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XXXIV Congreso Nacional de la Sociedad Española de Medicina Interna (SEMI)

21-23
Noviembre 2013

Palacio de Ferias y Congresos de Málaga
Málaga

XXIX Congreso de la Sociedad Andaluza de Medicina Interna (SADEMI)

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Reversión del tratamiento anticoagulante en situaciones de urgencia no demorable

Dr Javier Rodríguez Martorell

UGC Hematología

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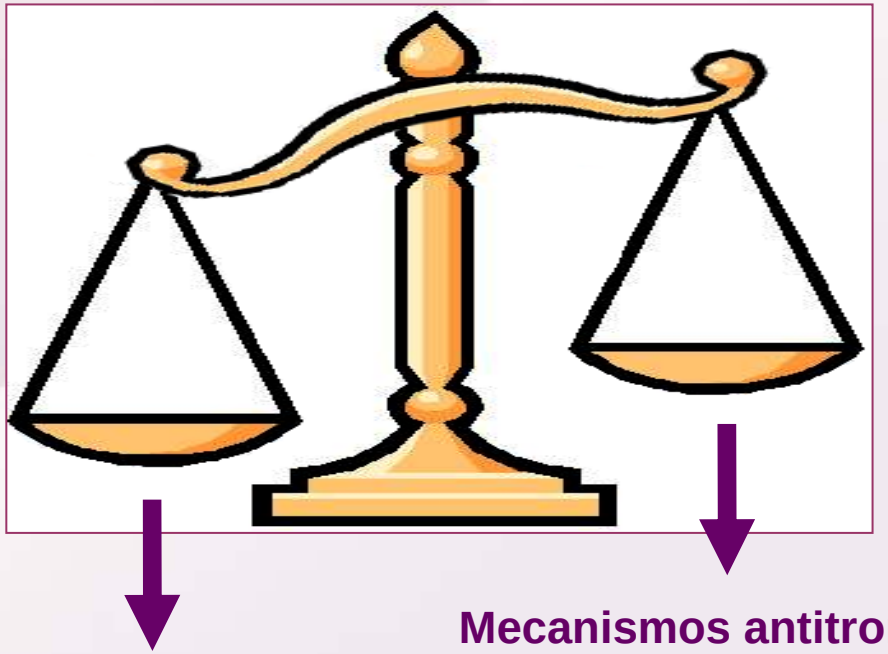
INSTITUTODEBIOMEDICINADESEVILLA

HEMOSTASIA: PROCESO INTEGRADO



Mecanismos prohemostáticos

Mecanismos antitrombóticos

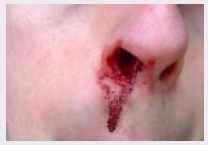
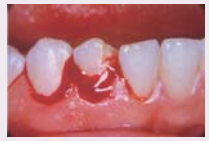
Equilibrio dinámico: en el lugar adecuado y el momento oportuno

HEMOSTASIA: PROCESO INTEGRADO

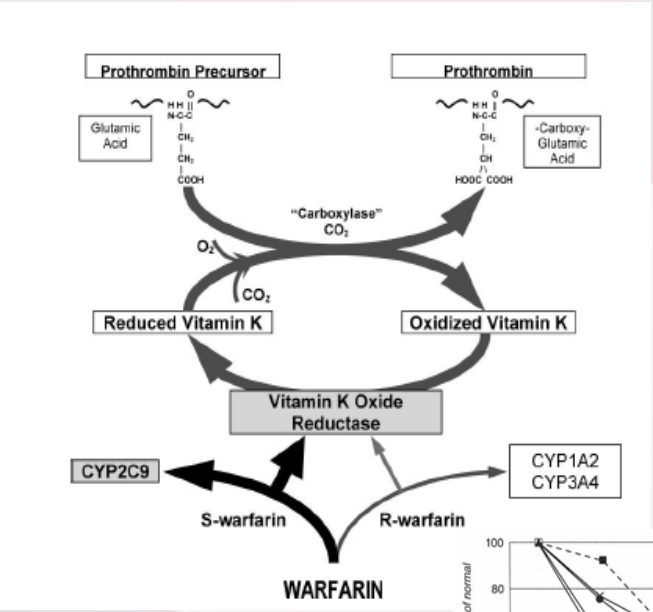
Mecanismos prohemostáticos

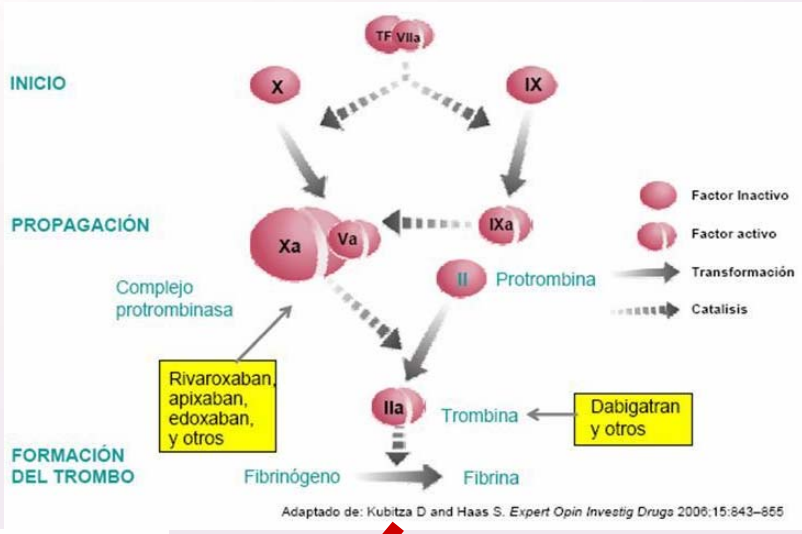
Mecanismos antitrombóticos

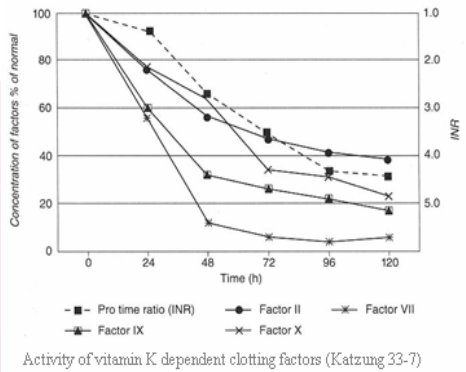
HEMORRAGIA

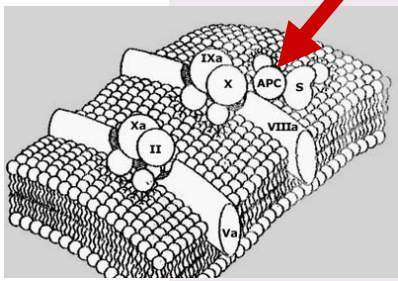
Fármacos anticoagulantes orales: tipos







Activity of vitamin K dependent clotting factors (Katzung 33-7)



