

18:55-19:10 h.

Experiencia de una unidad de gestación y enfermedades autoinmunes

Dr. Luis Sáez Comet

Unidad de Enfermedades Autoinmunes Sistémicas Servicio de Medicina Interna

Hospital Universitario Miguel Servet. Zaragoza



CONFLICTOS DE INTERÉS

Speaking fees from GlaxoSmithKline

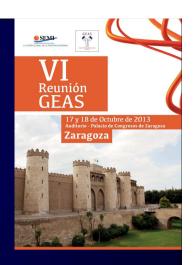
Capilaroscopy courses for Acthelion

Sent cases to BIOGEAS, RESCLE, RELES,

REVAS, REGAS

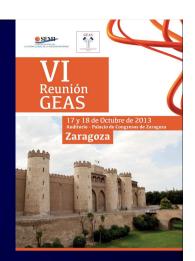
Participating in anti-TWEAK trial

Participated in DUO registry



UNIDAD DE GESTACIÓN Y EAS (SEGUIMIENTO GESTANTES EN UEAS)

- Gestación del protocolo
- Protocolo asistencial
- Resultados
- Asistenciales
- Docentes
- Investigación
- Casos clínicos
- Temas no resueltos



PROTOCOLO CONSULTA AUTOINMUNES Y EMBARAZO HOSPITAL DE CRUCES

| SEMANA | 8 | 12 | 16 | 20 | 24 | 28 | 30 | 32 | 33 | 34 | 35 | 36 | 37 | 38 | 39 | 40 | COMENTARIOS |
|-------------------|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|---------------------------|
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| DNA, C3, C4 | | | | | | | | | | | | | | | | | LES |
| Eco | | | | | | | | | | | | | | | | | TODAS |
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| Doppler Uterhas | | | | | | | | | | | | | | | | | TODA5 |
| Ecocardio firtal | | | | | | | | | | | | | | | | | RoyJoLa+ |
| CTG | | | | | | | | | | | | | | | | | TODAS |



2007: contactos con:

- •UEAS Cruces
- •Ginecología HUMS: JS, UAR, ecos...
- Coagulación
- Enfermería



nexo Solicitud de inclusión en el Programa de Apoyo a las finicia tivas del Mejora de la Calidad en el Servicio Aragon és de Salud (2009)

PROYECTO DE MEJORA DE LA CALIDAD

1.- TITULO

SEGUIMIENTO CONJUNTO DE EMBARAZOS DE ALTO RIESGO POR SOSPECHA DE SINDROME ANTIFOSFOLIPIDO O ENFERMEDADES AUTOINMUNES ASOCIADAS

2.- RESPONSABLE DEL PROYECTO

Nombre y apellidos

Luis Sáez Comet

Profesión

Facultativo Especialista de Área de Medicina Interna

Lugar de trabajo

Unidad de Enfermedades Autoinmunes Sistémicas, Servicio de Medicina Interna Hospital Universitario Miguel Servet de Zaragoza

Sector de SALUD:

Zaragoza II

En el caso de hospital, centro socio sanitario, centro rehabilitación psicosocial o similar. Indicar el servicio o unidad.

Correo electrónico:

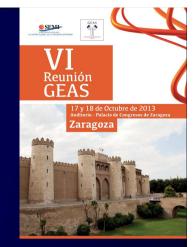
<u>||saezcomet@gmail.com;||saezc@salud.aragon.es;</u>

Teléfono y extensión del centro de trabajo:

976765500 ext 2799

3.- OTROS COMPONENTES DEL EQUIPO DE MEJORA

| Nombre y apellidos | Profesión | Centro de trabajo |
|------------------------------|--------------|---------------------------|
| 1 José Velilla Marco | Jefe Sección | Hosp. Univ. Miguel Servet |
| 2 José Manuel Campillos Maza | Jefe Sección | Hosp. Univ. Miguel Servet |
| 3 Pilar Andrés | FEA | Hosp. Univ. Miguel Servet |
| 4 Isabel Lahoz Pascual | FEA | Hosp. Univ. Miguel Servet |
| 5 María Lapresta | FEA | Hosp. Univ. Miguel Servet |
| 6 Alberto Pérez Falo | Jefe Sección | Hosp, Univ. Miguel Servet |



