5 h.[10] Consequently, we inferred that profound LA may be induced by prolonged period of hepatic parenchymal transection and with prolonged total HVO and CLCVP.

Many studies showed that CLCVP in partial hepatectomy does not impact on hepatic or renal function.[14,15] However, the SBP or MAP should be appropriately kept to ensure adequate organs blood perfusion. When CLCVP leads to hypovolemia, and induces fluctuant hemodynamics, maintaining a targeted blood pressure becomes thorny. Our 1st patient suffered with hypovolemia and subsequent refractory hypotension because of CLCVP, which undoubtedly diminished organic perfusion and promoted lactate production. In addition, the use of vasoconstrictor exacerbated the unfavorable condition, caused further tissue ischemia and aggravated LA.

Sodium acetate infusion as a therapeutic measure for acidosis has been validated.[16,17] In early 1982, Hamat and his colleagues[18] confirmed the effective use of sodium acetate on LA from an in vitro study, and they considered the mechanism is due to sodium acetate participating in the tricarboxylic acid (TCA) cycle for adenosine triphosphate (ATP) synthesis, and thus glycolysis and lactate accumulation decreased. Additionally, this unique metabolic pathway has no impact on liver or renal function, and it is recommended for treating patients with stable hemodynamics. This was the main approach we took to treat our 2nd patient. For those with impaired renal function, peritoneal dialysis and hemodialysis with sodium acetate should be considered.[3]

When the pH falls below 7.20, severely adverse hemodynamic changes may occur, and sodium bicarbonate should be administered,[1] however, the validity of this treatment is still in question. Kim and his colleagues[19] reported a retrospective analysis on 103 LA patients, and discovered that patients treated with sodium bicarbonate were associated with a higher mortality when compared to those without, and considered that $NaCO_3$ merely corrects the pH value, but not inhibits lactate production or promotes its elimination. Besides, acidosis reduces the activity of phosphofructokinase, therefore inhibits lactate production. If $NaCO_3$ is used to correct acidosis, lactate may accumulate by canceling the benefit. Arieff's[20] animal experiment also showed that $NaCO_3$ resulted in a decline of liver and erythrocyte pHi (intracellular pH), increased gut lactate production, diminished cardiac output and hepatic portal vein blood flow. Therefore, $NaCO_3$ administration in treating LA should be cautious. This conclusion corresponded to the phenomenon in our 2 cases, that the pH value was corrected while the lactate level was still elevated. Kim's study also showed that the highest mortality rate of LA was in patients with sepsis, and then hepatic failure, cardiogenic shock, etc.[19] The favorable prognosis of our 2 patients indicated that temporary hyperlactataemia occurring during partial hepatectomy is not as fatal as LA which is induced by other diseases.[2,4,19] Our explanation is as follows: (1) Both our patients had no underlying diseases that may lead to lactate accumulation, and their liver function were relatively normal preoperatively. (2) Intraoperative production of lactate could cease quickly after reperfusion of the liver with improvement in tissue perfusion or oxygen supply by rehydration and blood transfusion. (3) Excess lactate could be cleared quickly by the liver and kidneys that function well. (4) These results are comparable with those of Cox's,[11] they found that a DKA patient with LA was not associated with a worse prognosis. Thus, we wonder if a single reading of hyperlactataemia is a valuable predictor of patients' outcome.

Dichloroacetate (DCA) is a specific agent to treat LA, it activates pyruvate dehydrogenase, increases pyruvate oxidation and reduces lactate production. It also promotes regional lactate transport, raises plasma bicarbonate concentration and pH value, reduces the fatality rate of LA patients; although it raises plasma ketone-body concentration, appreciable drug toxicity is rarely seen in short-term administration of DCA.[1,21,22] Regrettably, we had no DCA at that time. Other drugs for treating LA include insulin, vitamin B1, methylene blue, etc. However, they are of limited effects.[1]

4. Conclusions

Perioperative lactic acidosis is rarely seen. The purpose we reported these 2 cases was to emphasize the importance of perioperative management of hepatic surgery. LA is hardly perceived simply by monitoring the patient's vital signs. However, its fatality rate is high, and anesthesiologists should be on the alert. The CLCVP technique is widely performed during hepatic resection surgery for its various advantages, but the operative times included in most researches are relatively short, hence, the duration of CLCVP and HVO are short correspondingly. Thus, if the operation time, especially parenchymal transection is prolonged, a benefit-risk balance of CLCVP should be further studied, because a prolonged hypovolemia period is harmful to patients. Blood gas analysis is the main approach to perceive LA during operation, but we rarely take blood samples for its detection. Delayed diagnosis and therapy may lead to unfavourable outcomes. Moreover, LA is refractory to normal therapeutic management on metabolic acidosis, sodium bicarbonate administration should be reconsidered when the pH value declines significantly, or adverse effects appear.

As we summarized, real-time blood gas analysis should be recommended in prolonged hepatic surgery. When lactate accumulates, the appropriate procedures should include stopping propofol infusion, keeping the patient's hemodynamics stable with proper and cautious use of vasoactive agents, and administration of sodium

acetate solution (such as Plasmalyte-A) combined with diuretics for reducing lactate production and promoting its elimination. Also, the glucose level should be well controlled perioperatively. The kidneys still account for significant lactate elimination, hence, we recommend to mainly use sodium acetate solution for fluid management and combine it with proper use of diuretics for patients undergoing prolonged hepatic surgery as a prophylacsis against LA.

