Prothrombin complex for reversal of dabigatran anticoagulation in an emergency department: a report of 2 cases

Sir,

Dabigatran is indicated for the prevention of stroke in patients with atrial fibrillation (AF)[1]. There are studies showing that bleeding in patients anticoagulated with antivitamin K (AVK) can be resolved with replacement hemostatic factors[2-5]. The main drawback of dabigatran is the lack of a specific antidote and of evidence-based hemostatic strategies. We report 2 cases of reversal of dabigatran anticoagulation in the emergency department (ED).

Case 1: This was a woman with a history of hypertension and permanent AF anticoagulated with dabigatran 110 mg/12 h. attended for fever during 24 hours, vomiting and abdominal pain, hypotension, tachycardia and hypoperfusion. Laboratory tests showed glomerular filtration (MDRD-4) of 20 ml/min, included in Table 1. Abdominal CT scan showed biliary lithiasis in the infundibular region and thickened wall. With a diagnosis of severe sepsis secondary to acute cholecystitis, percutaneous drainage was indicated. The patient received prothrombin complex (PC) 1500 IU/iv (Octaplex®; 25 U/kg) and 4 h later she underwent percutaneous cholecystostomy without adverse events or bleeding complications. The septic picture resolved progressively over the next few days.

Case 2: This was an 88 year-old man anticoagulated with dabigatran 110 mg/12 h for permanent AF. He consulted for black stool during 3 days, the last deposition with red blood. Physical examination showed blood pressure 116/52 mmHg, heart rate 120 bpm, $SatO_2$ 92%, peripheral coldness and sweating, and rectal examination showed melena. Laboratory tests showed hemoglobin (Hb) 5.2 g/dl, included in Table 1. He received 3 packs of concentrated red blood cells and was given 1,500 IU/iv of CP. Emergency gastroscopy showed acute gastric mucosal lesions. At 48 h recurrence of bleeding and higher degree of anemia (Hb 6.8 mg/dl; previous post-transfusion 8.7 mg/dl) were recorded and a new deposition showed abundant melena. He received further concentrated red blood cells and fresh frozen plasma, and a new gastroscopy showed a 15 mm ulcer, sclerosed with adrenaline.

Table 1. Study of blood coagulation parameters

	Case 1			Case 2	
Time from arrival at emergency department	0 h	8 h	11 h	0 h	8 h
Platelet cells/UL	103,000	102,000	93,000	214,000	190,000
APTT sec. [VN: < 39]	49.1	63.3	69.9	64.6	27.3
Prothrombin time sec.	18.5	21.3	23	28.5	14.4
Thrombin Time sec. [VN 15-25]	> 25	> 25	> 25	> 25	17.4
INR [VN: < 1.30]	1.62	1.95	1.95	2.78	1.14
Quick Index % [VN: 70-100]	51	41	37	28	81

INR: International Normalized Ratio. APTT: activated partial thromboplastin time. Sec: seconds.

In the first case, coagulation parameters remained altered despite the administration of PC, probably due to the persistence of blood levels of the drug during several days after the last dose[6] - reduced elimination secondary to renal failure - and coagulation disorders secondary to the septic picture.

However, we were able to perform a percutaneous cholecystostomy without bleeding complications, which suggests that CP administration could be effective despite the coagulation alterations.

In the second case, rebleeding occurred 48 h later although coagulation disorders had disappeared, which suggests the emergence of a new gastric lesion or a prior injury that went unnoticed in the first gastroscopy. It has been suggested that the administration of factor VIIa, fresh frozen plasma and CP may be effective in these cases[7,8]. The administration of CP associated with other therapeutic measures (fluids, transfusion of blood components, early empiric antibiotic, etc.) allowed to perform an invasive technique (cholecystostomy) without complications in one patient and stabilize the other with upper gastrointestinal bleeding.

