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REVIEW ARTICLE

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Bleeding in patients on anticoagulant therapy: the real utility of antidotes and how to manage bleeding in patients on new-generation oral anticoagulants

Miquel SÁNCHEZ[1], Ginés ESCOLAR[2], Joan Carles REVERTER[2]

[1]Área de Urgencias, [2]Servicio de Hemoterapia y Hemostasia (CDB), Hospital Clínic, Barcelona, Spain.

Correspondence:
Miguel Sánchez
Director Urgencias
Hospital Clínic
C/Villarroel, 170
08036 Barcelona, Spain
E-mail: msanchez@clinic.ub.es

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Bleeding is one of the most feared complications of anticoagulant therapy. Discontinuing the anticoagulant and establishing of support measures will often resolve the emergency, but some cases require more specific treatment. Vitamin K antagonists (VKAs) have traditionally been used for long-term prevention of thromboembolic complications, but these drugs have many limitations that complicate clinical management. The new-generation of oral anticoagulants are similar in efficacy to VKAs but are associated with a lower incidence of intracranial hemorrhage, do not require routine scheduling of laboratory tests, and can be prescribed at fixed dosages. However, these drugs are not complication-free. The management of acute bleeding is very similar for patients on either VKA or a new oral anticoagulant, with the single exception that a specific antidote is available to reverse the effect of a VKA. [Emergencias 2013;25:482-490]

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Introduction

Until the recent advent of new-generation oral anticoagulants, the only anticoagulant therapy available was oral vitamin K antagonists (VKA) (acenocoumarol and warfarin)[1]. Although effective, these agents have numerous disadvantages. First, they have a narrow therapeutic window, below which the patient is exposed to increased risk of thromboembolic events, and above which the risk of bleeding increases exponentially[2]. In addition, VKA have numerous interactions with other drugs and some foods, and anticoagulant response is unpredictable. This necessitates regular monitoring and frequent dose adjustments to maintain the patient within the International Normalized Ratio (INR) therapeutic range of 2.0 to 3.0[3]. Also, the slow action of VKA at the beginning and end requires bridge therapy before any intervention, generally with low molecular weight heparin[4]. New-generation oral anticoagulants provide a practical solution to many of the problems of VKA use. In contrast to classic anticoagulant therapy, the pharmacokinetics and anticoagulant activity of new anticoagulant are predictable; there are no interactions with food and limited interactions with other drugs, which reduces routine coagulation level monitoring, and they can be used at fixed doses. Also, they offer rapid beginning and end of action, so bridge therapy with heparin is not required[5]. Furthermore, several clinical trials have shown them to be equally effective or even superior to VKA, and greater safety[6-8].

Currently there are 3 new oral anticoagulants available: dabigatran, rivaroxaban and apixaban. Dabigatran is indicated for the primary prevention of venous thromboembolic events (VTE) in adult patients undergoing elective surgery for total hip or knee replacement, as well as for stroke prevention in patients with non-valvular atrial fibrillation (AF) with one or more risk factors (history of stroke, transient ischemic attack or systemic embolism, left ventricular ejection fraction less than 40%, symptomatic heart failure, age $\geq$ 75 years or 65 years and diabetes, heart disease or hypertension)[9]. Rivaroxaban is indicated for the prevention of VTE in adult patients undergoing elective surgery for hip or knee replacement, for treat-

ment of VTE and prevention of recurrence, and for the prevention of stroke and systemic embolism in patients with non-valvular AF with one or more risk factors (historyof stroke or transient ischemic attack, age ≥ 75 years, heart failure, hypertension, diabetes mellitus)[10]. Finally, apixaban is indicated for the prevention of VTE in patients undergoing elective hip or knee replacement surgery and for the prevention of stroke in patients with non- valvular AF, but with respect to the latter indication the market price is pending ratification in Spain[11,12].

