Síndrome Antifosfolípido en la infancia: Tratamiento



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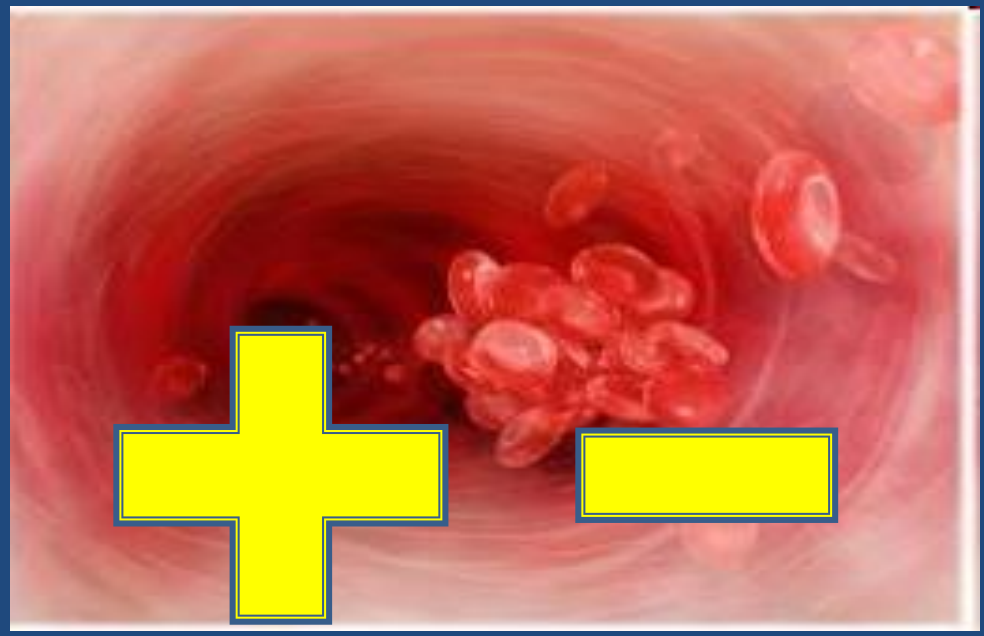


Índice

- Introducción
- Terapia Anti-trombótica en niños
- Tratamiento diversos escenarios
- Conclusiones

Introducción

¿Está claro el tratamiento del Síndrome Antifosfolípido en la Infancia?



Introducción



Introducción

"SÍ"

- Práctica clínica

NO

- No hay EC
- Extrapolamos de población adulta

Petty RE, Cassidy JT. Textbook of pediatric rheumatology. 6th ed. Pp 344-360.
Ravelli A, Martini A. Rheum Dis Clin North Am. 2007; 33: 499-523.
Alarcon-Segovia D, Boffa M.C, Branch W. Lupus 2003, 12: 499-503.

Introducción



Farmacocinética
Farmacodinámica

Infecciones intercurrentes

Efectos Adversos

Manco-Johnson M.J. Blood 2006; 107: 21-29.
Monagle P, Michelson A.D, Bovill E. Chest 2001; 119: 344S-370S.

Terapia Antitrombótica en niños

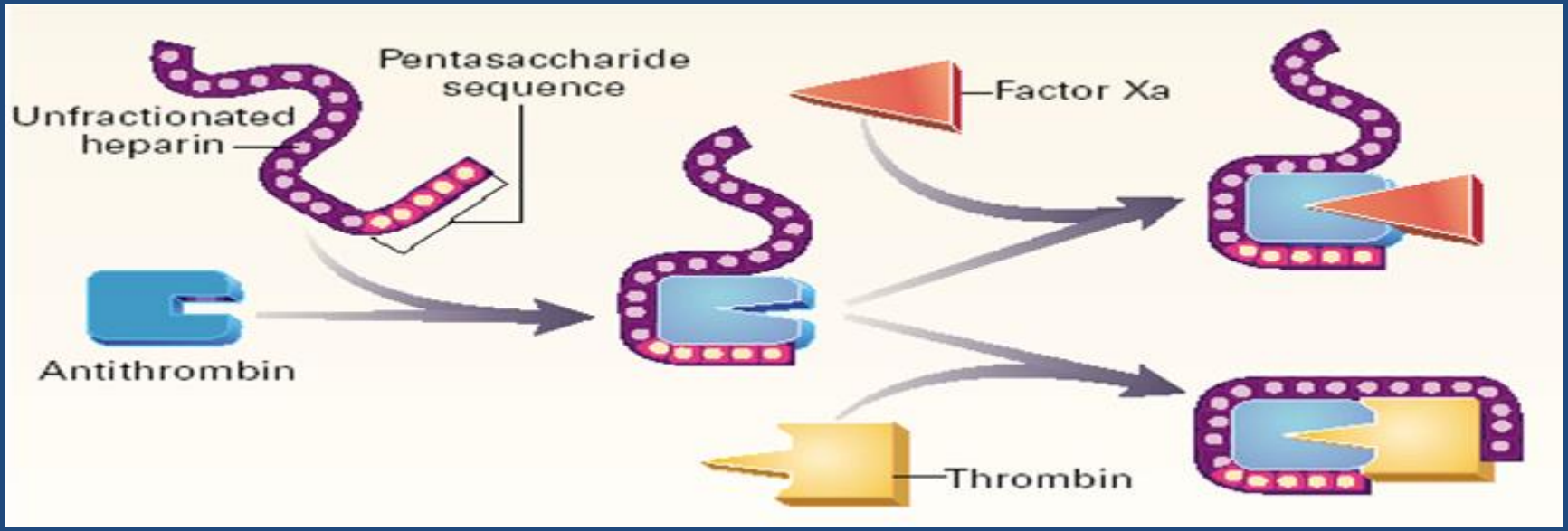
- Heparina no fraccionada (HNF)
- Heparina de bajo peso molecular (HBPM)
- Acenocumarol
- Ácido Acetíl Salicílico (AAS)
- Otros: clopidrogel, estreptoquinasa, uroquinasa, activador tisular del plasminógeno







Heparina no fraccionada



- Monitorización : TTPA
- Efectos adversos: Hemorragia, osteoporosis, trombopenia
- Antagonista: sulfato de protamina

Weitz JI N Engl J Med 1997; 337: 688; Holst J et al. Blood Coagul Fibrinolysis 1994; 5: 795
Monagle P, Michelson A.D, Bovill E. Chest 2001; 119: 344S-370S.

Heparina no fraccionada

Table 1—*Protocol for Systemic Heparin Administration and Adjustment for Pediatric Patients

I. Loading dose: Heparin 75 U/kg IV over 10 min
II. Initial maintenance dose: 28 U/kg/h for infants < 1 year; 20 U/kg/h for children > 1 year.
III. Adjust heparin to maintain APTT 60–85 s (assuming this reflects an anti-factor Xa level of 0.30 to 0.70):

APTT, s	Bolus, U/kg	Hold, min	Rate Change, %	Repeat APTT
< 50	50	0	+10	4 h
50–59	0	0	+10	4 h
60–85	0	0	0	Next day
86–95	0	0	−10	4 h
96–120	0	30	−10	4 h
> 120	0	60	−15	4 h

IV. Obtain blood for APTT 4 h after administration of the heparin loading dose and 4 h after every change in the infusion rate.
V. When APTT values are therapeutic, a daily CBC and APTT.

*Reproduced with permission of Michelson et al.[3]

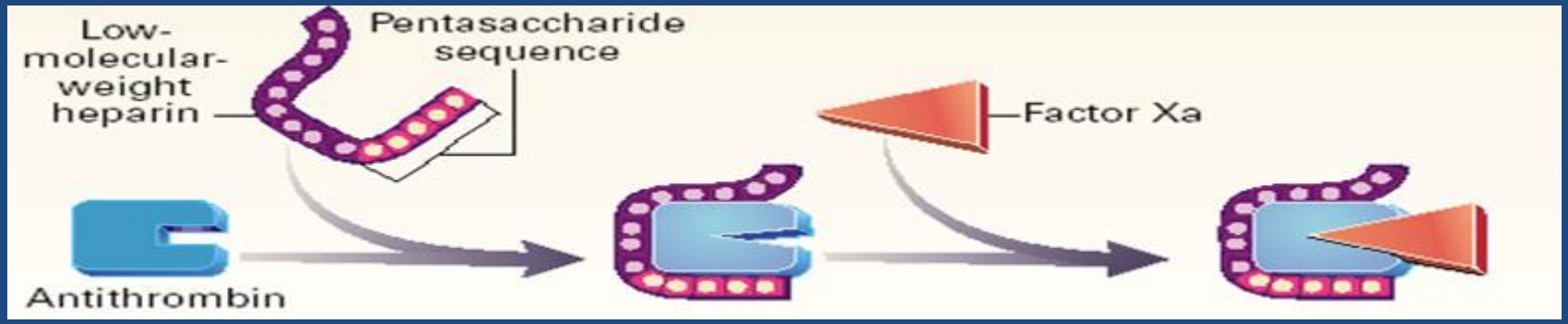
Table 3—*Reversal of Heparin Therapy

Time Since Last Heparin Dose, min	Protamine Dose, mg/100 U heparin
< 30	1.0
30–60	0.5–0.75
60–120	0.375–0.5
> 120	0.25–0.375

*Maximum dose of 50 mg. Infusion rate of a 10-mg/mL solution should not exceed 5 mg/min. Hypersensitivity reactions to protamine sulfate may occur in patients with known hypersensitivity reactions to fish or those previously exposed to protamine therapy or protamine-containing insulin.