Efecto terapéutico retardado:
- **+ 48 horas Sintrom®**
- **+ 72-96 horas warfarina**

Vida media con FR normal:
- **+ DBG: 12-14 h**
- **+ RVX: 9-11 h**
- **+ APX: 8-13 h**

Riesgo hemorrágico del tratamiento anticoagulante

- **Inherente a su mecanismo de acción e inseparable de su efecto antitrombótico (dogma en revisión).**
- **Riesgo anual estimado: 2.8-8.1% AVK; 2-5% NACO.**
- **Mortalidad atribuible: 0.2-0.5% anual.**
- **Aumentan el riesgo: comorbilidades (HAS-BLED, HAEMORRHAGES, score RIETE-ETEV, etc), co-tto con antiagregantes o AINEs, algunos fármacos con efecto sobre la hemostasia (ISRS, inhibidores de proteasas).**

Reversión del tratamiento anticoagulante: escenarios

- **Paciente con complicación hemorrágica mayor (criterios OMS: grados 3-4)[1] o que compromete la vida del paciente.**
- **Necesidad de una cirugía o procedimiento invasivo (pericardiocentesis, endoscopia terapéutica, etc) urgente no demorable.**

1) http://transfusionmed.wordpress.com/2012/04/13/escala-de-sangrado-de-la-oms/

3	Hemorragia que requiera la transfusión de 1 ó más concentrados de hematíes
4	Hemorragia con amenaza vital, definida como una hemorragia masiva que causa compromiso hemodinámico o hemorragia dentro de un órgano vital (por ejemplo hemorragia intracaneal, pericárdica, pulmonar)

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Reversión del tratamiento anticoagulante: actitud

bjh guideline

Guideline on the management of bleeding in patients on antithrombotic agents

Mike Makris,[1,2] Joost J. Van Veen,[2] Campbell R. Tait,[3] Andrew D. Mumford[4] and Mike Laffan[5] on behalf of the British Committee for Standards in Haematology

THSNA Meeting Proceedings

Guidance on the emergent reversal of oral thrombin and factor Xa inhibitors

Scott Kaatz,[1]* Peter A. Kouides,[2] David A. Garcia,[3] Alex C. Spyropolous,[4] Mark Crowther,[5] Jim D. Douketis,[5] Anthony K. C. Chan,[6] Andra James,[7] Stephan Moll,[8] Thomas L. Ortel,[9] Elizabeth M. Van Cott,[10] and Jack Ansell[11]

Evidence-based focused review

Perioperative management of patients who are receiving warfarin therapy: an evidence-based and practical approach

James D. Douketis[1]

[1]Department of Medicine, McMaster University and St Joseph's Healthcare Hamilton, Hamilton, ON

CHEST Supplement

ANTITHROMBOTIC THERAPY AND PREVENTION OF THROMBOSIS, 9TH ED: ACCP GUIDELINES

Perioperative Management of Antithrombotic Therapy

Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

James D. Douketis, MD, FCCP; Alex C. Spyropoulos, MD, FCCP; Frederick A. Spencer, MD; Michael Mayr, MD; Amir K. Jaffer, MD, FHM; Mark H. Eckman, MD; Andrew S. Dunn, MD; and Regina Kunz, MD, MSc (Epi)

ELSEVIER

http://dx.doi.org/10.1016/j.jemermed.2013.03.016

Clinical Reviews

MANAGING BLEEDING IN ANTICOAGULATED PATIENTS IN THE EMERGENCY CARE SETTING

Charles V. Pollack Jr., MA, MD, FACEP, FAAEM, FAHA

Manejo estructurado ante reversión urgente: adaptación a nivel local (multidisciplinaria) de las G.P.C.

Figure 1. Management of patients with bleeding or needing an urgent invasive procedure.