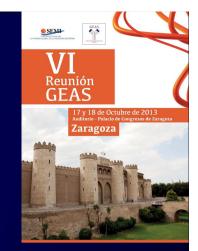
"Puertas abiertas" Sesiones mensuales Teléfono directo

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| revias: nº/éxito:/ | □HTA □DM |
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| érdidas fetales (>=10sem): nº sems: | Tabaco, cantidad cig/d |
| | Alcohol, cantidad u/d |
| rematuridad n ^a sems: N bajo peso n ^a sems: | □ Drogas, cantidad u/d |
| clampsia/preeclampsia | □TROMBOSIS: Fecha: Localización: |
| lloques cardíaco congénito/ Lupus neonatal (si R | 0+) |
| ENFERMEDADES AUTOINMUNES: | ESTUDIO DE AUTOINMUNIDAD: |
| LUPUS ERITEMATOSO SISTÉMICO | □ANA □RO |
| SÍNDROME ANTIFOSFOLÍPIDO | Dr-DNA DIA |
| ANTICUERPOS ANTIFOSFOLÍPIDO+ CONECTIVOPATÍA INDIFERENCIADA | DIGG ACL DSM DIGM ACL DRNP |
| SINDROME DE SJÖGREN | IGG AB2-GP1 ID01 |
| DESCLERODERMIA | ☐ IGM AB2-GP1 ☐ SCL-70 |
| ENFERMEDAD MIXTA DEL TEJIDO CONECTIVO | ■ ANTICOAGULANTE LÚPICO |
| OTRAS: | |
| Clínica fundamental: | |
| | MUTACIONES/TROMBOFILIA: |
| SESTACIÓN DE ALTO RIESGO EN PACIENTES LES: | |
| HI obstétrica previa desfavorable | C677T MTHFR heterocigato homocigota |
| □H4 obstétrica previa desfavorable □Nefritis lúpica | C677T MTHFR heterocigato homocigoto G7010A protrombina heterocigato homocigoto G7010A protrombina heterocigato homocigoto G7010A |
| Di∓P obstérica previa desfavorable Di∧efritis lúpica Direstficiencia renal + | C677T MTHFR heterocigato homocigoto G2010A protrombina heterocigato homocigoto R586Q (FV Leiden) heterocigato homocigoto D |
| Hª obstétrica previa desfavorable Nefritis lúpica Unesticiencia renal + Unsuficiencia cardísca, hipertensión pulmonar | C677T MTHFR heterocigato homocigoto G7010A protrombina heterocigato homocigoto G7010A protrombina heterocigato homocigoto G7010A |
| BH obstérnca previa desfavorable Profities Lúpica | C677T MTHFR heterocigato homocigato SCIOLA protrombina heterocigato homocigato Caras: homocigato homocigato Caras: |
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| cestación de ALTO REISGO EN PACIENTES LES: BH obstérez preva desfavorable Nedrits lúpica Insuficiencia renal + Insuficiencia cardisca, hipertensión pulmonar Enfermedad increstical pulmonar Enfermedad activa Alte grado de daño orgánico irreversible Alta dasse de corticnides AAF 4, SAF AR, LS Gestación múltiple Edad >40 | C67T MTHFR heterocigate homologote (2010) A protrombina heterocique homologote homologote (2010) A protrombina heterocique (2010) A protrombina heterocique (2010) A protrombina (2010) A prot |
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UMDAD DE ENFERMEDADES AUTOINMUNES SISTÉMICAS SERVICIO DE MEDICINA INTERNA HOSPITAL UMIVESSITARIO MOJUEL SERVET ZARAGICZA Tel STETOSOCIO EL TEL STETOSOCIO EL TEL