Monagle P, Michelson A.D, Bovill E. Chest 2001; 119: 344S-370S.

Heparina bajo peso molecular



- Monitorización : No requiere. Niveles de Anti Factor Xa
- Efectos adversos: Hipoaldosteronismo
- Antagonista: ninguno

Weitz JI N Engl J Med 1997; 337: 688; Holst J et al. Blood Coagul Fibrinolysis 1994; 5: 795
Monagle P, Michelson A.D, Bovill E. Chest 2001; 119: 344S-370S.

Heparina bajo peso molecular

Table 4—*Dosing of Reviparin and Enoxaparin*

Treatment	Weight-Dependent Dose of Reviparin*	
	< 5 kg	> 5 kg
Initial treatment dose	150	100
Initial prophylactic dose	50	30
	Age-Dependent Dose of Enoxaparin†	
	< 2 mo	> 2 mo
Initial treatment dose	1.5	1.0
Initial prophylactic dose	0.75	0.5

*Values given as U/kg/dose q12h.

†Enoxaparin has 110 anti-factor Xa U/mg.[43] Values given as mg/kg/dose q12h.

Monagle P, Michelson A.D, Bovill E. Chest 2001; 119: 344S-370S.

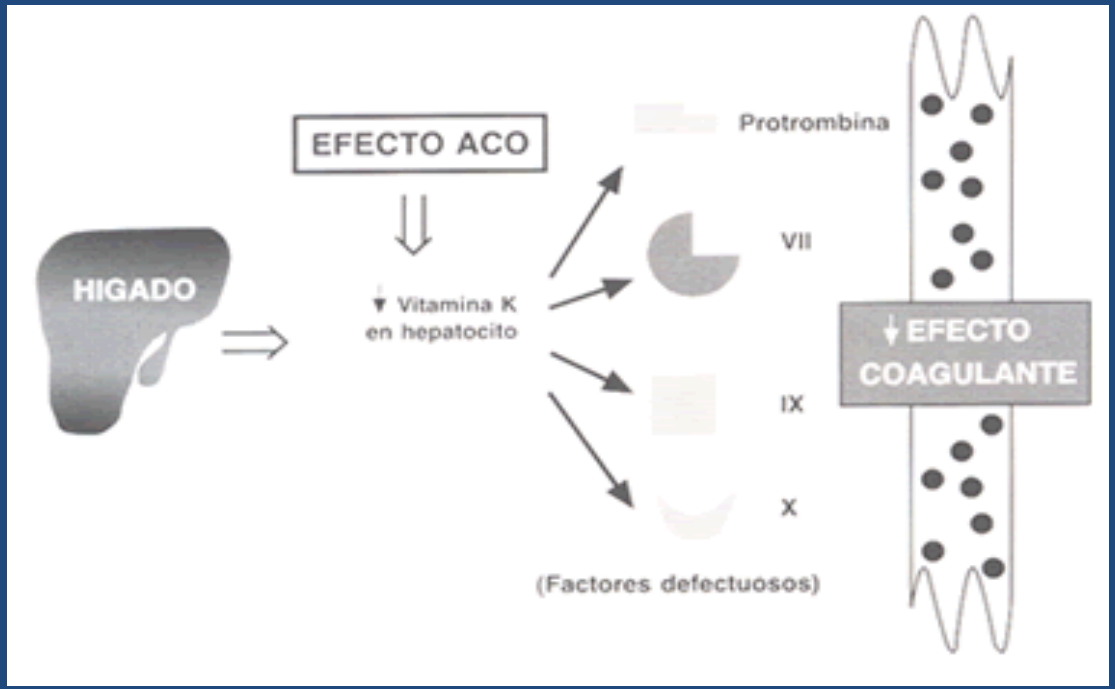
Heparina bajo peso molecular

Table 5—*Nomogram for Monitoring Reviparin/Enoxaparin in Pediatric Patients*

Anti-Factor Xa Level U/mL	Hold Next Dose?	Dose Change?	Repeat Anti-Factor Xa
< 0.35	No	Increase by 25%	4 h after next dose
0.35–0.49	No	Increase by 10%	4 h after next dose
0.5–1.0	No	No	Next day, then 1 wk later and monthly thereafter while receiving reviparin-Na treatment (at 4 h after AM dose)
1.1–1.5	No	Decrease by 20%	Before next dose
1.6–2.0	3 h	Decrease by 30%	Before next dose then 4 h after next dose
> 2.0	Until anti-factor Xa 0.5 U/mL	Decrease by 40%	Before next dose, if not < 0.5 u/mL, repeat q12h

Monagle P, Michelson A.D, Bovill E. Chest 2001; 119: 344S-370S.

Acenocumarol



- Monitorización : Tiempo de protrombina (INR)
- Efectos adversos: Hemorragia,alopecia, ¿DMO?
- Antagonista: vitamina K

Weitz JI N Engl J Med 1997; 337: 688; Holst J et al. Blood Coagul Fibrinolysis 1994; 5: 795
Monagle P, Michelson A.D, Bovill E. Chest 2001; 119: 344S-370S.

Acenocumarol

Table 6—*Protocol for Oral Anticoagulation Therapy to Maintain an INR Between 2 and 3 for Pediatric Patients

I. Day 1: if the baseline INR is 1.0 to 1.3: dose = 0.2 mg/kg orally

II. Loading days 2–4: If the INR is:

INR	Action
1.1–1.3	Repeat initial loading dose
1.4–1.9	50% of initial loading dose
2.0–3.0	50% of initial loading dose
3.1–3.5	25% of loading dose
> 3.5	Hold until INR < 3.5, then restart at 50% less than previous dose

III. Maintenance oral anticoagulation dose guidelines:

INR	Action
1.1–1.4	Increase by 20% of dose
1.5–1.9	Increase by 10% of dose
2.0–3.0	No change
3.1–3.5	Decrease by 10% of dose
> 3.5	Hold until INR < 3.5 then restart at 20% less than previous dose

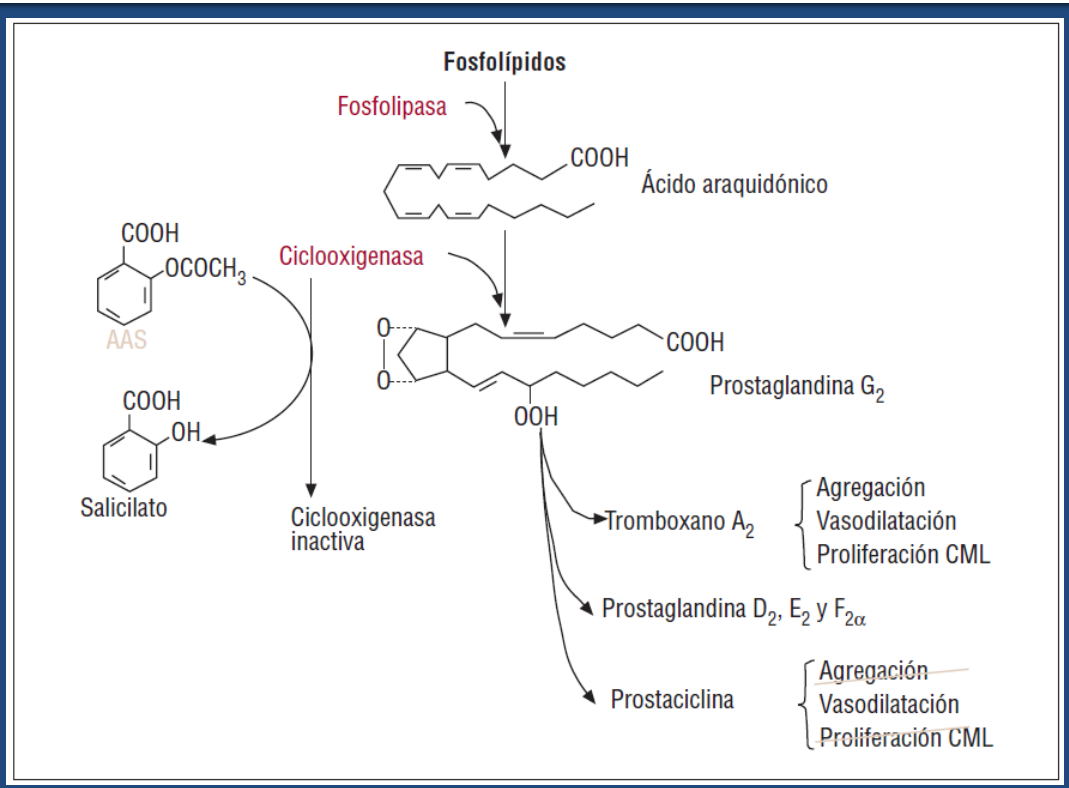
*Reproduced with permission of Michelson et al.[3]