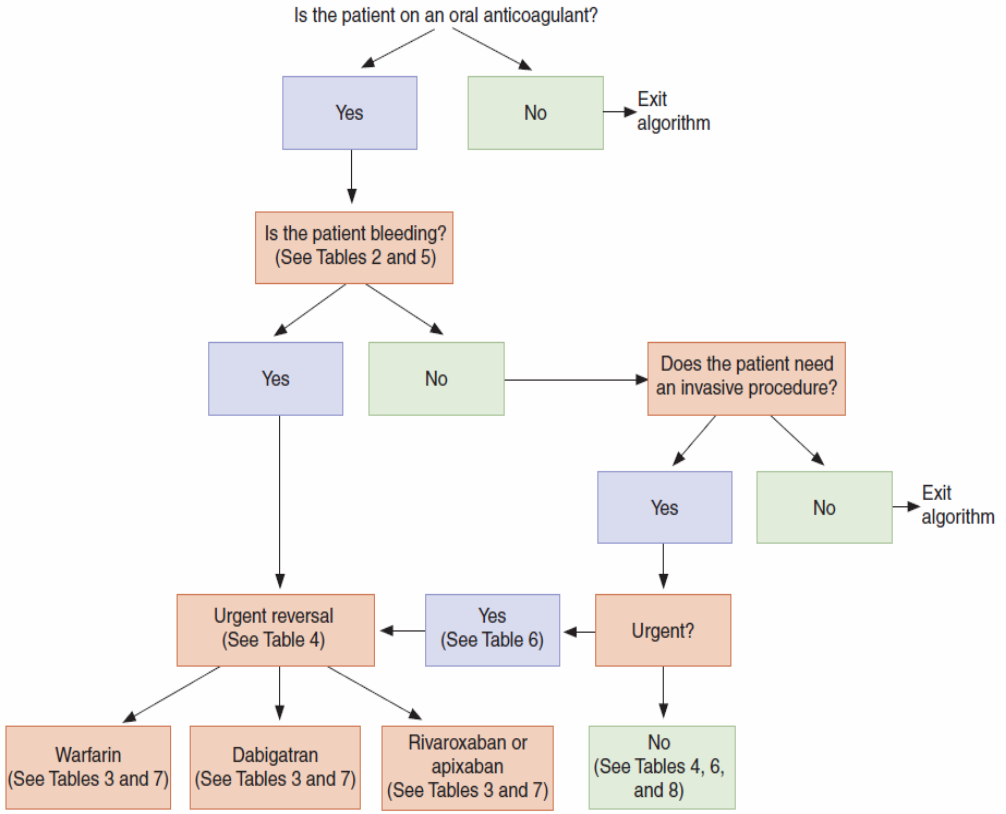


Table 7.
Therapeutic Interventions for Reversal of Oral Anticoagulants Based on Urgency[12,15,16,18,19,45,46,66-69]

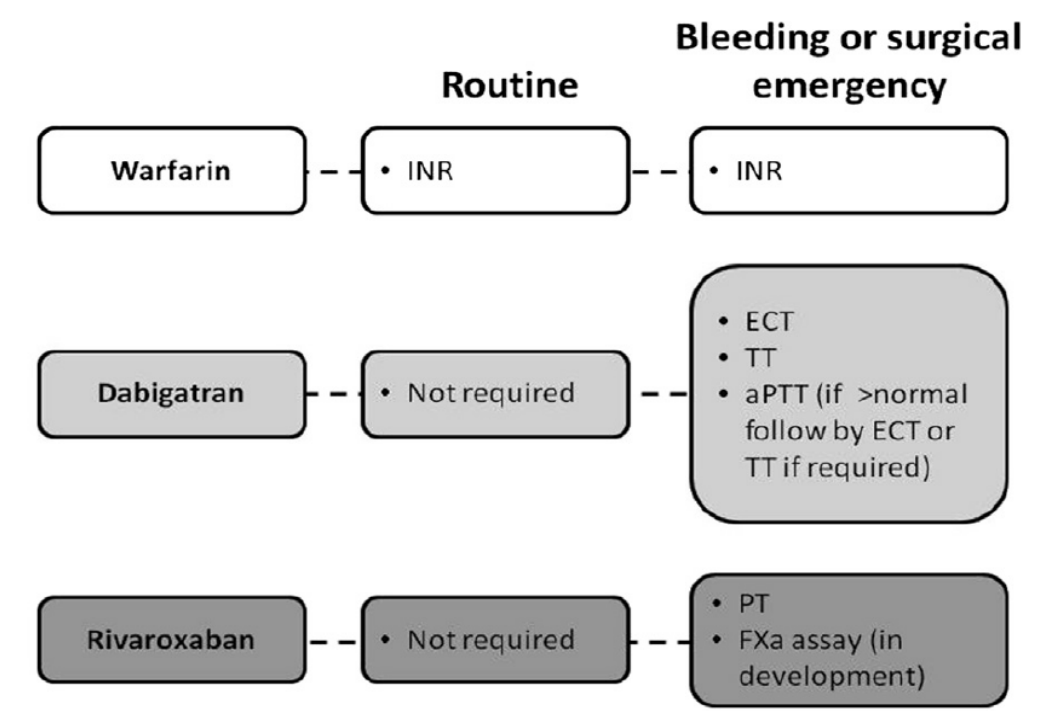
Level of Urgency	Warfarin	Dabigatran	Rivaroxaban or Apixaban
No rush (>24 hr)[a]	Withhold warfarin and consider oral phytonadione, with dose based on INR	Withhold drug and monitor clinical status and pertinent laboratory tests	Withhold drug and monitor clinical status and pertinent laboratory tests
Expedited (1–24 hr)[a]	Withhold drug and give oral phytonadione (1–5 mg) or low-dose i.v. phytonadione (0.25–5 mg), with dose based on initial INR and postreversal INR (checked 24 hr after dose)	Withhold drug, give activated charcoal[b] if last dose was taken within past 2 hr, and use prolonged hemodialysis (>2 hr)	Withhold drug and give activated charcoal[b] if last dose was taken within past 2 hr and repeat 6 hr after the last dose
Emergent (<1 hr)	Withhold drug, consider high-dose i.v. phytonadione[c] (depending on anticipated need to restart warfarin), and consider clotting factor supplement (listed in order of preference): • PCC4 • Build PCC4 with PCC3 plus rFVIIa[d] • aPCC • PCC3 • rFVIIa • FFP[e]	Withhold drug, give activated charcoal[b] if last dose was taken within past 2 hr, use prolonged hemodialysis (>2 hr), and consider clotting factor supplement (listed in order of preference): • aPCC • PCC4 • Build PCC4 with PCC3 plus rFVIIa[d]	Withhold drug, give activated charcoal[b] if last dose was taken within past 2 hr and repeat 6 hr after the last dose, and consider clotting factor supplement (listed in order of preference): • PCC4 • aPCC • Build PCC4 with PCC3 plus rFVIIa[d] • PCC3[f]

Table 3.
Recommended Dosing of Concentrated Clotting Factor Products for Oral Anticoagulant Reversal[29,33,34,39-52,a,b]

