Extensive bowel ischaemia after nifedipine overdose
過量服用硝苯地平後腸臟廣泛缺血

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A 57-year-old woman presented with abdominal distension and vomiting two days after overdosing an unknown amount of sustained-release nifedipine tablets. She had refractory shock requiring calcium chloride, glucagon, insulin-glucose and multiple high-dose inotropic agent infusions in the intensive care unit. Her abdominal computed tomography showed features of bowel ischaemia and exploratory laparotomy reviewed non-salvageable massive bowel ischaemia. She finally succumbed after 22 days of hospital treatment. This case illustrates the importance of awareness of this potentially fatal complication of calcium channel blocker overdose, requiring early recognition and intervention. (Hong Kong Emerg. Med. 2010;17:360-363)

一名57歲女子過量服用不明分量的硝苯地平持續釋放藥片兩天後，呈現腹脹及嘔吐。她有顯著的休克，需要在深切治療部輸注氯化鈣，胰高糖素，胰島素－葡萄糖及多種高劑量的強心劑。她的腹部電腦掃描顯示腸臟缺血的徵象，而剖腹顯示不可救活的大量腸臟缺血。她於醫院治療22天後最終死亡。本案例說明：知道這鈣通道阻斷劑過量可能致命的併發症的重要性，需要及早認出及介入。

Keywords: Calcium channel blockers, infarction, intestines, overdose
關鍵詞：鈣通道阻斷劑，梗死，腸臟，藥物過量

Introduction

Nifedipine, a calcium-channel blocker (CCB), has been widely used to treat various cardiovascular conditions, such as hypertension, angina pectoris and Raynaud’s phenomenon. Toxicity from the drug may occur with therapeutic use (often due to drug interaction), while life-threatening toxicity usually occurs after major overdose. The most important manifestation of nifedipine overdose is severe hypotension. Bradycardia and atrioventricular block may be present in severe poisoning. We report a case of extensive bowel ischaemia after nifedipine overdose.

Case report

A 57-year-old lady with history of hypertension, diabetes mellitus, and depression presented to the emergency department in March 2008 with dizziness, chest and abdominal discomfort with no bowel motion for two days. She had taken an unknown amount of sleeping pills and sustained-release nifedipine two days before her attendance. She got an episode of syncope at home on the day of her overdose. On arrival, she was hypotensive (blood pressure 47/21 mmHg, pulse rate 51 beat/min; on recheck blood pressure 94/44 mmHg, pulse rate 96 beat/min) and hyperglycaemic with bedside blood glucose test 24.2 mmol/L. On examination, her abdomen was distended with diminished bowel sound and per rectal examination
revealed an empty rectum. Chest and abdominal X-rays showed dilated bowels and no fluid level (Figure 1). Arterial blood gas showed high anion gap metabolic acidosis (pH 7.22, anion gap of 30 mmol/L and lactate 15.9 mmol/L). One litre of intravenous normal saline fluid was given and she was admitted to the medical department initially but subsequently transferred to the intensive care unit (ICU) for further management.

Treatment in the ICU included calcium bolus injection and infusion (ionised calcium level was kept at around 2-2.5 mmol/L), glucagon (3 boluses, total 5 mg given on day 2), insulin infusion up to 100 unit/hr and multiple inotropic agents for her refractory shock (systolic blood pressure ranged from 60-90 mmHg), namely adrenaline (maximum 6 mg/hr), noradrenaline (maximum 9.6 mg/hr) and vasopressin (maximum 2.4 unit/hr). Besides, she was put on albumin-enhanced continuous venovenous haemodialysis and plasmapheresis. It was planned to treat her with intra-aortic balloon pump, but unfortunately, her condition was too critical for transfer. For similar reason, CT abdomen to look for intra-abdominal sepsis was deferred until her condition was stabilised.