Table 8—*Reversal of Oral Anticoagulation Therapy*

1. No bleeding
   - A. Rapid reversal of OAs is necessary, and the patient will require OAs again in the near future: give vitamin K_1, 0.5 to 2 mg subcutaneously or IV (not intramuscularly), depending on the patient's size.
   - B. Rapid reversal of OAs is necessary and the patient will not require OAs again: vitamin K_1 2–5 mg subcutaneously or IV (not intramuscularly).
2. Significant bleeding
   - A. Significant bleeding that is not life-threatening and will not cause morbidity: treat with vitamin K_1 as in 1A plus (20 mL/kg IV).
   - B. Significant bleeding that is life-threatening and will cause morbidity: treat with vitamin K_1 IV (5 mg) by slow infusion over 10–20 min because of the risk of anaphylactic shock. Consider giving prothrombin concentrate (containing factors II, VII, IX, and X) 50 U/kg IV rather than FFP (20 mL/kg IV).

Monagle P, Michelson A.D, Bovill E. Chest 2001; 119: 344S-370S.

Ácido Acetil Salicílico (AAS)



- Monitorización : No requiere
- Efectos adversos: Sd. Reye
- Antagonista: ninguno

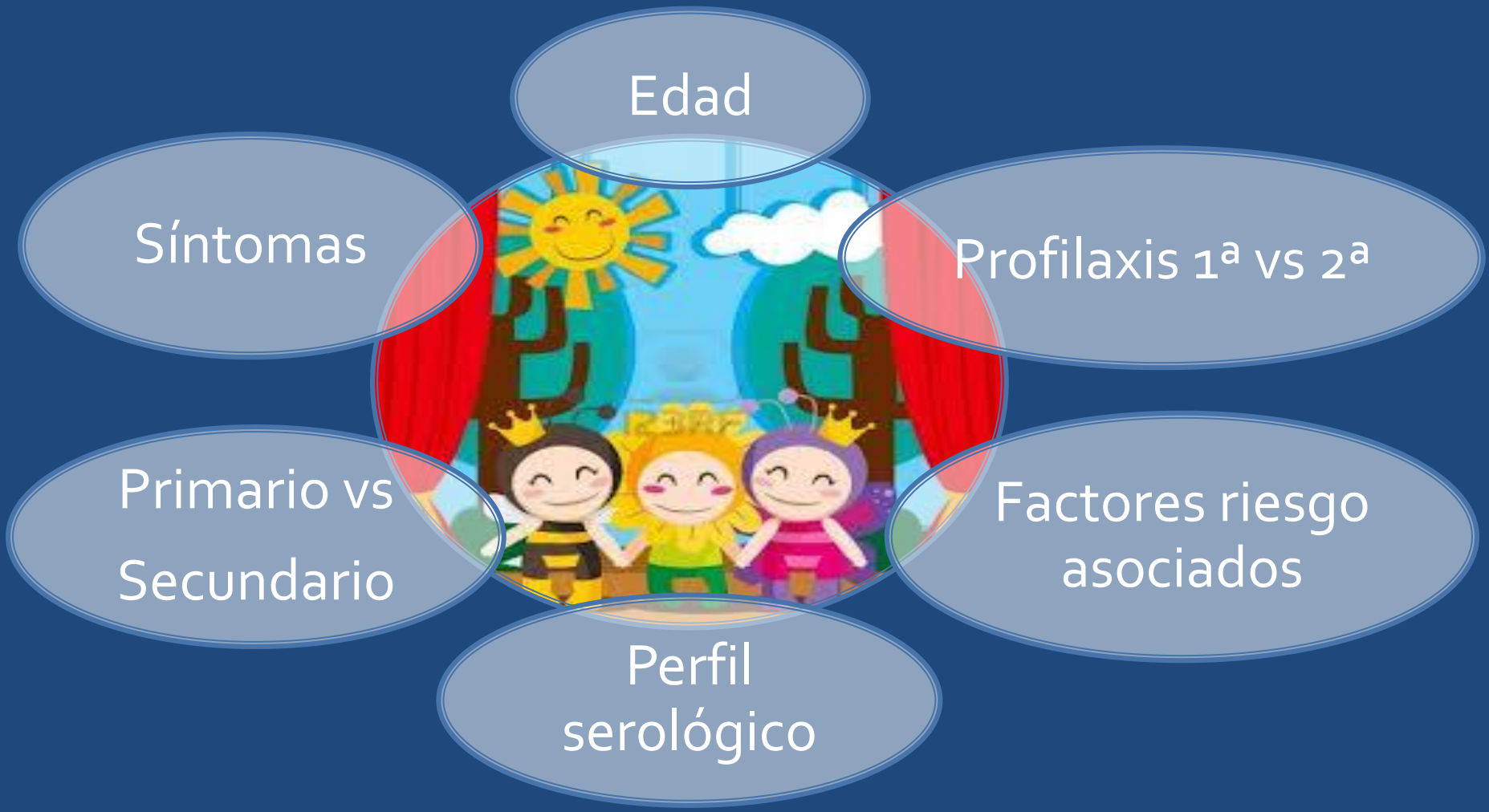
Arzamendi D et al. Mecanismo de acción de los fármacos antitrombóticos. Rev Esp Cardiol Supl. 2006;6:2H-10H
Monagle P, Michelson A.D, Bovill E. Chest 2001; 119: 344S-370S.

Terapia Antitrombótica en niños

	HNF	HBPM	Acenocumarol	AAS
Mecanismo de acción	Unión a anti trombina III	Unión anti trombina III pero sólo efecto anti Xa	↓ síntesis factores vitamina K dependientes	Inhibición irreversible de la ciclooxigenasa e inhibe formación de tromboxano A2
Monitorización	TTPA	No requiere Niveles Anti Factor Xa	Tiempo de protrombina (INR)	No precisa
Efectos Adversos	Hemorragia Osteoporosis Trombopenia	Hipoaldosteronismo	Hemorragia Alopecia ¿DMO?	Sd Reye
Antagonista	Sulfato protamina	No existe específico. Factores coagulación.	Vitamina K	

Monagle P, Michelson A.D, Bovill E. Chest 2001; 119: 344S-370S.

Tratamiento diversos escenarios



Tratamiento diversos escenarios

- Asintomático con AAF +
- Asintomático con LES y AAF +
- SAF primario:
  - Trombosis venosa: fase aguda y profilaxis 2ª
  - Trombosis arterial: fase aguda y profilaxis 2ª
- SAF asociado a LES pediátrico:
  - Trombosis venosas y arteriales: fase aguda
  - Profilaxis secundaria
- SAF catastrófico