Conflict of interest

All the authors declared that there is no conflict of interest to this work.

Funding

There is no funding for our case report.

Ethical approval

Written consent was been obtained from all patients.

Author contribution

Yi Zou and Jitong Liu contributed mostly to the paper, Wanmin Pei and Yongqiong Liao managed one of the cases clinically, Gaoyin Kong is the corresponding author.

References

1. Madias NE. Lactic acidosis. *Kidney Int* 1986;**29**(3):752–74.
2. Stacpoole PW, Wright EC, Baumgartner TG, Bersin RM, Buchalter S, Curry SH, et al. Natural history and course of acquired lactic acidosis in adults, DCA-Lactic Acidosis Study Group. *Am J Med* 1994;**97**(1):47–54.
3. De Backer D. Lactic acidosis. *Minerva Anestesiol* 2003;**69**(4):281–4.
4. Krzymień J, Karnafel W. Lactic acidosis in patients with diabetes. *Pol Arch Med Wewn* 2013;**123**(3):91–7.
5. Amrein K, Ribitsch W, Otto R, Worm HC, Stauber RE. Severe lactic acidosis reversed by thiamine within 24 hours. *Crit Care* 2011;**15**(6):457.
6. Romero PC, Morales RM, Donaire RL, Llanos VO, Cornejo RR, Gálvez AR, et al. Severe lactic acidosis caused by propofol infusion: report of one case. *Rev Med Chil* 2008;**136**(1):88–92.
7. Bordes J, Meaudre E, Asencio Y, Montcriol A, Kaiser E. Lactic acidosis associated with propofol during general anaesthesia for neurosurgery. *Ann Fr Anesth Reanim* 2008;**27**(3):261–4.
8. Annecke T, Conzen P, Ney L. Propofol-related infusion syndrome induced by "moderate dosage" in a patient with severe head trauma. *J Clin Anesth* 2012;**24**(1):51–4.
9. Haase R, Sauer H, Eichler G. Lactic acidosis following short-term propofol infusion may be an early warning of propofol infusion syndrome. *J Neurosurg Anesthesiol* 2005;**17**(2):122–3.
10. Kelliher LJ, Fawcett WJ. Lactic acidosis in a diabetic patient treated with metformin undergoing hepatic resection. *Br J Hosp Med (Lond)* 2012;**73**(4):232–3.
11. Cox K, Cocchi MN, Salciccioli JD, Carney E, Howell M, Donnino MW. Prevalence and significance of lactic acidosis in diabetic ketoacidosis. *J Crit Care* 2012;**27**(2):132–7.
12. Mijzen EJ, Jacobs B, Aslan A, Rodgers MG. Propofol infusion syndrome heralded by ECG changes. *Neurocrit Care* 2012;**17**(2):260–4.
13. Pietsch UC, Herrmann ML, Uhlmann D, Busch T, Hokema F, Kaisers UX, et al. Blood lactate and pyruvate levels in the perioperative period of liver resection with Pringle maneuver. *Clin Hemorheol Microcirc* 2010;**44**(4):269–81.
14. Melendez JA, Arslan V, Fischer ME, Wuest D, Jarnagin WR, Fong Y, et al. Perioperative outcomes of major hepatic resections under low central venous pressure anesthesia: blood loss, blood transfusion, and the risk of postoperative renal dysfunction. *J Am Coll Surg* 1998;**187**(6):620–5.
15. Wang WD, Liang LJ, Huang XQ, Yin XY. Low central venous pressure reduces blood loss in hepatectomy. *World J Gastroenterol* 2006;**12**(6):935–9.
16. McCague A, Dermendjieva M, Hutchinson R, Wong DT, Dao N. Sodium acetate infusion in critically ill trauma patients for hyperchloremic acidosis. *Scand J Trauma Resusc Emerg Med* 2011;**19**:24.
17. Ekblad H, Kero P, Takala J. Slow sodium acetate infusion in the correction of metabolic acidosis in premature infants. *Am J Dis Child* 1985;**139**(7):708–10.
18. Hamat RB, Wolman SL, Fields AL, Sonnenberg KL, Cheema-Dhadli S, Halperin ML. Evaluation of sodium acetate as a source of alkali therapy in an experimental aerobic model of lactic acidosis due to decreased pyruvate oxidation. *Metabolism* 1982;**31**(6):548–52.
19. Kim HJ, Son YK, An WS. Effect of sodium bicarbonate administration on mortality in patients with lactic acidosis: a retrospective analysis. *PLoS ONE* 2013;**8**(6):e65283.
20. Arieff AI, Leach W, Park R, Lazarowitz VC. Systemic effects of $NaHCO_3$ in experimental lactic acidosis in dogs. *Am J Physiol* 1982;**242**(6):F586–91.
21. De Stefano N, Matthews PM, Ford B, Genge A, Karpati G, Arnold DL. Short-term dichloroacetate treatment improves indices of cerebral metabolism in patients with mitochondrial disorders. *Neurology* 1995;**45**(6):1193–8.
22. Stacpoole PW. The pharmacology of dichloroacetate. *Metabolism* 1989;**38**(11):1124–44.