Although new anticoagulants have been shown to be safer than VKA, with reduced risk of intracranial bleeding, they are not exempt from bleeding complications[6-8]. One of the big arguments against the use of these new agents is the lack of a specific antidote to rapidly reverse their anticoagulant effect if serious bleeding occurs, whereas with VKA we have vitamin K as an effective antidote. Since the use of new oral anticoagulants is expected to increase, it is important to know all about the management of bleeding in patients anticoagulated with classical and new drugs, in order to optimize treatment.

Pharmacokinetics of vitamin K antagonists

VKA inhibit vitamin K-dependent coagulation factors II, VII, IX, and X and also the anticoagulant proteins C and S. Consequently, one of the main objectives in the management of bleeding associated with these drugs is to increase the concentration of vitamin K-dependent coagulation factors[13].

Warfarin is completely absorbed after oral administration, reaching peak concentration at 4 hours. Warfarin is almost entirely eliminated metabolically and only a small amount is excreted unchanged in urine and bile. Metabolism occurs primarily in the liver via cytochrome P450 and the isoenzyme CYP2C9. The half-life varies between 20 and 60 hours (mean 40 hours), so that the duration of its effect is between 2 and 5 days. Oral acenocoumarol is rapidly absorbed and peak concentration occurs 1-3 hours after ingestion. It is mainly metabolized mainly by cytochrome P4502C9, but also by CYP1A2 and CYP2C[19]. Acenocoumarol half life is 8-11 hours. However, it prolongs the INR for 36-72 hours depending on the initial dose. INR value normalizes within a few days after discontinuation of acenocoumarol. Interactions with VKA are frequent, significantly interfering with INR control. Age also plays a role, because the elderly may have exaggerated response to warfarin. All this means that INR monitoring must be more frequent at the beginning and end, and after dose adjustment of concomitant medication[14,15].

Management of bleeding using vitamin K antagonists

As with all anticoagulants, VKA use carries an inherent risk of bleeding. Consequently, it is critical know how to deal with this situation. The theoretical advantage of VKA over other anticoagulants is that they have a specific antidote, vitamin K. Unfortunately, its mechanism of action is slow. It has been demonstrated that when administered intravenously, normalization of the INR begins 6 hours later, and the full effect can take 24 hours or more to appear, even at high doses, depending on the starting values of INR[14]. Vitamin K administered orally is even slower. Intramuscular or subcutaneous vitamin K is not recommended as the response is unpredictable and may be even slower in some cases. Additionally, intramuscular injection can cause hematoma. Oral vitamin K is the treatment of choice when rapid reversal is not necessary, as in the case of an INR > 5 in an asymptomatic patient. In an emergency, when there is bleeding, the sole use of vitamin K is insufficient[13,14,16-18].

Given that the reversal of vitamin K anticoagulation is slow, one may use either fresh frozen plasma (FFP) or prothrombin complex concentrate (PCC)[13]. PCCs can normalize coagulation in a short period of time, and some authors consider they are better tolerated than FFP. However, no randomized clinical trials or controlled studies have compared the different treatments to reverse the effects of VKA. In a recently published study prospectively analyzing the use of PCC in patients with bleeding associated with the use of VKA, the results indicated that the management of these patients should be improved, especially regarding the dose of PCC, INR monitoring or the administration of vitamin K. In addition, no differences were observed in the values of INR after infusion of PCC in patients who received vitamin K compared to those who did not, regardless of when the INR was measured[19].

As with any bleeding, it is important to assess the hemodynamic status of the patient and the severity of bleeding. If the bleeding is significant, it may be necessary to administer fluid therapy or even transfusion of packed red blood cells. Me-

chanical compression is recommended to stem the bleed or, in some cases, surgical intervention. VKA therapy must be suspended and iv vitamin K (5-10 mg) administered, while PCC and/or FFP should be considered. If overdose within the last 2 hours is suspected and the patient is conscious and oriented, consider the use of activated carbon[13,14].