Asintomático AAF +



Asintomático AAF +

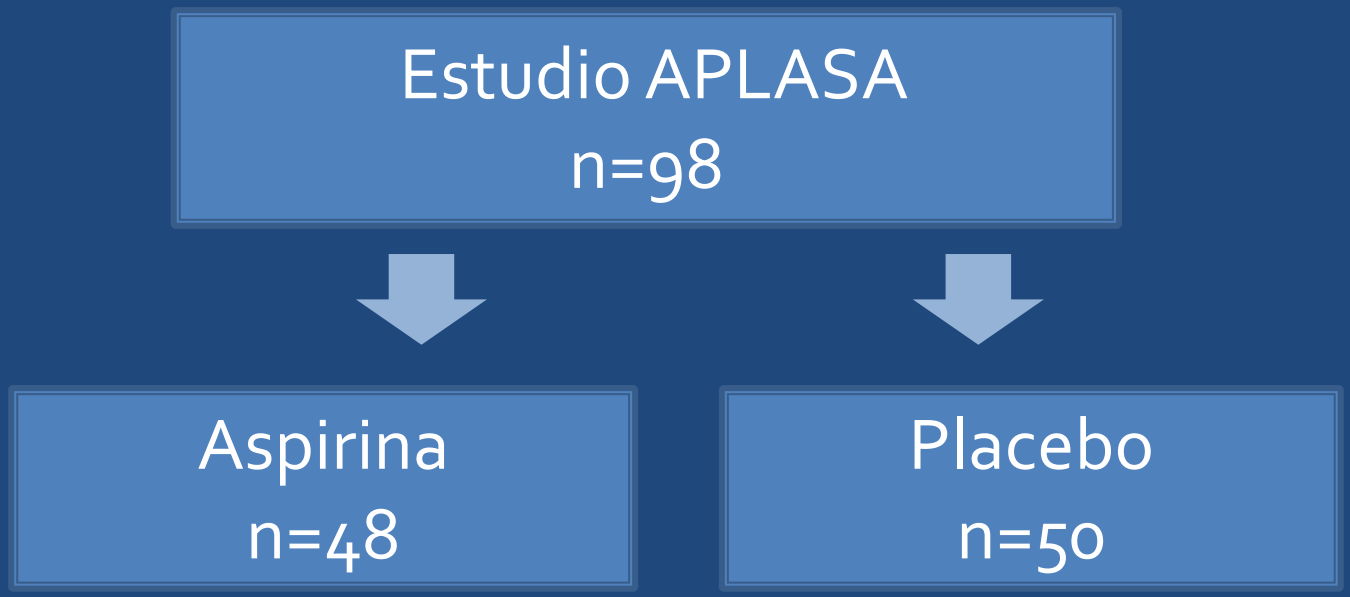
ARTHRITIS & RHEUMATISM
Vol. 56, No. 7, July 2007, pp 2382–2391
DOI 10.1002/art.22663
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Aspirin for Primary Thrombosis Prevention in the Antiphospholipid Syndrome

A Randomized, Double-Blind, Placebo-Controlled Trial in Asymptomatic Antiphospholipid Antibody–Positive Individuals

Doruk Erkan,[1] Melanie J. Harrison,[1] Roger Levy,[2] Margaret Peterson,[1] Michelle Petri,[3] Lisa Sammaritano,[1] Aynur Unalp-Arida,[4] Veronica Vilela,[2] Yusuf Yazici,[5] and Michael D. Lockshin[1]

Asintomático AAF +



Arthritis & Rheumatism. Vol. 56, No. 7, July 2007, pp 2382–2391

Asintomático AAF +

Estudio APLASA			
	AAS (n=48)	Placebo (n=50)	OR
Incidencia episodio trombótico agudo* (100 pacientes/año)	2.75	0	1.02 (0.67–1.54) p= 0.91

*Trombosis venosa profunda, trombosis vena central de la retina, ictus trombótico

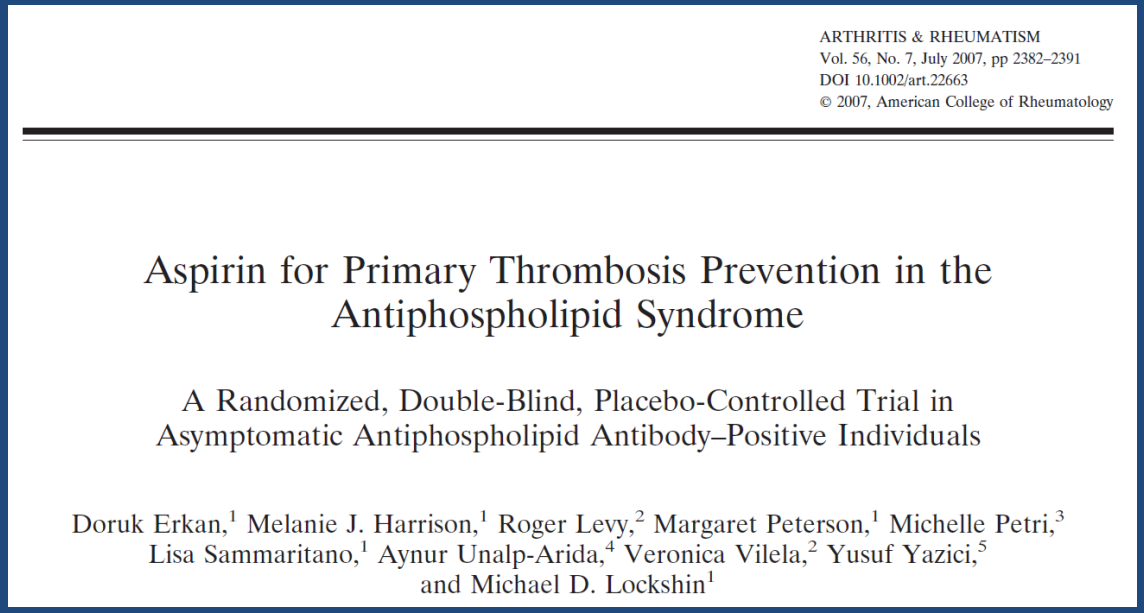
Asintomático AAF +

Estudio APLASA			
	AAS	Placebo	OR
Trombosis aguda	3*	0	1.04 (0.69–1.56) p= 0.83
AITs	2	1	1.08 (0.72–1.62) p=0.68

*2 venosos; 1 arterial

Arthritis & Rheumatism. Vol. 56, No. 7, July 2007, pp 2382–2391

Asintomático AAF +



ARTHRITIS & RHEUMATISM
Vol. 56, No. 7, July 2007, pp 2382–2391
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- La incidencia anual de trombosis en pacientes asintomáticos con AAF + de forma persistente es baja.
- Los eventos trombóticos en esta población son infrecuentes en ausencia de otros factores de riesgo para trombosis
- Estos individuos no se benefician del tratamiento con dosis bajas de AAS

Asintomático AAF +

Lupus (2011) 20, 206–218
http://lup.sagepub.com

SPECIAL ARTICLE

Evidence-based recommendations for the prevention and long-term management of thrombosis in antiphospholipid antibody-positive patients: Report of a Task Force at the 13th International Congress on Antiphospholipid Antibodies

G Ruiz-Irastorza[1], MJ Cuadrado[2], I Ruiz-Arruza[1], R Brey[3], M Crowther[4], R Derksen[5], D Erkan[6], S Krilis[7], S Machin[8], V Pengo[9], S Pierangeli[10], M Tektonidou[11] and M Khamashta[2]

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Asintomático AAF +

1. General measures for aPL carriers

1.1. A strict control of cardiovascular risk factors should be accomplished in all individuals with a high-risk aPL profile, irrespective of the presence of previous thrombosis, concomitant SLE or additional APS features. **Non-graded recommendation.**

1.2. We recommend that all aPL carriers receive thromboprophylaxis with usual doses of low molecular weight heparin in high-risk situations, such as surgery, prolonged immobilization and the puerperium. **1C recommendation.**

3. Primary thromboprophylaxis in aPL-positive individuals without SLE

3.1. In non-SLE individuals with aPL and no previous thrombosis, we suggest long-term thromboprophylaxis with low-dose aspirin in those with a high-risk aPL profile, especially in the presence of other thrombotic risk factors. **2C recommendation.**

Asintomático AAF +

- Tratamiento factores de riesgo asociados
- Opciones:
  - No tratar
  - AAS dosis bajas
- Si situación de riesgo de trombosis:
  - HBPM profiláctica

Ravelli A, Martini A. Rheum Dis Clin North Am. 2007; 33: 499-523
Alarcon-Segovia D,, Boffa M.C, Branch W. Lupus 2003, 12: 499-503.

