This incident emphasizes the fact that despite repeated checking, errors can and do occur and it is necessary to be vigilant for new errors as our anaesthesia delivery systems become more complicated and modernized. We have informed Draeger and look forward to their comments.

V. K. Jagannathan, S. A. Nortcliffe
Department of Anaesthetics
Manor Hospital
Walsall, UK

References

1. Webb C, Ringrose D, Stone A. Faulty interlock on Drager vaporizers. *Anaesthesia* 2005; **60**: 628–629.
2. Medicine and Healthcare products Regulatory Agency. Ref: MDA/06/030.
3. Drager Medizintechnik. *Dräger Vapor® 2000 Anaesthetic Vaporiser. Instructions for Use*. Lübeck: Drager Medizintechnik, 2000: 22–33.
4. Association of Anaesthetists of Great Britain and Ireland. *Checking Anaesthetic Equipment*. London: AAGBI, 2004.

Metformin-associated lactic acidosis following contrast media-induced nephrotoxicity

doi: 10.1017/S026502150700097X

EDITOR:
Metformin-associated lactic acidosis (MALA) has an incidence of 0.03 per 1000 person years with a mortality rate of about 50% [1]. In a neurosurgical ward, patients with aneurysmal subarachnoid haemorrhage (SAH) may be admitted in an emergency unit requiring early diagnosis and management. Patients on multiple drug therapy require consideration, as the current trend is towards early surgical intervention in treating SAH. Recently, we encountered MALA in a patient with aneurysmal SAH in whom lactic acidosis was precipitated by contrast media-induced nephrotoxicity despite normal renal function before operation.

Case report

A 47-yr-old male, weighing 67 kg, was admitted to the neurosurgical ward with a 2-day history of severe headache and transient loss of consciousness on the previous day. His medical history was significant for Type II diabetes mellitus over the previous 3 yr. Blood glucose concentration was well controlled with glyburide 5 mg and metformin 500 mg twice a day. All routine investigations were normal. Blood was seen in the interhemispheric fissure and basal cistern on a computed tomographic (CT) head scan. A diagnosis of SAH Grade III was made. The patient was taken for emergency digital substraction angiography under monitored anaesthesia care. It showed aneurysms at the right middle cerebral artery bifurcation and the left anterior communicating artery. Emergency craniotomy and clipping of the aneurysm was planned. Although a dose of metformin had been taken by the patient just before coming to hospital, in view of the emergency nature of the surgery, the neurosurgeon decided to proceed. The anaesthetic and surgical course was uneventful. For the next 12 h, the patient's general condition remained stable but the blood sugar had risen to 16.2 mmol L^{-1} despite insulin infusion at the rate of 6 units h^{-1}. The patient became irritable and tachypnoeic. Arterial blood gas analysis showed pH 7.26, $PaCO_2$ 2.84 kPa, PaO_2 11.43 kPa, HCO_3 12 mmol L^{-1}, base excess −10, anion gap 29 and lactate 5 mmol L^{-1}. There were no ketone bodies in the urine. Serum osmolality was 283 mOsm kg^{-1}. A transcranial Doppler examination showed normal blood flow velocities in all major blood vessels. One hour later, the urine output had decreased to 20 ml h^{-1} despite the administration of adequate intravenous (i.v.) fluids, maintenance of haemodynamic parameters and central venous pressure 16 cm H_2O. Furosemide 40 mg was administered i.v. but the urine output did not improve. Blood gas analysis now showed a metabolic acidosis with pH 7.258, $PaCO_2$ 2.34 kPa, PaO_2 12.38 kPa, HCO_3 7.6 mmol L^{-1}, Na 131 mmol L^{-1}, K 3.7 mmol L^{-1}, Cl 96 mmol L^{-1}, base excess -14, anion gap 27.4 and lactate 7.3 mmol L^{-1}. Serum creatinine was

Corresponence to: Hemanshu Prabhakar, Department of Neuroanaesthesiology, Neurosciences Centre All India Institute of Medical Sciences, New Delhi 110029, India. E-mail: prabhakarhemanshu@rediffmail.com; Tel: +91 11 26588700 Ext. 3474; Fax: +91 11 26588663

Accepted for publication 18 May 2007 EJA 4487
First published online 22 June 2007

0.25 mmol L^{-1}. A diagnosis of lactic acidosis was made. In view of the increasing respiratory distress, the patient was intubated and mechanical ventilation was started. One hour later, arterial blood gas showed a worsening acidosis with pH 6.95, $PaCO_2$ 2.48 kPa, PaO_2 14.93 kPa, HCO_3 3.8 mmol L^{-1}, Na 133 mmol L^{-1}, K 4.6 mmol L^{-1}, Cl 100 mmol L^{-1}, base excess −20, anion gap 29.2 and lactate 15.6 mmol L^{-1}. Sodium bicarbonate 150 mmol was infused. In view of the deteriorating renal function, haemodialysis was planned. However, before haemodialysis could be instituted, the patient became hypotensive and suffered a sudden cardiac arrest from which he could not be resuscitated.