Pharmacokinetic properties of new oral anticoagulants

The pharmacological properties, pharmacodynamics and pharmacokinetics of new anticoagulants have been reviewed extensively[20]. Dabigatran etexilate is the prodrug of dabigatran, with no pharmacological activity by itself, but after ingestion is rapidly absorbed in the stomach and intestine; after hydrolysis in plasma and in the liver it is transformed into dabigatran, the active form with anticoagulant activity[9,21-25]. Dabigatran competitively and reversibly inhibits free and clot-bound thrombin and thrombin-induced platelet activity. Bioavailability is low, around 6.5% and it needs 0.5-2 hours to achieve maximum blood concentration. Elimination half-life in healthy volunteers is 12-14 hours, but this increases with worsening renal function. As binding to plasma proteins is low, the drug is dialyzable. It is important to note that the main route of elimination is urinary (85%) (Table 1)[9,21-25]. For dosage of dabigatran, it is essential to consider renal function. For example, in the case of avalvular heart disease, it is not necessary to adjust the dose in patients with a creatinine clearance between 50 and 80 ml/min and the recommended dose is 150 mg twice daily, but for patients with creatinine clearance between 30 and 50 ml/min, although the recommended starting dose is 150 mg twice daily, it should be reduced to 110 mg twice daily to reduce the risk of bleeding. Moreover, in patients with renal failure, close clinical monitoring is recommended. Finally, in those with creatinine clearance less than 30 ml/min, dabigatran is contraindicated[9].

Rivaroxaban is an orally active direct inhibitor of factor Xa. Bioavailability is 80-100% for 10 mg rivaroxaban, and food intake independent, but for the dose of 20 mg it is 66%. With food it increases by 39%, so that the doses of 15 and 20 mg should be taken with food. Absorption is rapid, and peak concentrations are reached 2 to 4 hours after drug intake. Rivaroxaban has high plasma protein binding ability (92-95%), so it is not dialyzable. Approximately two thirds of rivaroxaban is metabolized (half is excreted in urine and the other half in feces) and a third is directly excreted by the kidneys. Rivaroxaban is metabolized primarily via CYP3A4, CYP2J2 and other mechanisms independent of CYP. It is also a substrate of transporter proteins P- gp and Bcrp. Elimination half-life is 5-9 hours in young adults, and 11-13 hours in advanced elderly patients (Table 1)[10,21,26,27]. The dose of rivaroxaban should be adjusted to 15 mg daily in patients with moderately impaired renal function (creatinine clearance 30 to 49 ml/min) and severe (clearance creatinine 15-29 ml/min) when used for stroke prevention in patients with non-valvular AF. The use of rivaroxaban is not recommended when creatinine clearance is less than 15 ml/min[10].

Apixaban is an oral, direct and selective inhibitor of factor Xa. Apixaban prevents both the formation of thrombin and thrombi. Bioavailability is 50%, and maximum concentrations are reached 3-4 hours of drug intake. Binding to plasma proteins is high (87%), so it is not dialyzable. Renal excretion of apixaban constitutes 27% of total clearance. Elimination half-life is about 12 hours. Apixaban is metabolized primarily by CYP3A4/5 and less by CYP1A2, 2C8, 2C9, 2C19, and 2J2. Furthermore, it is a substrate of the transporter proteins P- gp and Brcp (Table 1)[11,28-30]. Clinical trials of patients with severe renal insufficiency (creatinine clearance 15-29 ml/min) indicate that plasma concentrations of apixaban increase, so apixaban should be used with caution in these patients. Apixaban is not recommended in patients with creatinine clearance < 15 ml/min.

New oral anticoagulants and coagulation tests

As mentioned, routine INR monitoring is not necessary due to the predictable kinetics of new anticoagulants. However, in some circumstances such as accidental or intentional overdose, if there is active bleeding or there is a need for urgent surgical intervention, monitoring may be useful[1,31-34]. It may also be useful to know if the patient is taking medication, if there are thromboembolic complications, and to evaluate adverse effects or possible interactions with other drugs[34].