Asintomático con LES y AAF +



Asintomático con LES y AAF +

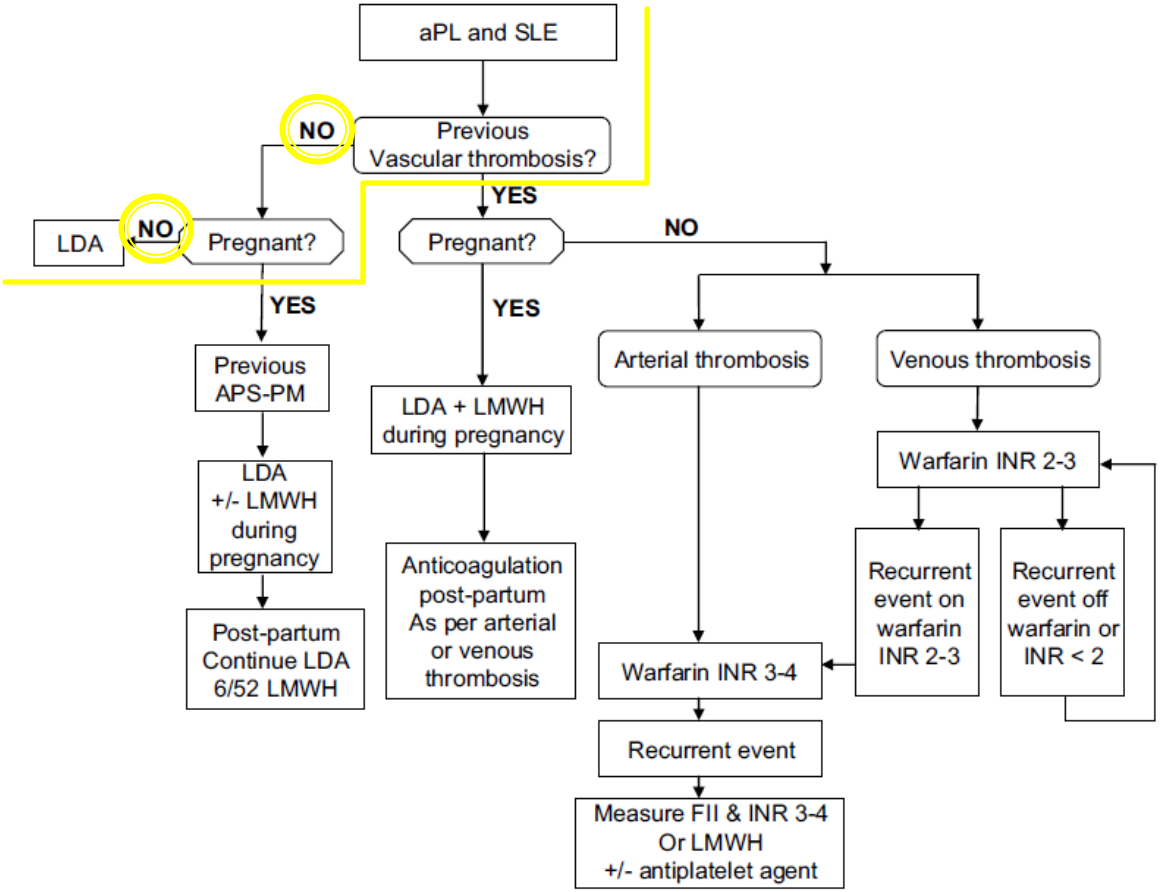


Fig. 1. An algorithm for the management of patients with systemic lupus erythematosus (SLE) and antiphospholipid antibodies (aPLs). All patients should be screened for the presence of other cardiovascular risk factors. Abbreviations: APS, antiphospholipid syndrome; FII, factor II; INR, international normalised ratio; LDA, low-dose aspirin; LMWH, low-molecular-weight heparin; PM, pregnancy morbidity.

I. Giles, A. Rahman / Best Practice & Research Clinical Rheumatology 23 (2009) 525–537

Asintomático con LES y AAF +

Lupus (2011) 20, 206–218
http://lup.sagepub.com

SPECIAL ARTICLE

Evidence-based recommendations for the prevention and long-term management of thrombosis in antiphospholipid antibody-positive patients: Report of a Task Force at the 13th International Congress on Antiphospholipid Antibodies

2. Primary thromboprophylaxis in SLE patients with aPL

2.1. Clinicians should regularly assess patients with SLE for the presence of aPL. **Non-graded recommendation.**

2.2. We recommend that patients with SLE and positive LA or isolated persistent aCL at medium–high titers receive primary thromboprophylaxis with hydroxychloroquine **(1B recommendation)** and low-dose aspirin **(2B recommendation).**

Asintomático con LES y AAF +

- Tratamiento factores de riesgo asociados
- Hidroxicloroquina
- AAS dosis bajas

Giles, A. Rahman / Best Practice & Research Clinical Rheumatology 23 (2009) 525–537
G Ruiz-Irastorza et al. Lupus (2011) 20, 206–218
Alarcon-Segovia D,, Boffa M.C, Branch W. Lupus 2003, 12: 499-503.

SAF Primario: Trombosis venosa



SAF Primario:
Trombosis venosa: fase aguda

HBPM cada 12 hs

5 días

↓

HBPM cada 12 hs +

ACO

↓

ACO

"INR 2-3"

SAF Primario:
Trombosis venosa: profilaxis 2ª

THE MANAGEMENT OF THROMBOSIS IN THE ANTIPHOSPHOLIPID-ANTIBODY SYNDROME

MUNTHER A. KHAMASHTA, M.D., MARIA JOSE CUADRADO, M.D., FEDZA MUJIC, M.D., NICK A. TAUB, M.Sc., BEVERLEY J. HUNT, M.D., AND GRAHAM R.V. HUGHES, M.D.

In this study, we found that high-intensity oral anticoagulants (producing an international normalized ratio of ≥3) with or without low-dose aspirin are an effective prophylaxis against both venous and arterial thrombosis in most of our patients with the antiphospholipid-antibody syndrome.

Khamashta MA, Cuadrado MJ, Mujic F, et al. N Engl J Med 1995; 332:993

SAF Primario:
Trombosis venosa: profilaxis 2ª

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

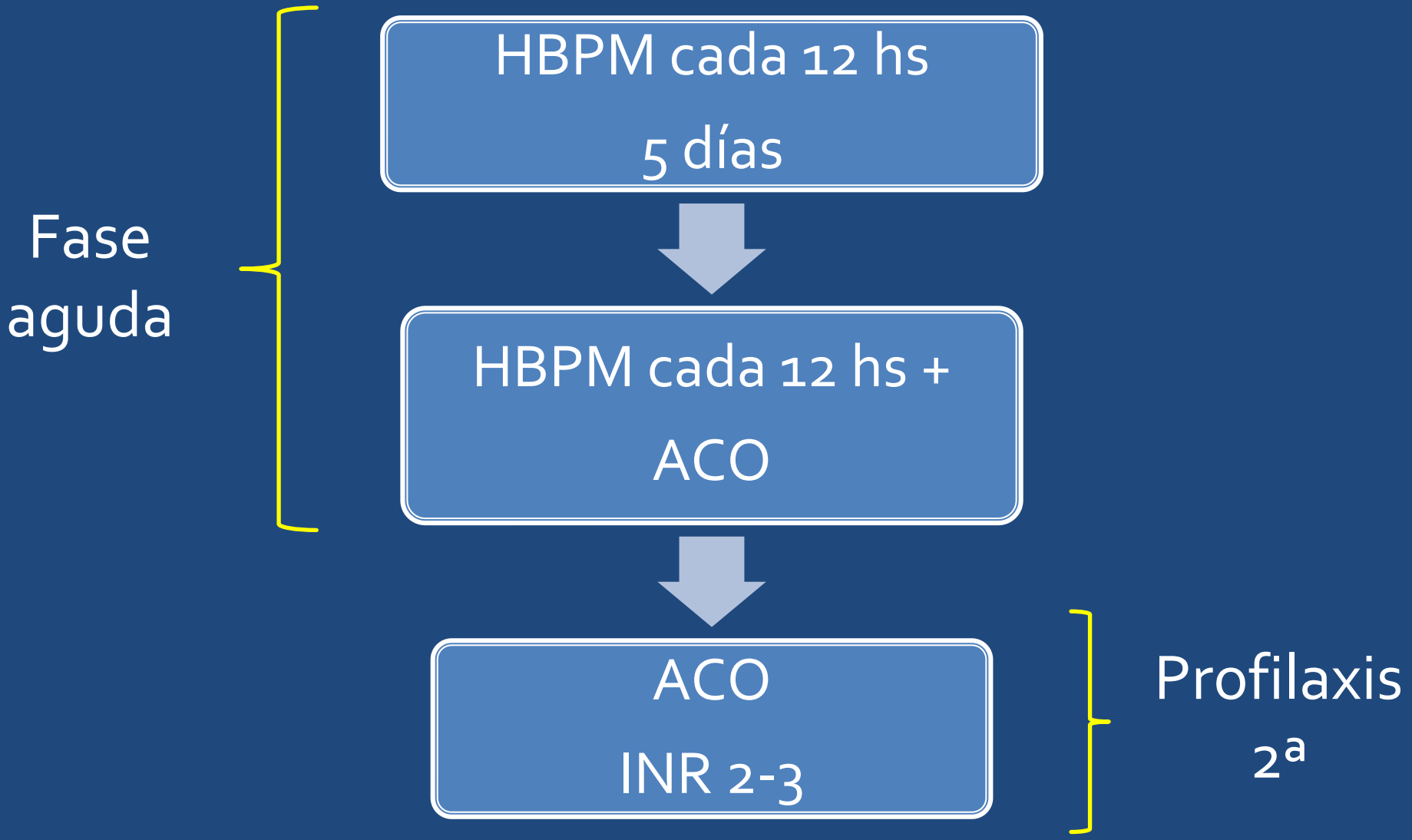
A Comparison of Two Intensities of Warfarin for the Prevention of Recurrent Thrombosis in Patients with the Antiphospholipid Antibody Syndrome

CONCLUSIONS

High-intensity warfarin was not superior to moderate-intensity warfarin for thromboprophylaxis in patients with antiphospholipid antibodies and previous thrombosis. The low rate of recurrent thrombosis among patients in whom the target INR was 2.0 to 3.0 suggests that moderate-intensity warfarin is appropriate for patients with the antiphospholipid antibody syndrome.