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Severe trauma register in Catalonia (TRAUMCAT)

Sir,

In relation to the article on a severe trauma register for Navarra by Belzunegui Otano et al published in Emergencias[1], we would first like to congratulate the authors for carrying out the register and published the article on it. We know from firsthand experience that both are very difficult tasks. Secondly, we want to congratulate the journal Emergencias for being open to publish work on such registers. In line with this article,

since 2009 we have worked on a population-based computerized register of severe trauma in Catalonia (TRAUMCAT), as part of a plan to improve severe trauma/multiple trauma care in Catalonia. After some redesigns and pilot phases, we now have a register based in the information systems of CatSalut (insurance guarantor of the provision of public health services) that complies with all the regulations regarding protection and confidentiality of the data. We started the prospective collection of data from cases in July 2012. The inclusion of patients is based on: a) severity of initial physiological or anatomic involvement[2], (b) admission to a critical care unit, or c) deaths during admission.

Eighteen hospitals have participated in the first year and more than 950 cases have been collected. Although we cannot affirm that the register includes 100% of severe trauma in Catalonia, we know that the participating hospitals very substantially represent centers serving severe trauma in Catalonia. One of the features of the register system is that is linked via a web server with the information systems of the system d' Emergències Mèdiques (SEM) so, once the patient is identified on the register, the pre-hospital care information is automated. In a similar vein, we are now working to enable the register to communicate via the web server with different hospital information systems, in such a way that certain data may also be fed in automatically. This phase is rather more complex, given the great variability of the different systems of hospital information. Such information is currently collected manually, and requires a great deal of willingness by participating professionals, whom we thank for their indispensable work. We hope to soon be able to have the final results to disseminate them and compare them with the Navarre register or other European standards.

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Metformin-induced acute pancreatitis

Sir,

Acute pancreatitis (PA) is a rare complication of treatment with metformin, and there are few cases in the literature. It could be favoured by the presence of renal failure[1,2], although there is one report on a case with preserved renal function[3].

A 70 year-old woman consulted the emergency department for radiating epigastric pain during 4 days accompanied by vomiting, diarrhea, fever and decreased urine output. Medical history included diabetes treated with metformin and repaglinide and chronic renal failure. Physical examination showed mild dehydration and tenderness in the epigastrium. Main laboratory data were: glucose 22 mg/dl, creatinine 8 mg/dl, urea 201 amylase 1,023 IU/L, sodium 136,5 lipase 1,334 IU/L mg/dl mmol/L, potassium 6.67 mmol/L and chlorine 102 mmol/L. Arterial blood gases showed metabolic acidosis (pH 7.02, bicarbonate 14.3 mmol/L, excess base - 12, lactic acid 32 mEq/L), and anionic hiatus 20.2 mEq/l. Abdominal ultrasound showed no hepatic or pancreatic injury, lithiasis or dilatation of the intrahepatic or extrahepatic bile. The patient evolved favorably after withdrawal of metformin and initiated treatment with fluid, glucose, bicarbonate, calcium gluconate, tazobactam piperacillin and absolute diet for 24 hours. On the seventh day the patient was discharged after presenting clinical and laboratory test improvement (creatinine 1.5 mg/dl, urea 65 mg/dl).

Among the causes of PA, up to 2% of cases are secondary to drugs[4]. In the case of metformin, it could be related to pancreatic acinar cell damage in an indirect way by accumulation of the drug[1,6], or directly by an idiosyncratic mechanism[3]. The deterioration of renal function could be explained by the depletion of the intravascular space secondary to vomiting[5], which favors the accumulation of metformin and consequent appearance of toxic levels and side effects, such as the PA[6]. To be able to confirm an association between a drug and the development of PA, it must develop during exposure to a given agent, disappear once suspended and reappear if resumed[4,7]. In our case, the association between PA and metformin is likely even though we could not assess the recurrence criterion for ethical reasons. We have not found cases in the literature of PA in relation to repaglinide, which the patient in our case was also taking.

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