To correctly interpret the results of coagulation tests it is essential to know the pharmacokinetics of new anticoagulants. Time to peak concentration is short, and half-life is 9-12 hours; in the case of dabigatran this is very dependent on renal

Table 1. Pharmacodynamic and pharmacokinetic characteristics of new oral anticoagulants[9-11]

	Dabigatran	Rivaroxaban	Apixaban
Mechanism of action	• Direct thrombin inhibitor.	• Direct factor Xa inhibitor.	• Direct factor Xa inhibitor.
Oral bioavailability	• 6,5%.	• 80-100% for 10 mg, regardless of food intake. • 66% for 20 mg. With food it increases by 39%.	• Approximately 50%.
Maximum concentration (Cmax)	• 0.5-2 hours.	• 2-4 hours.	• 3-4 hours.
Plasma protein binding	• 34-35%.	• 92-95%.	• 87%.
Metabolism and elimination	• Mainly urinary (85%); fecal excretion is 6%.	• Approximately 2/3 metabolized and 1/3 is directly excreted via the kidneys. • Metabolized by CYP3A4, CYP2J2 and other CYP-independent mechanisms. It is also a substrate of the transporter proteins Pgp and Bcrp.	• Approximately 25% of the dose recovered as metabolites, and most is eliminated in feces. Renal excretion accounts for 27% of total elimination. • Metabolized primarily by CYP3A4/5 and less by CYP1A2, 2, 2 c 9, 2 c 19, and 2J2. It is also a substrate of the P-gp and Brcp transporter proteins.
Relevant interactions	• Does not inhibit/induce major cytochrome P450 isoenzymes. • Potent inhibitor of P-gp (verapamil, amiodarone, quinidine), increases the concentration of dabigatran: caution required with co-administration (if the patient is taking verapamil, the dose of dabigatran should be 110 mg/12 h). • Potent inducers of Pgp (including carbamazepine, phenytoin, or rifampicin) should be avoided. • Contraindication: concomitant treatment with ketoconazole, ciclosporin, itraconazole, and tacrolimus. Not to be combined with dronedarone.	• Not recommended: the concomitant use of rivaroxaban with potent inhibitors of CYP3A4 and P-gp (azolic anti-fungals or protease inhibitors). • Caution required with potent inducers of CYP3A4 (carbamazepine, phenytoin, phenobarbital or rifampicin).	• Not recommended: the concomitant use of apixaban with potent inhibitors of CYP3A4 and P-gp (azolic anti-fungals or protease inhibitors). • Caution required with potent inducers of CYP3A4 (carbamazepine, phenytoin, phenobarbital or rifampicin). ,
Elimination half-life	• 12-14 hours (healthy volunteers). • Creatinine clearance ≥ 80 ml/min: 13.4 hours. • Creatinine clearance ≥ 50-80 ml/min: 15.3 hours. • Creatinine clearance ≥ 30-50 ml/min: 18.4 hours. • Creatinine clearance < 30 ml/min: 27.2 hours.	• 5-9 hours (young adults). • 11-13 hours (elderly).	• 12 hours.

function[9-11]. It is therefore important to perform renal function tests and to know the dose administered, when the last dose was taken and concomitant medication[34].

Dabigatran prolongs activated partial thromboplastin time (aPTT) and, minimally, prothrombin time (PT). At therapeutic concentrations, aPTT is not a sensitive measure of anticoagulation, and only provides a qualitative but not quantitative measure of anticoagulant activity. PT only increases slightly at therapeutic concentrations. Therefore, ecarin time (ET) is recommended; this is a specific test of thrombin generation providing more accurate and dose-dependent information of the anticoagulant effect. It allows distinguishing plasma drug levels. Thrombin time (TT) is also very sensitive and useful for detecting the presence of the drug in plasma, although not used to monitor the dosage. Hemoclot® test (Hyphen BioMed, Neuville -sur -Oise, France), a diluted TT method, can be used in the emergency department to provide information on the anticoagulant activity of dabigatran (Table 2)[1,9,31-35].