N Engl J Med 2003;349:1133-8.

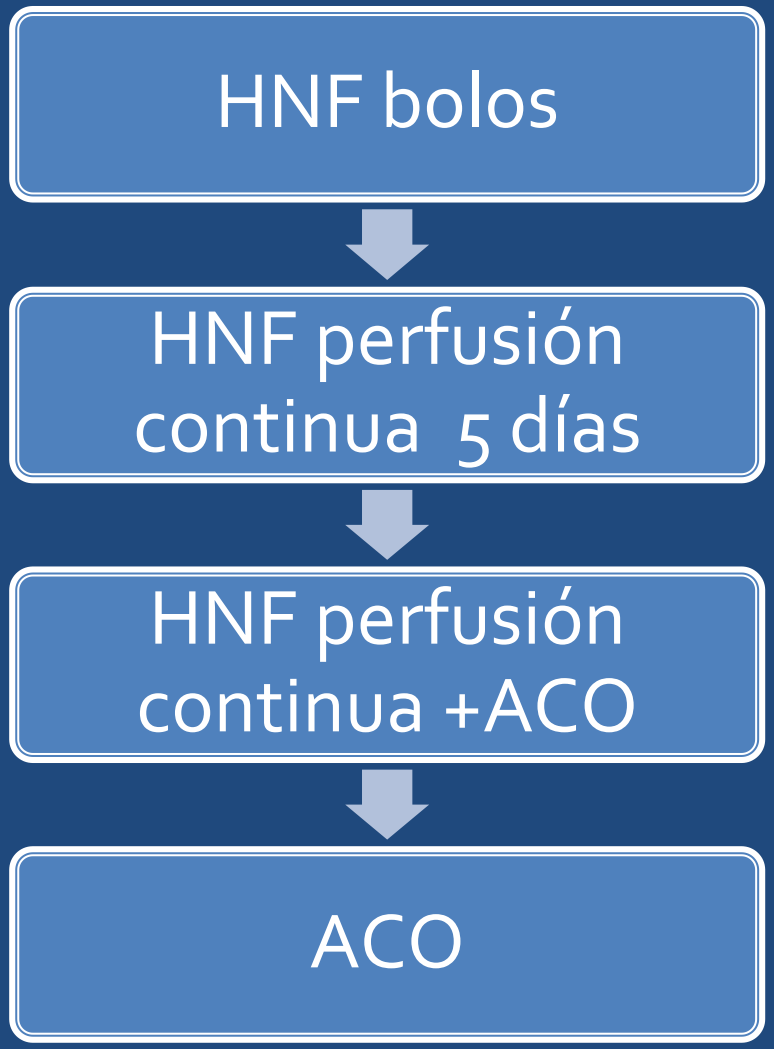
SAF Primario: Trombosis venosa



SAF Primario: Trombosis arterial



SAF Primario:
Trombosis arterial: fase aguda





Petty RE, Cassidy JT. Textbook of pediatric rheumatology. 6th ed. Pp 344-360.

SAF Primario:
Trombosis arterial: profilaxis 2ª

Lupus (2011) 20, 206–218
http://lup.sagepub.com

SPECIAL ARTICLE

Evidence-based recommendations for the prevention and long-term management of thrombosis in antiphospholipid antibody-positive patients: Report of a Task Force at the 13th International Congress on Antiphospholipid Antibodies

4.3. Patients with definite APS and arterial thrombosis should be treated with warfarin at an INR >3.0 or combined antiaggregant-anticoagulant (INR 2.0–3.0) therapy. **Non-graded recommendation due to lack of consensus.**

SAF Primario:
Trombosis arterial: profilaxis 2ª

Arthritis & Rheumatism (Arthritis Care & Research)
Vol. 57, No. 8, December 15, 2007, pp 1487–1495
DOI 10.1002/art.23109
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ORIGINAL ARTICLE

A Systematic Review of Secondary Thromboprophylaxis in Patients With Antiphospholipid Antibodies

GUILLERMO RUIZ-IRASTORZA,[1] BEVERLEY J. HUNT,[2] AND MUNTHER A. KHAMASHTA[2]

Conclusion. For patients with definite APS, we recommend prolonged warfarin therapy at a target INR of 2.0–3.0 in APS patients with first venous events and ≥3.0 for those with recurrent and/or arterial events. For patients with venous thromboembolism or stroke and a single positive aPL test, we recommend further testing to determine if they have a persisting antibody. If they do not, the same therapy as for the general population should be used (warfarin at a target INR of 2.0–3.0 and low-dose aspirin, respectively).

SAF Primario: Profilaxis Secundaria

Evento	Tratamiento
Tratamiento factores de riesgo asociados	
Trombosis venosa	ACO INR 2-3
Trombosis arterial	ACO INR >3 Ó ACO INR 2-3 + AAS
Trombosis recurrentes con ACO en rango	↑ intensidad de la ACO Añadir AAS Otros

Khamashta MA, Cuadrado MJ, Mujic F, et al. N Engl J Med 1995;332(15):993–7.
Crowther MA, Ginsberg JS, Julian J, et al. N Engl J Med 2003;349(12):1133–8.
Finazzi G, Marchioli R, Barbui T. J Thromb Haemost 2003;1(Suppl 1):OC365.
Crowther MA. J Rheumatol 2004;31(8):1474–5.

SAF Primario: Profilaxis Secundaria

Duración → No definida

SPECIAL ARTICLE

Evidence-based recommendations for the prevention and long-term management of thrombosis in antiphospholipid antibody-positive patients: Report of a Task Force at the 13th International Congress on Antiphospholipid Antibodies

5. Duration of treatment

5.1. We recommend indefinite antithrombotic therapy in patients with definite APS and thrombosis. **1C recommendation.**

5.2. In cases of first venous event, low-risk aPL profile and a known transient precipitating factor, anticoagulation could be limited to 3–6 months. **Non-graded recommendation.**

G Ruiz-Irastorza et al. Lupus (2011) 20, 206–218

SAF asociado a LES pediátrico



SAF asociado a LES pediátrico

Prevalence of antiphospholipid antibodies and frequency of thrombotic events in juvenile systemic lupus erythematosus

Authors (year)	No. of patients	aCL (%)	LA (%)	aβ2-GPI (%)	Thrombosis (%)
Shergy et al (1988) [39]	32	50	ND	ND	0
Montes de Oca et al (1991) [40]	120	ND	19	ND	9
Molta et al (1993) [41]	37	19	11	ND	8
Ravelli et al (1994) [42]	30	87	20	ND	3
Gattorno et al (1995) [43]	19	79	42	ND	16
Seaman et al (1995) [44]	29	66	62	ND	24
Berube et al (1998) [45]	59	19	24	ND	17
Gedalia et al (1998) [46]	36	37	ND	ND	8
von Scheven et al (2002) [47]	57	53	23	48	5
Campos et al (2003) [48]	57	70	29	ND	9
Levy et al (2003) [49]	149	39	16	ND	9

Abbreviations: aCL, anticardiolipin antibodies; aβ2-GPI, anti-β2-glycoprotein I antibodies; LA, lupus anticoagulant; ND, not determined.