Our patient had normal renal function on admission but developed renal failure in the early postoperative period. In the absence of other causes, the most likely cause appears to be contrast media-induced nephrotoxicity, which is known to occur within 3 days of contrast administration in up to 10% of people with normal renal function and is more common following intra-arterial rather than i.v. administration [2]. Our patient received non-ionic contrast iohexol twice for CT scan and digital substraction angiography. Rapid deterioration in clinical condition with high anion gap metabolic acidosis and high serum lactate levels suggests a diagnosis of lactic acidosis. As all common causes of lactic acidosis including shock, cardiac failure and hypoxia were ruled out, a diagnosis of MALA was made. Although the incidence of risk of lactic acidosis in metformin users that can be attributed to the drug is debatable, in our case the temporal correlation was strong.

A proposed clinical definition describes MALA as metabolic acidosis (pH $<$ 7.35) in association with blood lactate $>$5.0 mmol L^{-1} in metformin-treated patients [3]. Most cases of MALA occur in the setting of impaired renal function when plasma levels of metformin are expected to rise. The mechanism whereby metformin causes lactic acidosis is complex but is thought to be mainly a result of a shift in intracellular redox potential from aerobic to anaerobic metabolism, leading to an increase in cellular lactate production [4]. Severe lactic acidosis can be followed by multiple-organ dysfunction, a complication associated with a poor prognosis. Some common precipitating causes of MALA are cardiac failure, chronic obstructive pulmonary disease and chronic hepatic dysfunction. Additional factors that increase blood lactate concentrations are often present, for example, a major illness causing hypotension with low tissue perfusion, hypoxia, liver disease or alcohol abuse [5].

It has been suggested that it is safe to give i.v. contrast medium to patients on metformin with normal renal function [6]. Since contrast media nephropathy can develop even in patients with normal renal function, we believe that special attention should be paid to the preservation of renal function if the patient has already consumed metformin. This would include adequate hydration, oxygenation and maintenance of haemodynamic function along with the avoidance of use of concomitant nephrotoxic medications. At the same time, renal function should be closely monitored. Serial blood gas and lactate estimations are likely to be helpful. Notwithstanding the poor prognosis of MALA and the recent reports of patient survival following haemodialysis [7], we feel that haemodialysis facilities should be ready beforehand.

Prophylactic measures including adequate hydration, oxygenation and maintenance of haemodynamic stability along with the avoidance of use of concomitant nephrotoxic medications help to preserve renal function in patients on metformin. Renal replacement therapy not only corrects the acidosis but also efficiently removes lactate and metformin from plasma, preventing further overproduction of lactate. There are recent reports in the literature where use of haemodialysis early in the disease process has improved the outcome [7].

V. Jain, D. Sharma, H. Prabhakar, H. H. Dash
Department of Neuroanaesthesiology
Neurosciences Centre
All India Institute of Medical Sciences
New Delhi, India

References

1. Chan NN, Brain HPS, Feher MD. Metformin associated lactic acidosis: a rare or very rare clinical entity? *Diabet Med* 1999; **16**: 273–281.
2. Morcos SK. Contrast media induced nephrotoxicity, questions and answers. *Br J Radiol* 1998; **71**: 357–365.
3. Chang CT, Chen YC, Fang JT, Huang CC. Metformin-associated lactic acidosis: case reports and literature review. *J Nephrol* 2002; **15**: 398–402.
4. Kreisberg R, Wood B. Drug and chemical induced metabolic acidosis. *Clin Endocrinol Metab* 1983; **12**: 391–411.
5. Bailey CJ, Turner RC. Metformin. *N Engl J Med* 1996; **334**: 574–579.
6. McCartney MM, Gilbert FJ, Murchison LE, Pearson D, McHardy K, Murray AD. Metformin and contrast media – a dangerous combination? *Clin Radiol* 1999; **54**: 29–33.
7. Guo PY, Storsley LJ, Finkle SN. Severe lactic acidosis treated with prolonged hemodialysis: recovery after massive overdoses of metformin. *Semin Dial* 2006; **19**: 80–83.

https://doi.org/10.1017/S026502150700097X Published online by Cambridge University Press