| Nº VISITA | CLINICA | EXPLORACION | RESPONSABLE | |
|--|--|---|--------------------------------|--|
| FECHA: Repasar antecedentes obstétricos 1ª visita Repasar antecedentes obstétricos Repasar antecedentes ob | | TA _/_mm Hg Proteinuna: g/□ I, □24h Edemas: SI □ NO □ | Consulta Médica | |
| 7 | Otros ttos (retirar teratógenos) | Y | | |
| FECHA: | Confirmar gestación Valorar tto con HBPM u otros ttos Clínica: | TA_/_mm Hg Proteinuria: g/□ I. □24h Edemas: Si □ NO □ | Consulta Médica | |
| FECHA: 34 visita (aprox 84 sem) | Clinica: | TA _/_ mm Hg Proteinuria: g/□ I. □24h Edemas: Si □ NO □ | Consulta Enfermeria | |
| FECHA: 4* visita (aprox 12* sem) | Clinica: | TA mm Hg Proteinuria: g/□ I. □24h Edemas: Si □ NO □ | Consulta Enfermeria | |
| FECHA: 5ª visita (aprox 16ª sem) | Clinics: | TA _/_ mm Hg Proteinuria: g/ 1. | Consulta Enfermeria | |
| FECHA: 6* visita (aprox 20* sem) | Clinica: Doppler arterias Uterinas: Ecocardio fetal: | TA mm Hg Proteinuria g/□ L □24h Edemas: Si □ No □ | Consulta Médica | |
| FECHA: 7ª visita (aprox 24ª sem) | Clinica: | TA_/_ mm Hg Proteinuria: g/ □ L □24h Edemas: Si □ NO □ | Consulta Enfermería | |
| FECHA: 8ª visita (aprox 30ª sem) | Clinica: Ecocardio fetal: | TA _/_ mm Hg Proteinuria: g/□ I. □24h Edemas: SÍ □ NO □ | Consulta Enfermeria | |
| FECHA: Clinica: 9ª visita (aprox 34ª sem) | | TA_/_mm Hg Proteinuria: g/□ I. □24h Edemas: Si □ NO □ | Consulta Enfermeria | |
| FECHA: Clinica: 104 visita Planificar fin de embarazo (aprox 384 Tratemiento postparto: sem) | | TA_/_mm Hg Proteinuria: g/□ L □24h Edemas: SÎ □ NO □ | Consulta Médica | |
| FECHA: Chinca: sem Parto Edad gestacional: sem Peso al nacer: log Complicaciones parto: Lacanaca natural prevista: si 📗 No 📗 | | Edad gestational: Pedo al nacer: | Consulta Médica/ Enfermeria | |
| FECHA: 12ª visita 3-4m Postparto | Clinica: | TA _/_ mm Hg Proteinuria: g/O I. D24h Edemas: SI O NO O | Consulta Médica | |





UNIDAD DE ENFERMEDADES AUTOINMUNES SISTÉNICAS SERVICIO DE MEDICINA INTERNA HOSPITAL UNIVERSITARIO MIQUEL SERVET ZARAGOZA



LIFAS

UMDAD DE ENFERMEDADES AUTOIMMUNES SISTÉMICAS SENVICIO DE MEDICINA INTERNA HOSPITAL UNIVERSITARIO MIQUEL SERVET ZARAGOZA TAI SESSOS EN 2788

| PROTOCOLO | EMBARAZO + | ENFERMEDAD | AUTOINMUNE | SISTÉM |
|-----------|------------|-------------------|------------|--------|
| | | | | |

| NOMBRE: | APELLIDOS: | NHC: us | EDAD: | |
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| ■ si | NOROME ANTIFOS | FOLIPIDO | | E |
| | GESTACIÓN DE ALTO R | IESGO EN PACI | ENTES LES: | I MUTACIONE |
| | Hª obstétrica previa o | desfavorable | 170-1-170-1-180 : | C677T MTHI |
| | Nefritis lúpica | | | G2016A prot |
| | ☐ Insuficiencia renal + ☐ Insuficiencia cardiaca | hipertensión o | inletonar. | R506Q (FV t |
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| | Prematurid | | 300 | |
| | RN bajo pe | | Пнта П р | and the second |
| | | | | neonatal (si Ro+ |
| | Otros: | relace conge | into Lupus | iconatai (si Ruh |
| | | S:Inicio sema | | Localización: |
| | - Table - Constitution (Constitution) | | iA: Inicio sems | The second secon |
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| | Clinica brote: | | | 3436 |