Reversal Agent	Clotting Factor(s) Replaced	Dose(s) for Reversal of Specific Anticoagulant		
		Warfarin	Dabigatran	Rivaroxaban
PCC3	II, IX, and X (inactivated)	25–50 units/kg[33,34,40,41]	…[c]	50 units/kg[42]
PCC4	II, VII, IX, and X (inactivated)	25–50 units/kg[36,43,44]	25–50 units/kg[45,46]	25–50 units/kg[42,45-47]
rFVIIa	VII (activated)	17.7–53.4 μg/kg[48-50,d]	20–120 μg/kg[45,d,e]	20–120 μg/kg[45,d,e]
aPCC	II, IX, X (inactivated) and VII (activated)	500 units for INR of <5 and 1000 units for INR of ≥5[51]	Up to 25 units/kg initially[f] with subsequent doses based on response[29]; 80 units/kg[45,g]	Up to 25 units/kg initially; no data available in patients with active bleeding; 80 units/kg[45,g]
Building of PCC4	PCC3: II, IX, and X (inactivated); rFVIIa: VII (activated)	PCC3 50 units/kg (or a fixed dose of 4000 units for an 80-kg patient) + rFVIIa 1 mg[52]; if rFVIIa is not available, the addition of a small dose of FFP (1–2 units) to PCC3 could be considered	No data available; possibly extrapolate doses from warfarin reversal	No data available; possibly extrapolate doses from warfarin reversal

Nutescu EA, et al. *Am J Health-Syst Pharm* 2013

¿Alguna prueba de laboratorio útil?



INR = international normalized ratio; ECT = ecarin clotting time; TT = thrombin clotting time; aPTT = activated partial thromboplastin time; PT = prothrombin time; FXa = activated factor X.

- **Con AVK el INR es el parámetro estándar.**
- **Con los NACOs los tests más útiles (ECT o TT diluido para DBG y anti-Xa para RVX-APX) habitualmente no están disponibles urgentes.**

Pollack CV Jr.
***J Emerg Med* 2013**

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Antivitaminas-K

Table 1. Treatment Options for Rapid Reversal of Warfarin Anticoagulation (7,31–38)

Option	Advantages	Disadvantages
Vitamin K	• Effect lasts beyond the relatively short half-lives of FFP and PCCs	• Takes ~6 h to reach therapeutic levels after i.v. administration
FFP—contains FII, VII, IX, and X	–	• Short duration of action
	–	• As large volumes (20–40 mL/kg) may be required, there is a risk of intravascular volume overload and heart failure
	–	• Must be compatibility tested
	–	• Must be thawed before use
	–	• Carries the general risks of blood transfusion
	–	• FIX levels may remain low despite adequate correction of other coagulation factors
Commercially available PCCs—pooled plasma products containing high (but varying) concentrations of FII, IX, and X, with or without FVII*	• Can correct INR faster than FFP	• Associated with increased risk of thrombosis
	• Available in smaller volumes than FFP	–
	• Does not require compatibility testing or thawing	–
	• Avoids the risks and delays associated with FFP	–
rFVIIa	–	• No strong evidence to support its widespread use are required
	–	• Short half-life means repeated doses
	–	• High cost

Pollack CV Jr. *J Emerg Med* 2013

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Uso de vitamina-K: recomendaciones

Emergency reversal of warfarin anticoagulation is required when a patient has major bleeding or needs an urgent procedure

Blood products, such as prothrombin complex concentrate, should be used only when the international normalized ratio (INR) is at least 1.5 and the patient has major bleeding (e.g., intracranial hemorrhage) or needs a procedure within six hours (e.g., repair of a ruptured aortic aneurysm or perforated viscus). For elective reversal, guidelines support withholding warfarin or administering vitamin K.[1]

Vitamin K should be given intravenously at the time of emergency reversal of anticoagulation

Because of the temporary effects of blood products, vitamin K is required for sustained reversal of anticoagulation. The recommended dose is 10 mg intravenously.[1] The intravenous route acts more quickly than the oral route (6–12 hours v. 18–24 hours).[2]

The effect of prothrombin complex concentrate and frozen plasma is temporary

The duration of effect is based on the short half-life of factor VII (about six hours).[1] As a result, the effect of both products decreases after six hours.

La vitamina-K iv debe administrarse en todos los casos graves (aunque se administre plasma o CCP)

Dosis: 5-10 mg en 20' (50 cc SSF)

Lin Y, Callum J. *CMAJ* 2011

Aporte de factores: opciones

Table. Available Treatments for Reversal of Vitamin K Antagonist–Associated Coagulopathy

Characteristic	Vitamin K	Fresh Frozen Plasma	3-Factor PCC	4-Factor PCC
Constituents	Vitamin K	All vitamin K–dependent clotting factors	Factor II, IX, X, proteins C and S*	Factor II, VII, IX, X, proteins C and S*
Route of administration	Oral or intravenous	Intravenous	Intravenous	Intravenous
Dose	5–10 mg	10–15 mL/kg	25–50 IU of factor IX/kg	25–50 IU of factor IX/kg
Onset of effect	6–8 h	Duration of infusion†	15–30 min†	15–30 min†
Adverse effects	Rare anaphylaxis	Fluid overload; febrile and allergic reactions; viral transmission; transfusion-related acute lung injury	Possible increase in thromboembolic complications	Possible increase in thromboembolic complications
Cost	Minimal	Moderate	High	High
Other	Intravenous administration produces more rapid reversal	Requires coadministration of vitamin K to sustain reversal	Requires coadministration of vitamin K to sustain reversal; may require coadministration of plasma or recombinant factor VIIa as a source of factor VII	Requires coadministration of vitamin K to sustain reversal

PCC indicates prothrombin complex concentrate.
*Some preparations also contain antithrombin and small amounts of heparin.
†Onset can also be affected by the dose administered.

Quinlan DJ. *Circulation* 2013

CCP vs PFC en reversión AVK

Table 5. Studies Comparing FFP and PCC to Correct Warfarin Anticoagulation in Nontraumatic ICH

