Anaesthesia
Journal of the Association of Anaesthetists of Great Britain and Ireland

Spurious propofol-induced coagulopathy in a patient with hepatic rupture

We would like to report the case of a young female who presented to our Intensive Care Unit following emergency laparotomy for spontaneous hepatic rupture during labour.

The patient presented to our maternity unit in natural labour at term. The pregnancy had been uncomplicated and the patient was a primigravida. Routine blood tests, including coagulation profile, had been performed earlier in pregnancy and were normal. There was no evidence of pre-eclampsia. After a prolonged and complicated second stage of labour the patient underwent emergency Caesarean section for fetal bradycardia under general anaesthesia. During this procedure the patient developed haemodynamic compromise. Blood was noted in the peritoneum and a full laparotomy was performed following delivery. Laparotomy revealed haemoperitoneum caused by a large right hepatic laceration, thought to be spontaneous. The liver capsule was repaired and a coagulopathy was successfully corrected with fresh frozen plasma and platelets. Despite these measures bleeding continued, necessitating surgical packing of the liver.

As the patient had liver packs and a persistent metabolic acidosis she was kept intubated, sedated with a continuous 1% propofol infusion and remifentanil and transferred to the Intensive Care Unit. A repeat coagulation profile on arrival was within normal limits and there was no clinical evidence of continued bleeding.

After an uneventful night it was decided to return the patient to theatre for removal of the intra-abdominal packs. Routine blood tests were performed by the laboratory prior to theatre including a routine coagulation profile (analysed using an optical sensor on an MDA 2 Trinity Biotech Analyser). The full blood count and urea and electrolytes were normal but the Activated Partial Thromboplastin Time (APTT) was grossly deranged at >240 s (normal range 21–34 s) The Prothrombin Time (PT) and the fibrinogen concentration remained in normal range. As these blood samples had been taken form a heparinised arterial line they were repeated both from the arterial line and from a peripheral vein. It was noted that the degree of coagulopathy was out of keeping with the clinical picture. Thromboelastography was performed from peripheral blood samples. R time was 14.2 min (normal range 4–8 min) and MA 42 mm (normal range 55–73 mm) suggesting a significant difference from the routine coagulation results. The repeat laboratory samples using an optical method, again demonstrated grossly prolonged APTT and now an unmeasurable PT. When these samples were examined by the laboratory staff they were found to be lipaemic to the naked eye. The serum triglyceride concentration was measured and found to be 14.7 $mmol.l^{-1}$ (normal range 0.0–1.8); cholesterol was in normal range. The propofol infusion was discontinued immediately and replaced with an infusion of midazolam. No other source of lipid had been administered. The total dose of propofol administered was 8.82 g over 31 h.

During the above period liver function tests had deteriorated markedly. The initial Alanine Transaminase concentration had been 401 $U.l^{-1}$ (normal range 5–40 $U.l^{-1}$) immediately after liver packing. This rose to 1369 and 2128 $U.l^{-1}$ at 16 and 24 h respectively. Alkaline Phophatase showed a modest rise from a normal baseline to 120 $U.l^{-1}$ (normal range 40–129 $U.l^{-1}$) at 24 h.

In view of the disparity between the results of the routine coagulation tests and the results of thromboelastography, it was decided by the haematology staff to use a different coagulation analyser which incorporates a mechanical sensor (Destiny Plus, Trinity Biotech). The coagulation parameters using a mechanical sensor were normal. Based on these results we were confident that the apparent coagulopathy was spurious; the patient returned to theatre and had an uneventful pack removal. There had been an avoidable delay of several hours before the patient returned to theatre while the spurious coagulopathy was investigated. Furthermore 4 units of fresh frozen plasma were administered that may not have been needed.

Following cessation of the propofol infusion and removal of the surgical packs the serum triglyceride concentration fell rapidly to 3.6 $mmol.l^{-1}$ the next day and became normal 48 h later. The ALT fell to 1007 $U.l^{-1}$ in the first 24 h and became normal over the next few days.

The use of a prolonged infusion of propofol in lipid emulsion for sedation had been shown to increase the serum triglyceride concentration in adults [1] and children [2]. However, profound lipaemia developing after only 31 h would appear to be very rare. No metabolic acidosis was observed and pancreatitis, which has been associated with hypertriglyceridaemia secondary to propofol infusion [3] was absent. Propofol itself is not associated with alteration of coagulation [4]. We surmise that the presence of the intra-abdominal packs may have disrupted hepatic blood flow leading to a degree of hepatic ischaemia and reduced capacity to metabolise triglycerides [5].

The authors draw two conclusions from this case. First, a continuous infusion of propofol should be used with caution in patients with hepatic packs or signs of hepatic ischaemia from other causes. Second, assay of lipaemic blood samples using an optical method may mislead clinicians into believing that there is a coagulopathy when none exists.

H. Thomson
A. Ali
N. J. Harper
Manchester Royal Infirmary
Manchester, UK
E-mail: nedthomson@btinternet.com

References

1 Eddleston J, Shelly M. The effects on serum lipid concentration of a prolonged infusion of propofol – hypertriglyceridaemia associated with propofol administration. *Intensive Care Medicine* 1991; **17**: 424–6.
2 Gottschling S, Meyer S, Krenn T, et al. Effects of short-term propofol administration on pancreatic enzymes and triglyceride levels

in children. *Anaesthesia* 2005; **60**: 660–3.
3 Devlin J, Lau A, Tanios M. Propofol-associated hypertriglyceridemia and pancreatitis in the intensive care unit: an analysis of frequency and risk factors. *Pharmacotherapy* 2005; **25**: 1348–52.
4 Niccolai I, Barontini L, Paolini P, Lavacchi L, et al. Long-term sedation with propofol in ICU: hemocoagulation problems. *Minerva Anestesiology* 1992; **58**: 375–9.
5 Kam P, Cardone D. Propofol infusion syndrome. *Anaesthesia* 2007; **62**: 690–701.