Ravelli A, Martini A. Rheum Dis Clin North Am. 2007; 33: 499-523

SAF asociado a LES pediátrico

Trombosis venosa: fase aguda
Trombosis arterial: fase aguda



Igual que en el SAF primario

Ravelli A, Martini A. Rheum Dis Clin North Am. 2007; 33: 499-523
G Ruiz-Irastorza et al. Lupus (2011) 20, 206–218

SAF asociado a LESp: Profilaxis 2ª

Evento	Tratamiento
Tratamiento factores de riesgo asociados Hidroxicloroquina	
Trombosis venosa profunda	ACO INR 2-3
Trombosis arterial	ACO INR >3 Ó ACO INR 2-3 + AAS
Trombosis recurrentes con ACO en rango	↑ intensidad de la ACO Añadir AAS Otros

Ravelli A, Martini A. Rheum Dis Clin North Am. 2007; 33: 499-523
G Ruiz-Irastorza et al. Lupus (2011) 20, 206–218

Registro de SAF pediátrico: PED APS Registry



Euro-Phospholipid on Line

Official Web-site of the "European Forum on Antiphospholipid Antibodies"

MULTICENTRE STUDIES

REGISTER FOR PEDIATRIC PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME (EUROPEAN PROJECT EXTENDED INTERNATIONALLY)

COORDINATORS

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Ricard Cervera, Department of Autoimmune Diseases, Hospital Clínic, Barcelona, Spain
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on behalf of the European Forum on Antiphospholipid Antibodies and Lupus Working Group of Paediatric Rheumatology European Society (PRES)

Registro de SAF pediátrico: PED APS Registry

Pediatric Antiphospholipid Syndrome: Clinical and Immunologic Features of 121 Patients in an International Registry

Tadej Avčin, MD, PhD[a], Rolando Cimaz, MD[b], Earl D. Silverman, MD, FRCPC[c], Ricard Cervera, MD, PhD, FRCP[d], Marco Gattorno, MD[e,f], Stella Garay, MD[g], Yackov Berkun, MD[h,i], Flavio R. Sztajnbok, MD[j,k], Clovis A. Silva, MD, PhD[l], Lucia M. Campos, MD, PhD[l], Claudia Saad-Magalhaes, MD, PhD[m], Donato Rigante, MD[n], Angelo Ravelli, MD[e,f], Alberto Martini, MD[e,f], Blaž Rozman, MD, PhD[o], Pier Luigi Meroni, MD, PhD[p,q]

TABLE 1 General Characteristics of Patients With Pediatric APS

	No. (%) of Patients
Study cohort	121 (100.0)
Primary APS	60 (49.5)
APS associated with autoimmune disease	60 (49.5)
SLE	46 (38.0)
Lupus-like disease	4 (3.0)
Autoimmune thyroiditis	4 (3.0)
Rheumatic fever	2 (2.0)
Immune thrombocytopenic purpura	1 (1.0)
Hemolytic-uremic syndrome	1 (1.0)
Pauci-immune glomerulonephritis	1 (1.0)
Behçet disease	1 (1.0)
APS associated with malignant disease	1 (1.0)

Pediatrics 2008;122:e1100–e1107

Registro de SAF pediátrico: PED APS Registry

Treatment and Outcome

Patients were treated according to each physician's clinical judgment. All patients with venous thrombosis received long-term anticoagulation therapy. In contrast, patients with arterial thrombosis received (1) no treatment (25%), (2) antiaggregation therapy (low-dose aspirin, 3–5 mg/kg per day) (35%), or (3) anticoagulation therapy with or without concomitant antiaggregation therapy (40%). Mean follow-up time from the time of APS diagnosis and the date of inclusion into the Ped-APS Registry was 6.1 years (range: 0.7–24.7 years). Overall, 23 (19%) of 121 patients developed further APS-related thrombosis after the initial thrombotic event. Among 9 of 29 patients who were tested for inherited prothrombotic disorders and had no identifiable inherited or acquired prothrombotic risk factor other than positive aPLs, 3 (33%) of 9 patients developed recurrent thrombotic events.

	Ninguno	AAS(%)	Anticoagulación (%)
Trombosis venosa			100
Trombosis arterial	25	35	40

Pediatrics 2008;122:e1100–e1107

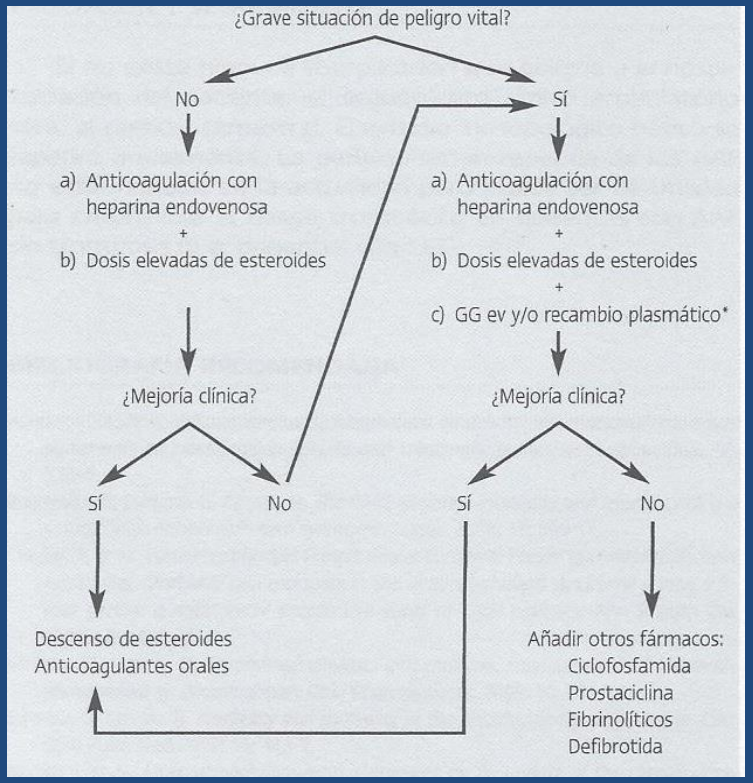
SAF catastrófico



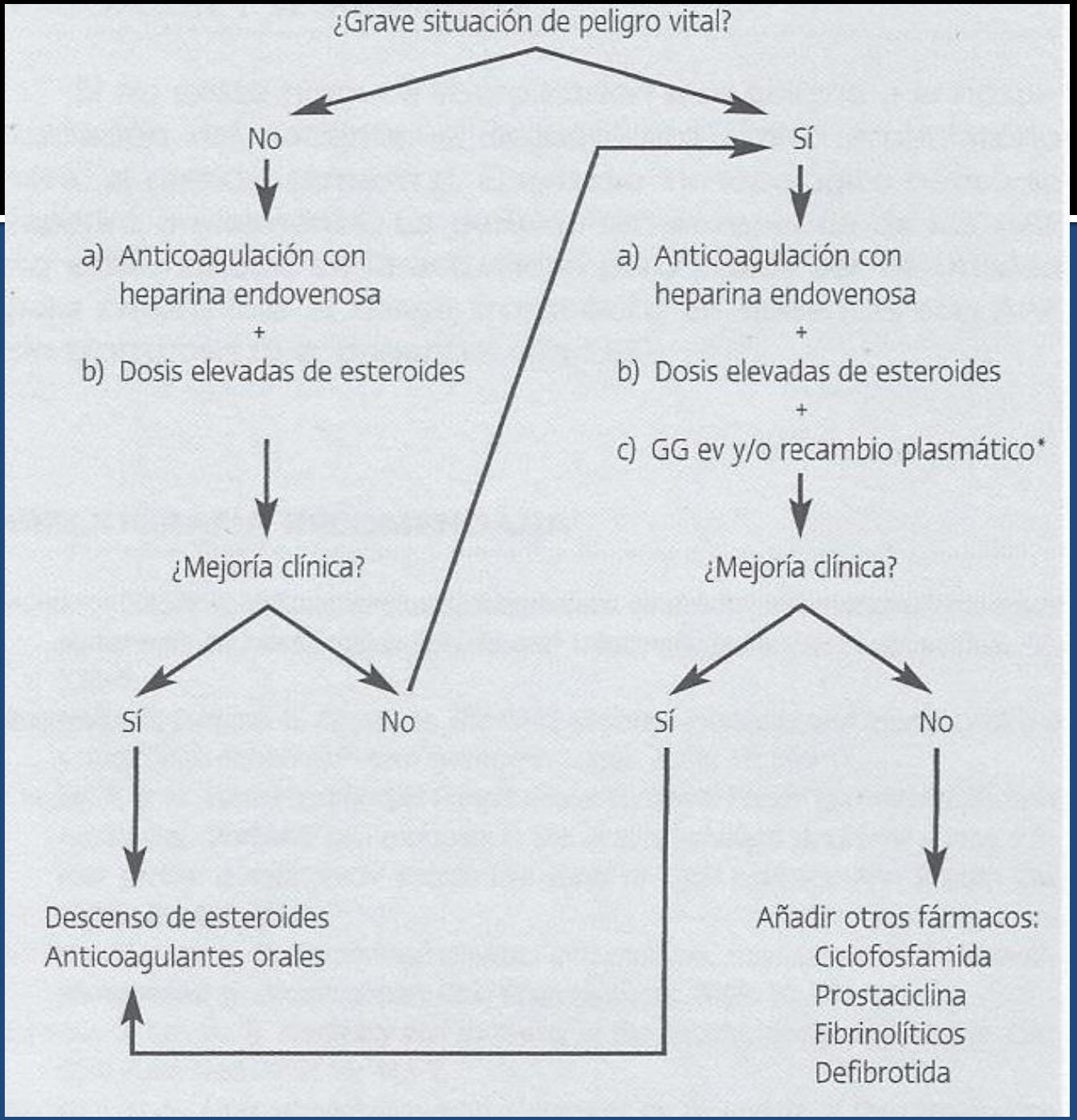
SAF catastrófico

- Tratamiento de soporte
- Eliminar factor desencadenante








¿Grave situación de peligro vital?
No
Sí
a) Anticoagulación con heparina endovenosa
+
b) Dosis elevadas de esteroides
a) Anticoagulación con heparina endovenosa
+
b) Dosis elevadas de esteroides
+
c) GG ev y/o recambio plasmático*
¿Mejoría clínica?
¿Mejoría clínica?
Sí
No
Sí
No
Descenso de esteroides
Anticoagulantes orales
Añadir otros fármacos:
Ciclofosfamida
Prostaciclina
Fibrinolíticos
Defibrotida