Reference	Design (PCC product)	Pts.	Bleeding	Results	Evidence Grade[a]
Fredriksson (1992)[50]	Retrospective (3-factor PCC)	PCC, n = 10 FFP, n = 7	ICH	All pts. received vitamin K 10-20 mg iv PCC decreased INR from 2.83 to 1.22 within 4.8 hours FFP decreased INR from 2.97 to 1.74 within 7.3 hours; $p < 0.001$ Signs and symptoms of ICH progressed less, with nonsignificant trend toward less severe outcomes in pts. treated with 3-factor PCC	Low
Makris (1997)[51]	Prospective (4-factor PCC)	PCC, n = 29[b] FFP, n = 12	WAICH, other	4-factor PCC corrected INR in 28 pts. (mean, 1.3; range, 0.9-3.8) FFP partially corrected INR (mean, 2.3; range, 1.6-3.8) Posttreatment factor II, VII, IX, and X levels higher with PCC vs FFP	Moderate
Boulis (1999)[52]	Prospective (3-factor PCC)	PCC, n = 5 FFP, n = 8	WAICH	All pts. received vitamin K All PCC pts. also received FFP 3-factor PCC plus FFP corrected INR significantly faster (2.95 ± 0.46 hours) vs FFP alone (8.9 ± 1.51 hours); $p < 0.01$ No significant difference in neurologic outcomes	Moderate
Cartmill (2000)[53]	Prospective (3-factor PCC)	PCC, n = 6 FFP, n = 6	WAICH	All pts. received vitamin K At 15 minutes posttreatment, 3-factor PCC decreased mean INR from 4.86 before treatment to 1.32 vs FFP, which decreased mean INR from 5.32 before treatment to 2.30 PCC reversal significantly faster (41 vs 115 minutes); $p < 0.001$	Low
Siddiq (2008)[54]	Retrospective (factor IX complex concentrate)	PCC, n = 10 FFP, n = 9	WAICH	All pts. received concurrent vitamin K All PCC pts. also received FFP 3-factor PCC (4.3 ± 2.1 hours) vs FFP group (8.5 ± 5.6); $p < 0.005$	Low
Demeyere (2010)[55]	Prospective, randomized (4-factor PCC)	PCC, n = 18 FFP, n = 20	Cardiac surgery; no pt. received vitamin K	No pt. received concurrent vitamin K 4-factor PCC achieved target INR faster than FFP at 15 minutes after CPB; no significant difference in mean INR values 60 minutes after CPB (PCC, 1.6 vs FFP, 1.7)	Good

El CCP revierte las AVK de forma más rápida y eficaz que el PFC

Nitzki-George D, et al. *Ann Pharmacotherapy* 2013

CCP vs PFC en reversión AVK

EC-III-b

n = 216

Table 2. Dose of Study Treatment per Baseline INR

Baseline INR	4F-PCC Dose, IU of Factor IX per kg Body Weight*	Plasma Dose, mL per kg Body Weight*
2 to <4	25	10
4–6	35	12
>6	50	15

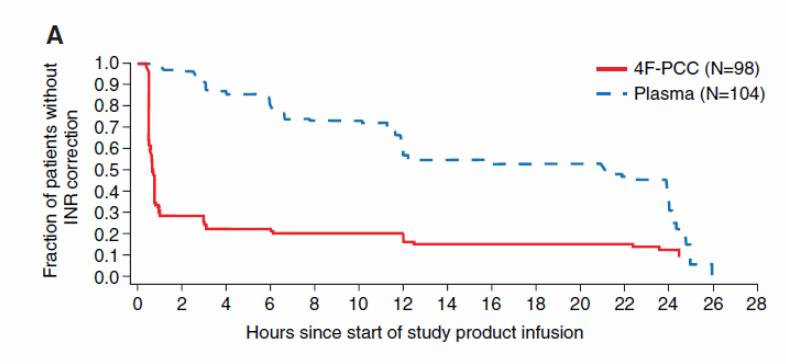


Table 8. Summary of AEs (Intention-to-Treat Safety Population)

AE	No. (%) of Patients 4F-PCC (n=103)	Plasma (n=109)
Any nonserious AE*	66 (64.1)	71 (65.1)
Related AE†	10 (9.7)	23 (21.1)
AE leading to treatment discontinuation	0	3 (2.8)
Serious AE*	32 (31.1)	26 (23.9)
Related serious AE†	2 (1.9)	4 (3.7)
AEs of interest		
Deaths to day 30	6 (5.8)	5 (4.6)
Deaths to day 45	10 (9.7)	5 (4.6)
Related deaths (to day 45)‡	1 (1.0)	0
Thromboembolic AE	8 (7.8)	7 (6.4)
Related thromboembolic AE†	4 (3.9)	3 (2.8)
Fluid overload or similar cardiac event	5 (4.9)	14 (12.8)
Related fluid overload or similar cardiac event†	0	7 (6.4)

El CCP revierte las AVK de forma más rápida y eficaz que el PFC y tiene un perfil de seguridad aceptable comparado con éste

Sarode R, et al. *Circulation* 2013

Uso de rFVIIa en la reversión de AVK

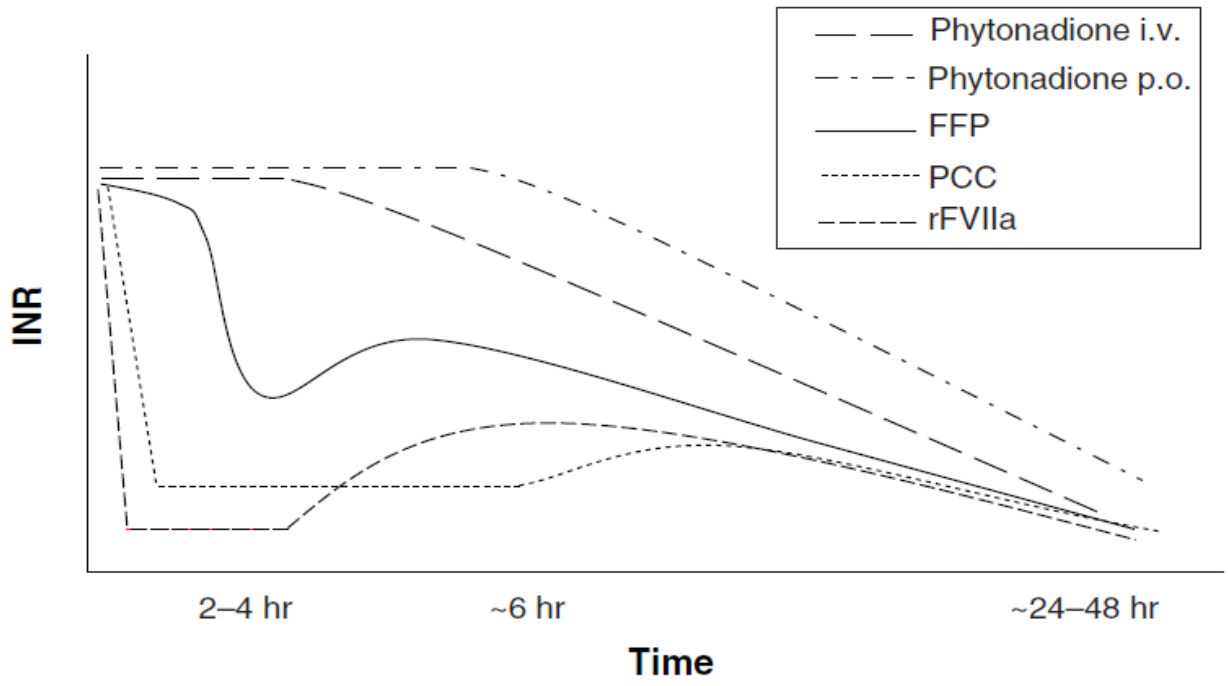
Cuando se administra NovoSeven a pacientes para indicaciones no autorizadas, son frecuentes los acontecimientos tromboembólicos arteriales (≥1/100 a <1/10). Se ha realizado un meta-análisis con datos de ensayos controlados con placebo llevados a cabo fuera de las indicaciones actualmente autorizadas, en distintos ámbitos clínicos, cada uno con pacientes de distintas características y por lo tanto con distintos perfiles de riesgo subyacentes. Este análisis ha mostrado que existe un riesgo mayor de sufrir eventos tromboembólicos arteriales (5,6% en pacientes tratados con NovoSeven versus 3,0% en pacientes que recibieron placebo). (Ver tabla: Trastornos vasculares).