| Nº VISITA | CLINICA | EXPLORACION | RESPONSABLE |
|---|--|---|--------------------|
| FECHA: | Repasar antecedentes obstétricos Repasar clínica sistémica | TA/_ mm Hg Proteinuria:g/□ 1, □24h | Consults Médica |
| Preconcepcional | Valorar tto preconcepcional con AAS Otros ttos (retirar teratógenas) | Edemas: SÍ 🗆 NO 🗆 | Piedice |
| FECHA: | Confirmar gestación | 7A/_ mm Hg | Consulta |
| 24 visite (aprox. 44 sem) | Valorar tto con HBPM u otros ttos Clinica: | Proteinura: g/ ☐ I. ☐24h Edemas: SI ☐ NO ☐ | Médica |
| FECHA: | Clinica: | TA/_ mm Hg | Consulta |
| 3ª visita (aprox 8ª sem) | S70.585 | Proteinura: g/ 1. 24h Edemas: SI 0 NO 0 | Enfermeria |
| FECHA: | Clinica: | TA/_ mm Hg | Consulta |
| 4ª visita (aprox 12ª sem) | | Proteinuria g/ 1. 24h Edemas: SI NO D | Enfermeria |
| FECHA: | Clinica: | TA/_ mm Hg | Consulta |
| 5ª visita (aprox 16ª sem) | Ecocardio fetal: | Proteinuna: g/□ 1, □24h Edemas: SÍ □ NO □ | Enfermeria |
| FECHA: | Clinica: | TA_J_ mm Hg | Consults |
| 6ª visita (aprox 20ª sem) | Doppler arterias Uterinas: Ecocardio fetal: | Proteinuna g/ 0 1. 024h Edemas: SI 0 NO 0 | Médice |
| FECHA: | Clínica: | TA/_ mm Hg | Consulta |
| 7ª visita (aprox 24ª sem) | Ecocardio fetal: | Proteinura: g/ 1. 24h Edemas: SI NO 0 | Enfermeria |
| FECHA: | Clinica: | TA/_ mm Hg | Consulta |
| 8º visita (aprox 30º sem) | Ecocardio fetal: | Proteinuria g/ 1. | Enfermeria |
| FECHA: | Clinica: | TA/_ mm Hg | Consulta |
| 9ª visita (aprox 34ª sem) | | Proteinuria: g/ 0 L 024h Edemas: St 0 NO 0 | Enfermeria |
| FECHA: | Clinica: | TA_/_ mm Hg | Consulta |
| 10 ^a visita (aprox 38 ^a sem.) | Planificar fin de embarazo Tratamiento postparto: | Proteinuria: g/ ☐ I. ☐ 24h Edemas: SÍ ☐ NO ☐ | Médica |
| FECHA: | Clinica: | Edad gestacional: | Consulta |
| 11º visita Parto | Edad gestadonal: sem Peso al nacer: kg Sexo (Complicaciones parto: | Peso al nacer: | Médica/ Enfermeria |
| | Lactancia natural prevista: Si O NO O | | |
| FECHA: | Clinica: | TA_/_ mm Hg | Consulta |
| 12ª visita 3-4m Postparto | 000000 | Proteinuria: g/□ L □24h | Médica |

Mujer edad fértil con EAS

Hª gral

Hª autoinmune

Hª obstétrica/infertilidad

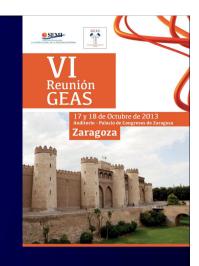
Ttos previos

Deseo gestación (→ + AAS si APA+) → momento gestación

Test embarazo + → UAR, analítica + confirmación test

Valoración tto y sgto según:

- •Subgrupo (UCTD, SLE, APA+, UCTD APA+, SLE APA+, PAPS)
- Ants obstétricos/trombóticos
- •Infertilidad/IA/FIVs previas
- Edad
- •Ro+, La+
- Deseo madre



HCQ? PRED?

INMN-?

AAS?

Seguimiento en II UAR, UEAS, coagulación (Xa)?