Rivaroxaban prolongs both aPTT and PT, but has no effect on TT. TP, measured in seconds, is modified by rivaroxaban in a dose-dependent manner, and bears a close correlation with plasma concentrations when neoplastin is used for analysis. INR is not helpful to monitor the effects of rivaroxaban, as it has only been validated for warfarin. Rivaroxaban modifies anti-factor Xa activity. In fact, the determination of anti-factor Xa using

chromogenic methods with specific calibration for rivaroxaban and controls (Technoclone, Hyphen - Biomed, Stago) has higher sensitivity and accuracy than TP. The results are expressed in ng/ml of rivaroxaban (Table 2)[1,10,34,36-39].

Apixaban also directly and selectively inhibits factor Xa, and also prolongs PT and aPTT.

However, the changes are small and show great variability, so that they are not recommended for assessing the anticoagulant effect of apixaban. However, since anti-factor Xa activity bears a close direct linear relationship with plasma levels of apixaban, the use of chromogenic methods, such as the Rotachrom Heparin assay, could be useful in certain situations such as overdose, hemorrhage or emergency surgery (Table 2)[11,34,39].

New oral anticoagulants: how to reverse their anticoagulant effect?

As mentioned, new oral anticoagulants are not exempt from bleeding complications and the lack of a specific antidote could be a problem for the management of bleeding[13,40,41]. In this regard, there are other anticoagulants without antidotes or only partial effect antidotes, which have been used for decades in our country without added risk for patients. Protamine sulfate (specific antidote for unfractionated heparins), has no effect or only a partial effect on low molecular weight heparin, so is only relatively useful in the management of bleeding in patients treated with these drugs.

Fondaparinux is an injectable direct inhibitor of factor X, used as an anticoagulant in our country for ten years, and there is no specific antidote to reverse its effects[13].

New oral anticoagulants have a short half-life, so discontinuation is sufficient in the majority of cases of hemorrhage, with observation and supportive treatment. Only in cases of severe bleeding do we need agents capable of reversing the effect of these anticoagulant drugs[13,40].

When an anticoagulant has been recently taken, the administration of activated carbon may decrease oral absorption. However, since the new drugs rapidly reach peak concentrations in the blood, activated carbon is only useful in the first few hours after ingestion. The usefulness of activated carbon has only been demonstrated with dabigatran, but is also considered a useful choice in the case of rivaroxaban and apixaban[9-11,34,41].

FFP has been used to treat bleeding in patients on VKA[13]. In a study using mice, FFP reduced the volume of intracranial hemorrhage in those taking high doses of dabigatran, but not in those with low doses. Furthermore, FFP did not reduce mortality rates in mice[42], and its effect in patients treated with rivaroxaban or apixaban is unknown[13,41]. Consequently, FPP cannot be recommended to reverse the effect of new oral anticoagulants; it is recommended for treating coagulopathy (dilutional coagulopathy, disseminated intramuscular coagulation) that can develop in serious bleeding processes[13,41].

Information on the reversal of new oral anticoagulants comes from guidelines and expert opinion or recommendations[40,41,43,44]. In general, these are based on experimental animal model studies and isolated human cases[20,45]. Animal studies indicate that the administration of activated recombinant factor VII can effectively reverse the anticoagulant effect of dabigatran[13,46]. However, primate studies show that activated recombinant factor VII has a modest effect on the reversal of bleeding in those treated with rivaroxaban[13,47]. Information on apixaban is more limited, although it seems that recombinant factor VIIa and prothrombin complex could be useful48. The manufacturer's infor-

Table 2. Effect of new oral anticoagulants on coagulation test results[1,9-11,31-39]