No se ha establecido la seguridad y eficacia de NovoSeven fuera para indicaciones no autorizadas y, por tanto, NovoSeven no debe utilizarse de este modo.

En España el rFVIIa es una opción con la que no se debe contar, pese a estar recogida en las GPC internacionales, ya que existen fármacos alternativos sin restricciones médico-legales

Novoseven®; Ficha técnica para Europa

Figure 1. Onset and duration of effect on International Normalized Ratio (INR) of various warfarin reversal therapies. FFP = fresh frozen plasma, PCC = prothrombin complex concentrate, rFVIIa = recombinant factor VIIa. Adapted from reference 23.



Dager WE.. *Am J Health-Syst Pharm* 2013

Recommendations

- All hospitals managing patients on warfarin should stock a licensed four-factor PCC (1C).
- Emergency anticoagulation reversal in major bleeding should be with 25–50 U/kg four-factor PCC and 5 mg intravenous vitamin K (1B).
- Recombinant factor VIIa is not recommended for emergency anticoagulation reversal (1B).
- Fresh frozen plasma produces suboptimal anticoagulation reversal and should only be used if PCC is not available (1C).
- Emergency reversal of the effect of phenprocoumon, acenocoumarol and phenindione should be with 5 mg intravenous vitamin K and 25–50 units/kg four-factor PCC.

Makris M, et al. *Br J Haematol* 2012 (BCSH)

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Nuevos anticoagulantes orales (NACO)

Table 8.

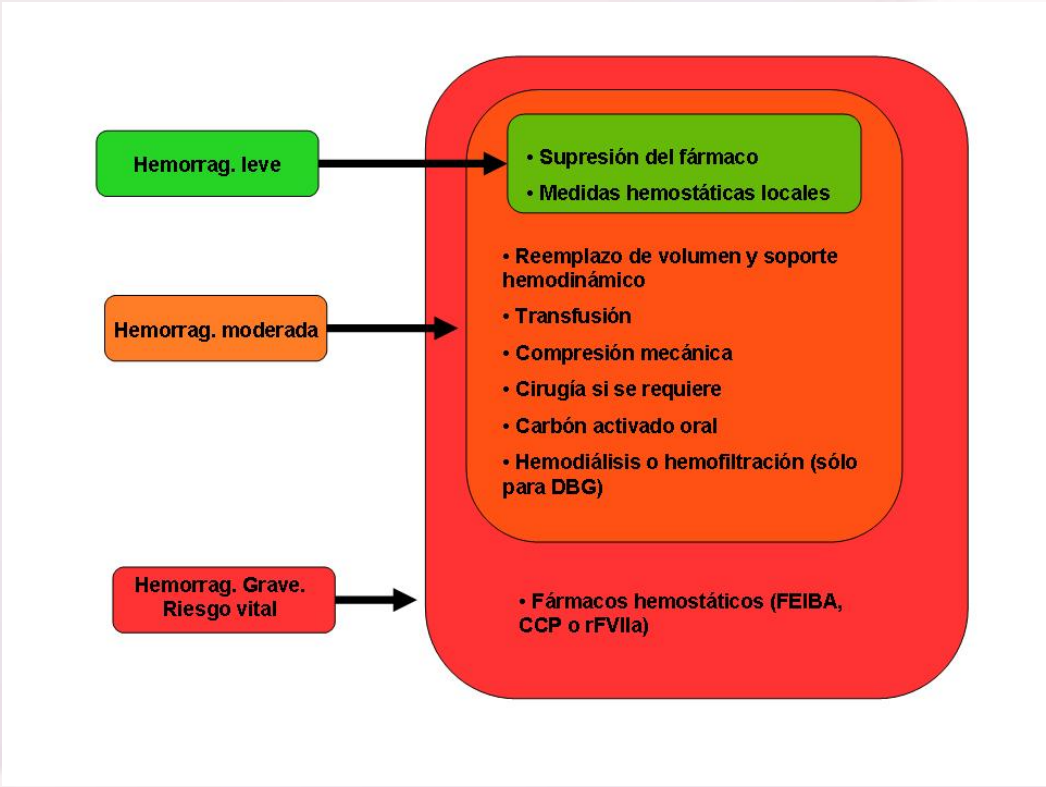
Interruption of Target-Specific Oral Anticoagulant Therapy for Invasive Procedures and Surgery[14-16,77-79,a]

Drug (Renal Function)	Time of Last Dose Before Minor Procedure	Time of Last Dose Before Major Surgery
Dabigatran		
CL_{cr} >50 mL/min	1 day (24 hr)	2 days
CL_{cr} 30–50 mL/min	2 days	4 days
CL_{cr} ≤30 mL/min	4 days	6 days
Rivaroxaban or apixaban		
CL_{cr} >50 mL/min	1 day (24 hr)	2 days
CL_{cr} 30–50 mL/min	1–2 days	3–4 days
CL_{cr} ≤30 mL/min	2 days	4 days

[a]Therapy should generally be resumed 24–48 hours after a minor procedure and 48–72 hours after major surgery. If unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH) is used as bridging therapy in patients with atrial fibrillation or with venous thromboembolism who are at high risk for thromboembolism, oral anticoagulant therapy with a target-specific agent should be resumed when the UFH infusion is discontinued and when the next scheduled dose of LMWH would have been given. CL_{cr} = creatinine clearance.