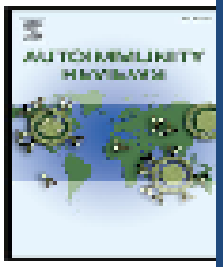
SAF catastrófico

Autoimmunity Reviews xxx (2013) xxx–xxx

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Review

Pediatric catastrophic antiphospholipid syndrome: Descriptive analysis of 45 patients from the "CAPS Registry"

Horacio Berman [a,1], Ignasi Rodríguez-Pintó [a,1], Ricard Cervera [a], Simone Gregory [b], Ernesto de Meis [b], Carlos Ewerton Maia Rodrigues [c], Nádia Emi Aikawa [c,d], Jozélio Freire de Carvalho [c], Janusz Springer [e], Maciej Niedzwiecki [e], Gerard Espinosa [a,*], on behalf of the Catastrophic Registry Project Group (European Forum on Antiphospholipid Antibodies) [2]

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SAF catastrófico: registro CAPS

Características demográficas	N (%)
Sexo (mujeres/varones)	32/13 (71/29)
Edad en el momento del diagnóstico (años)	11.5 +/- 4.6

Diagnóstico	N (%)
SAF primario	32 (69.6)
LES	13 (28.3)
Lupus Like	1 (2.2)
SAF catastrófico 1ª manifestación LES	39 (86.7)

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SAF catastrófico: registro CAPS

Manifestaciones Clínicas	N (%)
Afectación renal	29 (63)
Afectación pulmonar	29 (63)
Afectación cardiaca	27 (58.7)
Trombosis vasos periféricos	24 (52.2)
Fallo renal	22 (47.8)
Afectación cerebral	22 (47.8)
Afectación hepática	19 (41.3)
Trombosis venosa	19 (41.3)
Fallo cardiaco	18 (39.1)
Afectación cutánea	17 (37)
Síndrome distrés respiratorio agudo	13 (28.3)
Trombosis arterial	11 (23.9)

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SAF catastrófico: registro CAPS

Comparación entre población pediátrica y adulta: Características demográficas y clínicas			
	Casos infantiles	Casos adultos	p
Sexo (mujeres/varones)	32/13 (71/29)	267/121 (69/31)	0.752
SAF primario	31/46 (67.4)	232/400 (59.7)	0.220
LES	13/46 (28.3)	119/400 (29.8)	0.834
SAF catastrófico 1ª manifestación LES	38/46 (86.6)	181/400 (45.2)	<0.001

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SAF catastrófico: registro CAPS

Comparación entre población pediátrica y adulta: Factores Precipitantes			
	Casos infantiles	Casos adultos	p
Infección	28/46 (60.9)	105/392 (26.8)	< 0.001
Neoplasia	8/46 (17.4)	41/392 (10.5)	0.158
Anticonceptivos orales	1/46 (2.2)	30/392 (7.7)	0.231
Cirugía	3/46 (6.5)	45/391 (11.5)	0.306
Fármacos	0/46 (0)	19/392 (4.8)	0.243
Brote LES	2/46 (4.3)	7/392 (1.8)	0.247

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SAF catastrófico: registro CAPS

Comparación entre población pediátrica y adulta: Manifestaciones Clínicas			
	Casos infantiles	Casos adultos	p
Afectación renal	29/46 (63.0)	296/399 (74.2)	0.107
Afectación pulmonar	29/46 (63.0)	233/399 (58.4)	0.544
Afectación cardiaca	27/46 (57.4)	193/397 (48.6)	0.252
Trombosis vasos periféricos	24/46 (52.2)	136/396 (34.3)	0.017
Afectación cerebral	22/46 (47.8)	226/398 (56.8)	0.247
Afectación hepática	19/46 (40.4)	144/399 (36.1)	0.559

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SAF catastrófico: registro CAPS

Comparación entre población pediátrica y adulta: Tratamiento y Pronóstico			
	Casos infantiles	Casos adultos	p
Anticoagulantes	35/45 (77.8)	327/386 (84.7)	0.230
Corticoides	34/45 (75.6)	297/387 (76.7)	0.669
Plasmaféresis	18/45 (40.0)	133/387 (34.4)	0.522
Inmunoglobulinas IV	17/45 (37.8)	98/387 (25.3)	0.091
Ciclofosfamida	11/45 (24.4)	98/387 (25.3)	0.835
ACO+CE+ PF ó IG	12/45 (26.7)	81/386 (21.0)	0.426
Mortalidad	12/46 (26.1)	160/398 (40.2)	0.063

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SAF catastrófico: registro CAPS

Tratamientos utilizados en los episodios de SAF catastrófico	
	N(%) episodios tratados
Anticoagulantes	35/43 (81.4)
Corticoides	34/43 (79.1)
Ciclofosfamida	11/43 (25.6)
Plasmaféresis	18/43 (41.9)
Inmunoglobulinas IV	17/43 (39.5)
Antiagregantes	3/43 (7.0)

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SAF catastrófico: registro CAPS

- Existen diferencias mínimas entre ambas poblaciones:
  - Manifestaciones clínicas
  - Hallazgos de laboratorio
  - Tratamiento

Berman H, et al, Pediatric catastrophic antiphospholipid syndrome: Descriptive analysis of 45 patients from the "CAPS Registry", Autoimmun Rev (2013)

Conclusiones

- **Presente:**
  - Pocos datos
  - Extrapolamos de la población adulta
    - No olvidar particularidades de la población pediátrica

Conclusiones

- **Asintomáticos:** pocas dudas

- **SAF primarios y secundarios:**
  - Fase aguda: pocas dudas
  - Profilaxis secundarias: dudas en intensidad/duración

- **SAF catastrófico:**
  - Registro CAPS: 1er estudio SAF catastrófico pediátrico

Conclusiones

- **Futuro:**
  - Criterios validados para población pediátrica
  - Estudios:
    - Población sin factores de riesgo CV clásicos: gran valor
    - Registros, EC multicéntricos
  - Nuevas terapias anticoagulantes/antiagregantes


MUCHAS GRACIAS
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clinicaltrials.gov/ct2/show/NCT00616317?term=treatment+antiphospholipid+syndrome+in+children&rank=2
ClinicalTrials.gov
A service of the U.S. National Institutes of Health
Example: "Heart attack" AND "Los Angeles"
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Trial record 2 of 4 for: treatment antiphospholipid syndrome in children
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This study is currently recruiting participants.
Verified November 2012 by University of California, Davis
Sponsor:
University of California, Davis
Collaborator:
The Slovenian Ministry of Higher Education, Science and Technology
Information provided by (Responsible Party):
Lavjay Butani, MD, University of California, Davis
ClinicalTrials.gov Identifier:
NCT00616317
First received: February 4, 2008
Last updated: November 30, 2012
Last verified: November 2012
History of Changes

Lupus. 2009 Sep;18(10):894-9. doi: 10.1177/0961203309106917.

The Ped-APS Registry: the antiphospholipid syndrome in childhood.

Avcin T, Cimaz R, Rozman B; Ped-APS Registry Collaborative Group.

Collaborators (33)

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Abstract

In recent years, antiphospholipid syndrome (APS) has been increasingly recognised in various paediatric autoimmune and nonautoimmune diseases, but the relatively low prevalence and heterogeneity of APS in childhood made it very difficult to study in a systematic way. The project of an international registry of paediatric patients with APS (the Ped-APS Registry) was initiated in 2004 to foster and conduct multicentre, controlled studies with large number of paediatric APS patients. The Ped-APS Registry is organised as a collaborative project of the European Forum on Antiphospholipid Antibodies and Juvenile Systemic Lupus Erythematosus Working Group of the Paediatric Rheumatology European Society. Currently, it documents a standardised clinical, laboratory and therapeutic data of 133 children with antiphospholipid antibodies (aPL)-related thrombosis from 14 countries. The priority projects for future research of the Ped-APS Registry include prospective enrollment of new patients with aPL-related thrombosis, assessment of differences between the paediatric and adult APS, evaluation of proinflammatory genotype as a risk factor for APS manifestations in childhood and evaluation of patients with isolated nonthrombotic aPL-related manifestations.