Drug	Coagulation tests
Dabigatran	• Prolongs aPTT and minimally prolongs PT. • aPTT is only a qualitative but not quantitative measure. • ET provides more accurate information about the anticoagulant effect (more sensitive and accurate than aPTT). • TT is very sensitive and useful for detecting the presence of the drug in plasma, but does not serve to monitor dose. • Hemoclot® thrombin inhibitor test can provide information in the emergency department on anticoagulant activity.
Rivaroxaban	• Prolongs aPTT and PT, but has no effect on TT. • The INR is not useful for monitoring the effects of rivaroxaban. • Chromogenic methods (Technoclone, Hyphen-Biomed, Stago) have greater sensitivity and accuracy than PT to determine anti-factor Xa effect.
Apixaban	• Prolongs PT and aPTT discreetly, with a high degree of variability. • Chromogenic methods of measuring anti-factor Xa activity, such as Rotachrom Heparin chromogenic assay, could be useful in situations such as overdose, bleeding, or emergency surgery.

aPTT: activated partial thromboplastin time; PT: prothrombin time; ET: ecarin time; TT: thrombin time.

Table 3. General management of bleeding in patients treated with new oral anticoagulants[13,14]

	Adaptación del esquema propuesto por la Guía SEHH SEHE[34]	
General measures	• Establish the severity of bleeding (mild, moderate or severe), as well as its location. • Laboratory tests, including hemoglobin and renal function. • Establish when the last dose of the drug was taken.	
Mild bleeding	• Delay or temporarily discontinue the drug. • If possible, perform local hemostasis.	
Moderate bleeding	• Suspension of oral anticoagulant. • Hemodynamic monitoring (ensure adequate venous access, as well as volume replacement, including blood transfusion if necessary). • If the intake was less than 2 hours before, activated carbon could be useful. • Location and control of bleeding and correction by endoscopy or surgery.	
Hemodynamic compromise or severe bleeding	• Same measures as above and in addition: – If the bleeding is secondary to dabigatran and less than 4 hours have passed since ingestion, dialysis or hemofiltration with activated carbon might be useful. – In the case of dabigatran, activated prothrombin complex concentrate* or recombinant factor VIIa can be useful. – In the case of rivaroxaban or apixaban, prothrombin complex concentrate* may be useful.	
	Adaptation of the scheme proposed by W. Frank Peacock, *et al*[13]	
Rivaroxaban	Mild bleeding	• Delay the next dose or discontinue treatment as appropriate.
	Moderate to severe bleeding	• Symptomatic treatment. • Mechanical compression. • Surgical intervention. • Replenishment of fluids. • Hemodynamic support. • Activated charcoal if drug intake was recent (< 2 hours before).
	Life-threatening bleeding	• Consider prothrombin complex concentrate.
Dabigatran	Mild bleeding	• Delay the next dose or discontinue treatment as appropriate.
	Moderate to severe bleeding	• Symptomatic treatment. • Mechanical compression. • Surgical intervention. • Replenishment of fluids. • Hemodynamic support. • Activated charcoal if drug intake was recent (< 2 hours before). • Hemodialysis.
	Life-threatening bleeding	• Consider recombinant factor VIIa. • Filtration with activated carbon.

*Dose of prothrombin complex concentrate (PCC): 50 IU/kg; dose of activated PCC (FEIBAR): 80 IU/kg in the case of severe life-threatening bleeding.

mation sheet indicates that there is no current experience with the use of recombinant factor VIIa in patients receiving apixaban, while that for rivaroxaban indicates that clinical experience is limited, and recommendations on factor VIIa are non-clinically based data, so in cases of bleeding with these drugs one could consider re-administration of recombinant factor VIIa and adjust the dose depending on response[10,11].

As for PCC, in a randomized, double-blind, placebo-controlled trial conducted in 12 healthy volunteers, PCC was able to revert the effect of rivaroxaban 20 mg immediately and completely, but had no effect on the anticoagulant effect of dabigatran[49].

In a study of 70 patients undergoing hip replacement surgery, all treated with rivaroxaban as thromboprophylaxis, 37 patients received perioperative tranexamic acid. Before surgery there were no significant differences in loss of blood volume or thromboembolic and ischemic events or hematoma. However, blood loss after surgery was significantly lower in the group of patients treated with tranexamic acid compared with the control group. Furthermore, none of those receiving tranexamic acid required blood transfusion versus 4 in the control group[50].