Nutescu EA, et al. *Am J Health-Syst Pharm* 2013

Tto escalonado de la hemorragia por NACO



MINISTERIO DE SANIDAD, SERVICIOS SOCIALES E IGUALDAD

agencia española de medicamentos y productos sanitarios

INFORME DE POSICIONAMIENTO TERAPÉUTICO
UT/V3/06062013

Criterios y recomendaciones generales para el uso de nuevos anticoagulantes orales (NACO) en la prevención del ictus y la embolia sistémica en pacientes con fibrilación auricular no valvular

Fecha de publicación 18 de junio de 2013

- **Adopta el tratamiento escalonado.**
- **Particularidades de cada NACO.**

Pollack CV Jr. *J Emerg Med* 2013 (modificada)

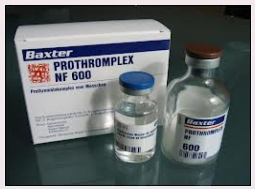
Papel de fármacos en reversión NACO

Species	Medication	Dose	DOA	Test	Result	Reference
HV	PCC	50 U/kg	rivaroxaban 20 mg bd (human therapeutic dose: 20 mg od)	PT, ETP	Complete reversal	Eerenberg [52]
	PCC	50 U/kg	dabigatran 150 mg bid (human therapeutic dose: 150 mg bid)	PT, ECT, TT	No reversal	
Rats	PCC	50 U/kg	rivaroxaban ED_{50} of 1.3 mg/kg	BT, TAT, PT	Complete reversal of TAT and BT, partial of PT	Perzborn [51]
Rabbits	FEIBA		dabigatran 1 µmol/kg bolus + 0.5 µ mol/kg/h infusion for 25 min	PTT, BT	BT reversal	Van Ryn [53]
	PCC			BT	BT reversal	
	rFVIIa			PTT	Partial PTT reversal	
Mice	PCC	100 U/kg	dabigatran 4.5 and 9 mg/kg 5–10-fold the human therapeutic plasma levels	TVBT, ECT, haematoma growth	Reduced haematoma growth	Zhou [54]
	Murine FFP	200 µl			No effect	
Human plasma	rFVIIa	8 mg/kg	edoxaban at supratherapeutic concentrations 500 and 1,000 ng/ml		No effect	
	rFVIIa	0.8 and 1.8 µg/ml		PT aPTT anti-Xa	Significant and rapid reversal on all tests	Halim [55]
	FEIBA	0.75 and 1.4 U/ml				
Rabbits	rFVIIa PCC		single bolus of 150 µg/kg rivaroxaban. Plasma levels close to human therapeutic dose	Ear BT Hepatosplenic blood loss aPTT	Decreased ear BT, no effect on blood loss, aPTT decreased	Godier [56]
Human plasma	PCC	0.15, 0.5, 1.5 U/ml	edoxaban 150 – 300 ng/ml (therapeutic to supratherapeutic doses)	PT	Concentration dependent shortening of PT, most effect by rFVIIa	Fukuda [57]
	FEIBA	0.15, 0.5, 1.5 U/ml				
	rFVIIa	100,300, 1,000 ng/ml				
Rats	FEIBA	100 U/kg	edoxaban 1 mg/kg/h	PT	Significant reversal of prolonged BT	
	rFVIIa	1–3 mg/kg				

- **Estudios en animales y en muestras de plasma.**
- **Con DBG el más efectivo parece el FEIBA.**
- **Para RVX y APX son útiles todos (CCP, FEIBA y rFVIIa).**
- **Con EDX los más efectivos son el rFVIIa y el FEIBA.**

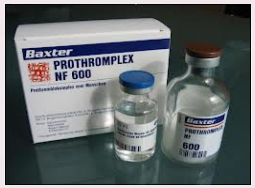
Miesbach W, Seifried E.
***Thromb Haemost* 2012**

Uso de fármacos hemostáticos: premisas



- **No son "antídotos" de los NACO ni "revierten" su efecto anticoagulante. Generan trombina en los focos de hemorragia controlando ésta.**
- **Todos tienen un cierto riesgo protrombótico (que se debe asumir): consentimiento informado.**
- **Su uso "profiláctico" no se justifica. Se restringe al tratamiento de una complicación hemorrágica ya existente muy grave o de riesgo vital.**

Uso de fármacos hemostáticos: dosis




- CCPa (FEIBA®): 50 UI/kg; repetir una segunda dosis en caso de no respuesta.
- CCP (Prothromplex®, Beriplex®): 25-50 UI/kg; repetir una segunda dosis en caso de no respuesta.
- rFVIIa (Novoseven®): 90-120 µg/kg; se puede repetir cada 2-3 horas hasta control de la hemorragia; no es un fármaco recomendable por cuestiones médico-legales.