Chronic left bundle branch block does not exclude the ECG in the diagnostic process of postoperative myocardial ischaemia

An elderly female was scheduled to undergo a hip arthroplasty. Past medical history included arterial hypertension treated with nicardipine, moderate aortic stenosis with left ventricle hypertrophy and slight diastolic and systolic dysfunction (ejection fraction of 48%) due to left bundle branch block. No history of ischaemic cardiac disease was detected and functional class was not measurable. She was receiving beta-blockers for essential tremor. Preoperative ECG showed sinus rhythm (75 beats.min^{-1}) and left bundle branch block. Slight cardiomegaly was observed on the X-ray.

In the operating room, general anaesthesia was performed without incident, the patient remaining haemodynamically stable and without ECG ST-segment changes. At the end of surgery the patient was extubated and transferred to the recovery unit.

Immediately after arrival, the patient complained of thoracic and epigastric discomfort highly suggestive of angina. Blood pressure was 140/80 mmHg and oxygen saturation by pulse oximetry was 89–90% despite oxygen administration (F_{IO_2} 0.5). ECG showed sinus rhythm 80 beats.min^{-1} with clear elevation of the ST segment in several leads. The possibility of acute coronary syndrome was confirmed by the cardiologist and sublingual nitroglycerine was administered, resulting in immediate clinical improvement and serial ECG showed progressive normalisation of ST changes similar to the pre-operative ECG. Cardiac biomarkers were negative and postoperative hemoglobin level was 9.3 g.dl^{-1}. One unit of packed red blood cell was transfused in order to optimise oxygen carriage and secondary prophylaxis was initiated with salicylic acid, statins, transdermic nitroglycerine and beta-blockers. The patient remained stable, and was discharged to conventional ward 48 h later.

Peri-operative myocardial ischaemia is a relatively common complication and it is associated with increased risk of cardiac morbidity and mortality in the surgical population with or at risk of coronary artery disease. Nowadays, several strategies have been advocated to reduce the incidence of peri-operative myocardial ischaemia including: pre-operative identification of high risk patients (and revascularisation when necessary), pharmacological prophylaxis and early diagnosis and treatment [1]. Prompt detection and treatment of peri-operative myocardial ischaemia is a cornerstone in the avoidance morbid cardiac events because myocardial ischaemia lasting more than 2 h increases the risk of cardiac event more than 30-fold [2].

Classically, diagnosis of myocardial ischaemia is based on suggestive chest pain, ECG alterations (ST-T wave changes) and elevation of biochemical markers. However, in the postoperative setting, diagnosis of peri-operative myocardial ischaemia it is not always easy. Pain could be attenuated or abolished due to residual anesthesia, and cardiac biomarkers may be elevated either by previous medical disease, or surgery. In addition, cardiac biomarker elevation does not occur in acute coronary syndrome without necrosis and it may occur late at 4–6 h. Under these circumstances, the ECG may be the only reliable parameter for early detection of peri-operative myocardial ischaemia. However up to one quarter of vascular surgical patients present baseline electrocardiographic abnormalities including left bundle branch block, that can mask the ECG signs of acute myocardial injury. Recently published articles suggest that specific ECG changes could help in the diagnosis of acute coronary syndrome in presence of left bundle branch block [3–5].

The GUSTO-1 study suggests three ECG criteria to be significant of myocardial infarct in patients with chronic left bundle branch block: ST elevation greater than 1 mm concordant (in the same direction) with QRS complex, drop of ST segment greater than or equal to 1 mm in V1, V2 or V3 and elevation of ST segment greater than or equal 5 mm contrary (in the opposite direction) to the QRS complex [3]. Edhouse [4] and Kontos [5] in retrospective and prospective studies corroborated these diagnostic criteria some years later. Other studies however, have not confirmed this association [6].

We believe that our patient experienced peri-operative myocardial ischaemia based on characteristic chest pain and suggestive ST-segment alterations while pain was experienced, followed by return to the baseline ECG after nitro-glycerine administration and pain disappearance. Repeated enzyme determination ruled out the diagnosis of myocardial necrosis.

It seems then, that in patients with chronic left bundle branch block with suggestive chest pain, the ECG changes are still of value for early diagnosis of peri-operative myocardial ischaemia and acute coronary syndrome. In the postoperative scenario, when a previous ECG is usually available, peri-operative myocardial ischaemia could be recognized when reversible ischaemic changes are superimposed on a pattern of chronic left bundle branch block. The ST-changes can be analysed using the criteria outlined thus helping with the diagnosis of acute coronary syndrome in the postoperative setting and probably also during anaesthesia and surgery when the ST-segment is constantly monitored.

H. S. De Beltrán
E. Samsó
N. Baldomà
J. Martí
Hospital del Mar-Esperanza. IMAS
Barcelona, Spain
E-mail: 94451@imas.imim.es