Her condition improved after the initial therapies. Insulin-glucose infusion was weaned off on day 5 of admission. Calcium, adrenaline and vasopressin infusions were stopped on day 6. CT abdomen was done on day 9 which showed fluid-filled dilated small bowel and collapsed large bowel with the transitional zone in the terminal ileum which could be due to ileus or intestinal obstruction. Moreover, a loop of small bowel in the pelvis had decreased contrast enhancement, suggesting bowel ischaemia (Figure 2). Exploratory laparotomy was performed on the same day which revealed massive small bowel gangrene, extending from the duodenojejunal junction through the terminal ileum, and involved most of the large bowel. There was also blood-stained foul-smelling peritoneal fluid. Resection of the bowel was not done because of the extensive bowel involvement. Her clinical course was further complicated by adult respiratory distress syndrome, nosocomial pneumonia, acute myocardial infarction and renal impairment. Laparotomy and drainage was repeated on day 21 in view of persistent sepsis and worsening of haemodynamic condition with the need of stepping up inotropic agent. There was extensive small bowel gangrene from the duodenal junction to the ileocaecal valve. Moreover, multiple sites of patchy gangrene over the transverse and descending colon resulted in perforation and a total of 1800 ml of foul-smelling turbid peritoneal fluid were drained. The perforation sites were repaired and the peritoneal cavity was lavaged with normal saline. Her condition further deteriorated and she finally succumbed on day 22.

**Discussion**

Calcium channel blockers have been widely used in treating a variety of conditions including hypertension, angina pectoris, coronary artery spasm, supraventricular arrhythmias, Raynaud’s phenomenon and migraine headache. Severe CCB toxicities manifest largely within
the cardiovascular system. The CCB-related cardiovascular disorders are thought to be a direct result of an excessive blockade of the L-type calcium channel in myocardial and vascular smooth muscle membranes, and thus preventing calcium influx into cells. The blockade decreases cardiac inotropy, chronotropy, cardiac conduction and vascular tone, resulting in hypotension or shock.1,2 Metabolic lactic acidosis, in turn, can result from circulatory shock and poor tissue perfusion. Altered mental state and acute pulmonary injury are other recognised features in CCB overdose. Owing to the blockade of insulin release in CCB poisoning, hyperglycaemia can occur. There is also a reported case of stroke after verapamil overdose.3

Gastrointestinal effects are usually limited to nausea and vomiting. However, more important gastrointestinal manifestations like pseudo-obstruction,4 bowel ischaemia and even infarction can also occur. There are several case reports of calcium channel blocker overdose (including nifedipine and verapamil) related bowel ischaemia or infarction in the literature.5-8 Successful treatment with surgical resection of the infarcted bowel has been achieved.5 The CCB effect on the splanchnic circulation remains controversial. In theory, CCB overdose induces a low flow state which is followed by vasoconstriction.9 Another postulated mechanism causing bowel ischaemia or infarction is that concretion formed by extended-release nifedipine tablets may have enhanced its local vasodilatory effects, and thus produced mesenteric hypoperfusion, ischaemia, and infarction.6 Moreover, a delay in occurrence for CCB-related bowel ischaemia has been observed, with a median of 48 hours after an initial phase of toxicant-induced shock. One postulated reason for the delay is that lack of the usual risk factors in the patients made the diagnosis more difficult.9

The calculated Naranjo adverse drug reaction probability score for the patient is 6, for which her bowel ischaemia was considered as probably related to the nifedipine overdose. Our patient has a much delayed presentation with hypotension and gastrointestinal manifestation after her overdose of a sustained-release form of nifedipine. Unfortunately,
her condition was too critical for further radiological investigation and early surgical intervention after her admission to the intensive care unit.

The presence of abdominal pain, abnormal physical examination (distended abdomen with diminished bowel sound) and dilated bowel in the abdominal X-ray should ring us the bell of the important complication. With early recognition and surgical intervention, we could improve the survival chance and decrease the morbidity of patients suffering from this potentially lethal complication. This case reminds us the importance of a heightened awareness of the potential bowel ischaemia or infarction in CCB overdose, and thus a potential for early recognition and intervention.

In conclusion, bowel ischaemia and infarction are recognised complications in CCB overdose. Mortalities can occur in untreated cases. Prompt and effective treatment of shock in CCB overdose is important to prevent organ hypoperfusion and subsequent bowel infarction. A high index of suspicion with early recognition and surgical intervention are the ways to the successful management of these complications.

References