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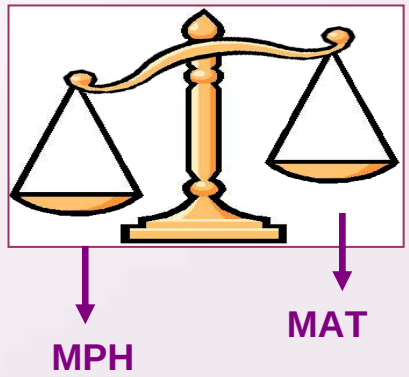
Profilaxis antitrombótica post-reversión

Tabla 4. Riesgo de eventos tromboembólicos[5]

Riesgo de trombosis	Antecedentes del paciente
Alto riesgo	IAM, angina, angor inestable o ictus isquémico reciente (menos de un mes) Angioplastia percutánea e inserción de stent (menos de un mes) Antecedentes de embolismo arterial Válvula protésica mitral tipo ball-cage Válvula protésica aórtica monovalva TEV* reciente (menos de tres meses) Cáncer activo (tratado durante 6 meses o es paliativo) Anticuerpo antifosfolípido (anticoagulante lúpico) Fractura o cirugía de pelvis, cadera o extremidad inferior Cirugía mayor pélvica o abdominal por cáncer Parálisis de extremidades inferiores Amputación de extremidades inferiores
Riesgo moderado	Válvula bivalva aórtica y dos o más factores de riesgo de embolia TEV* entre 3 y 6 meses TEV* ocurrido tras suspensión del anticoagulante Válvula protésica con fibrilación auricular Valvulopatía mitral reumática Traumatismos mayores o grandes quemados Enfermedades importantes cardíacas, pulmonares, neoplasias o enfermedad inflamatoria intestinal Enfermedad arterial oclusiva periférica
Riesgo bajo	Válvula bivalva aórtica y menos de dos factores de riesgo de embolia Anticoagulación por fibrilación auricular o TEV* sin válvula mitral protésica No antecedentes de ACV agudo No antecedentes de TEV* en los últimos 6 meses



HBPM a dosis profilácticas o intermedias hasta la reintroducción del TAO

Conclusiones

- La reversión urgente de las AVK se debe realizar con CCP a dosis de 25-50 UI/kg (según INR al ingreso).
Actualmente el PFC no se recomienda con esta finalidad.
- La administración de vit-K iv (5-10 mg) en 20-30 min debe realizarse en todos los casos.
- No existen antídotos disponibles para los NACO.
- Con los NACO se debe adoptar un abordaje secuencial. Los fármacos hemostáticos (FEIBA 50 UI/kg para DBG; CCP 25-50 UI/kg para RVX, APX) sólo en situaciones de riesgo vital.
- Es imprescindible un abordaje estructurado: Guía Local.
- No olvidar la profilaxis antitrombótica (“terapia puente” HBPM).

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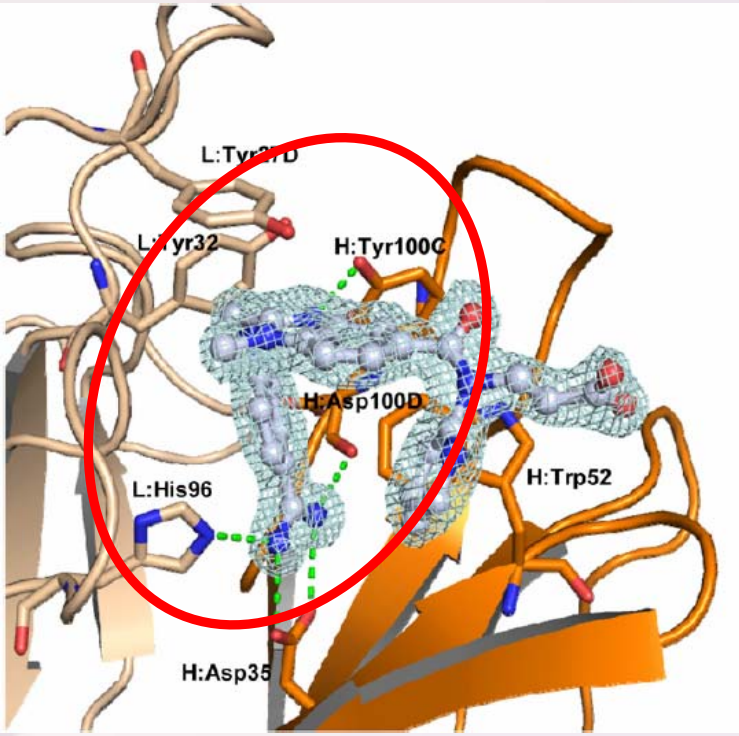
Muchas Gracias por su Atención

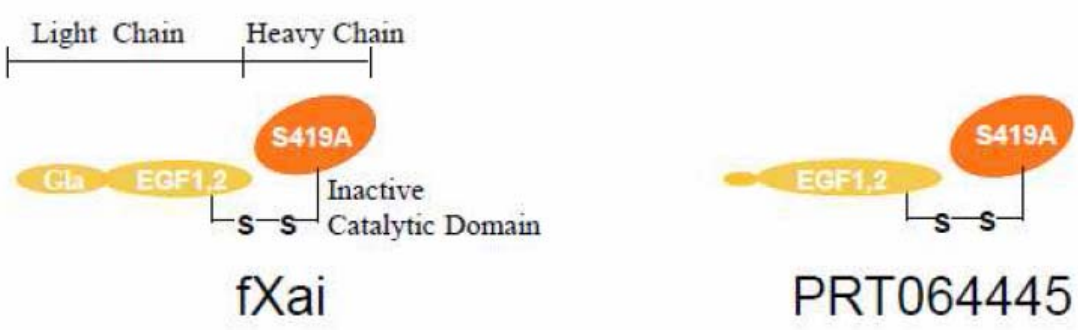
Antídoto para dabigatrán



- Ac monoclonal de origen murino y humanizado (a-Dabi-Fab).
- Unión del grupo benzamidina del DBG a "bolsillo" del AcMo (H-Asp35, L-His96 y H-Asp100D).
- Afinidad por el DBG 350 veces mayor que la trombina.
- Carece de efecto sobre las funciones de la trombina y es inerte en ausencia de DBG.
- Demostrada eficacia *in vivo* en ensayos experimentales en ratas.

Antídoto para inhibidores del FXa

r-Antidote: a recombinant human fXa variant lacking the membrane binding Gla-domain and active site serine



- **Incapaz de unirse al complejo protrombinasa y activar el F-II.**
- **Compite con el F-Xa por unirse a los inhibidores de éste (xabanes y HBPM-fondaparinux).**