In a study that included 6 patients on hemodialysis for ESRD receiving etexilate dabigatran, 62 % of dabigatran was eliminated at 2 hours, and 68% at 4 hours[51]. Hemoperfusion with activated carbon could also be an objective method for the elimination of dabigatran[52]. Due to high protein binding with rivaroxaban or apixaban, hemodialysis seems unlikely to be useful in patients treated with these drugs[10,11,13].

In summary, as pointed out by the Spanish Society of Hematology and Hemotherapy and the Spanish Society of Thrombosis and Hemostasis, to reverse the anticoagulant effect of new anticoagulants in cases of life-threatening bleeding unresponsive to usual supportive measures, one may

use recombinant factor VIIa in patients treated with dabigatran, or PCC in the case of rivaroxaban or apixaban[34].

However, recent data indicate that recombinant factor VIIa should be limited to compassionate use and cannot be considered the drug of choice for reversal of the anticoagulant effect of dabigatran, considered a thrombogenic drug, since there is currently no clear evidence of reversal in animal models or any experience in human sujects[53]. In addition, the anticoagulant activity of dabigatran could be reversed in an indirect way more effectively by activated than non-activated PCC[54,55].

Management of patients with active bleeding receiving new oral anticoagulants

For these patients, first establish the severity of bleeding (mild, moderate or severe), and the site of bleeding. Laboratory tests must be obtained, including hemoglobin and renal function. Establish when the last dose of the drug was taken; if it was within 2-3 hours, activated carbon may have a role in its management. Furthermore, knowing the time from intake is essential to interpret

coagulation tests correctly[9-11,34]. If the bleeding is slight, in addition to measures of local hemostasis, it is sufficient to delay the next dose or even suspend the drug temporarily. If the bleeding is moderate, the same measures apply but it is essential to stabilize the patient hemodynamically (secure venous access and replace volume as needed). If the last dose was taken within 2-3 hours, activated carbon may be useful. Endoscopic or surgical measures may also be useful to identify and treat the site of bleeding. If there is uncontrolled bleeding or significant hemodynamic instability despite these measures, and the drug taken within the last 4 hours was dabigatran, hemofiltration with dialysis or activated carbon may be useful. Otherwise, recombinant factor VIIa may be used. However, if the anticoagulant is rivaroxaban or apixaban, then PCC should be used[13,34,56]. Two algorithms are presented in Table 3 on the management of patients treated with new oral anticoagulants and presenting active bleeding. As can be seen, the management of these patients is very similar to that used for bleeding associated with VKA.

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Hemorragias en pacientes anticoagulados: utilidad real de los antídotos y modo de actuación con los nuevos anticoagulantes orales

Sánchez M, Escolar G, Carles Reverter J

Una de las complicaciones más temidas de los anticoagulantes son las hemorragias. Aunque en muchas ocasiones la suspensión de la anticoagulación y medidas de soporte es suficiente, en otras ocasiones exigen un tratamiento más específico. Clásicamente se han empleado los antagonistas de la vitamina K (AVK) en la prevención a largo plazo de las complicaciones tromboembólicas. Sin embargo, éstos presentan numerosas limitaciones que complican su manejo clínico. Los nuevos anticoagulantes orales, además de tener una eficacia al menos similar a los AVK con una menor incidencia de hemorragias intracraneales, no necesitan controles rutinarios de la coagulación y se pautan a dosis fijas. Sin embargo, no están exentos de presentar complicaciones hemorrágicas. Con la única diferencia de que los AVK tienen un antídoto específico, el manejo de las hemorragias con los nuevos anticoagulantes orales es muy similar al de la hemorragia asociada a los AVK. [Emergencias 2013;25:482-490]

Palabras clave: Dabigatran. Rivaroxaban. Apixaban. Anticoagulantes orales. Hemorragia. Tratamiento. Antagonistas de la vitamina K.