- •Eco 1T, screening combinado
- •12s amniocentesis? Bx corial?
- Ecocardiogramas si Ro+/La+ (16-28s)
- •20s: doppler uterinas
- •24s: doppler uterinas
- •28s y ss: biometrías fetales
- Consulta pre-parto: plan terapeútico parto y postparto
- •Visita en ingreso?
- Revisión postparto → tromboprofilaxis? Tto mantº

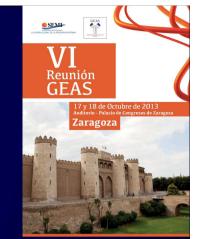


Table 2
Treatment groups

Features

Group 1 aPL positive No history of pregnancy loss No history of thrombosis Yes/no concomitant autoimmune disease

Treatment

Group 1 Education Low doses of aspirin may be prescribed Strict control Autoimmunity Reviews 11 (2012) 288-295



Contents lists available at SciVerse ScienceDirect

Autoimmunity Reviews



journal homepage: www.elsevier.com/locate/autrev

Review

Obstetric antiphospholipid syndrome

Claudio Galarza-Maldonado ^{a,*}, Maria R. Kourilovitch ^a, Oscar M. Pérez-Fernández ^b, Mariana Gaybor ^{a,c,d}, Christian Cordero ^{a,c}, Sonia Cabrera ^a, Nikolai F. Soroka ^e

- ^a Unit of Rheumatic and Autoimmune Diseases UNERA, Lupus Center, Mont Sinai Hospital, Cuenca, Ecuador
- b Center for Autoimmune Diseases Research (CREA), School of Medicine and Health Sciences, Universidad del Rosario, Bogotá, Colombia
- ^c Unit of Obstetrics and Gynecology, Mont Sinai Hospital, Cuenca, Ecuador
- d Unit of Obstetrics and Gynecology, Rio Universitary Hospital, Cuenca, Ecuador e National Center of Rheumatic Diseases, Hospital N 9, Minsk, Belarus

Table 2 Treatment groups

Features

Group 1 aPL positive No history of pregnancy loss No history of thrombosis Yes/no concomitant autoimmune disease

Treatment

Group 1 Education Low doses of aspirin may be prescribed Strict control Group 3
Obstetric APS secondary to SLE or other autoimmune diseases with or without history of thrombosis



Autoimmunity Reviews 11 (2012) 288-295



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Autoimmunity Reviews

journal homepage: www.elsevier.com/locate/autrev



Review

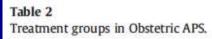
Obstetric antiphospholipid syndrome

Claudio Galarza-Maldonado ^{a,*}, Maria R. Kourilovitch ^a, Oscar M. Pérez-Fernández ^b, Mariana Gaybor ^{a,c,d}, Christian Cordero ^{a,c}, Sonia Cabrera ^a. Nikolai F. Soroka ^e

- ^a Unit of Rheumatic and Autoimmune Diseases UNERA, Lupus Center, Mont Sinai Hospital, Cuenca, Ecuador
- b Center for Autoimmune Diseases Research (CREA), School of Medicine and Health Sciences, Universidad del Rosario, Bogotá, Colombia
- Cunit of Obstetrics and Gynecology, Mont Sinai Hospital, Cuenca, Ecuador
- d Unit of Obstetrics and Gynecology, Rio Universitary Hospital, Cuenca, Ecuador e National Center of Rheumatic Diseases, Hospital N 9, Minsk, Belarus

Group 3
Education
Individual management
strategy (e.g.
glucocorticoids for SLE
flares)
Daily administration of
LMWH plus low-dose
aspirin
Warfarin discontinued
before 6th week of
pregnancy





Features

Group 1 aPL positive No history of pregnancy loss No history of

No history of thrombosis Yes/no concomitant autoimmune

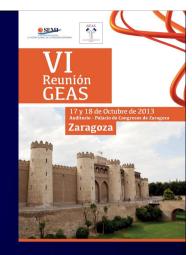
Group 2 aPL positive

History of two or more

miscarriages

Group 3

Obstetric APS secondary to SLE or other autoimmune diseases with or without history of thrombosis



Autoimmunity Reviews 11 (2012) 288-295



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Autoimmunity Reviews

journal homepage: www.elsevier.com/locate/autrev



Treatment

disease

Group 1
Education
Low doses of
aspirin may
be
prescribed
Strict control

Group 2 Education Plan A.

Aspirin 81–100 mg
 before conception and
 then throughout
 pregnancy
 Plan B.

 Aspirin 81–100 mg before conception and then aspirin 81–100 mg + LMWH throughout pregnancy Group 3
Education
Individual management
strategy (e.g.
glucocorticoids for SLE
flares)
Daily administration of
LMWH plus low-dose
aspirin
Warfarin discontinued
before 6th week of

pregnancy

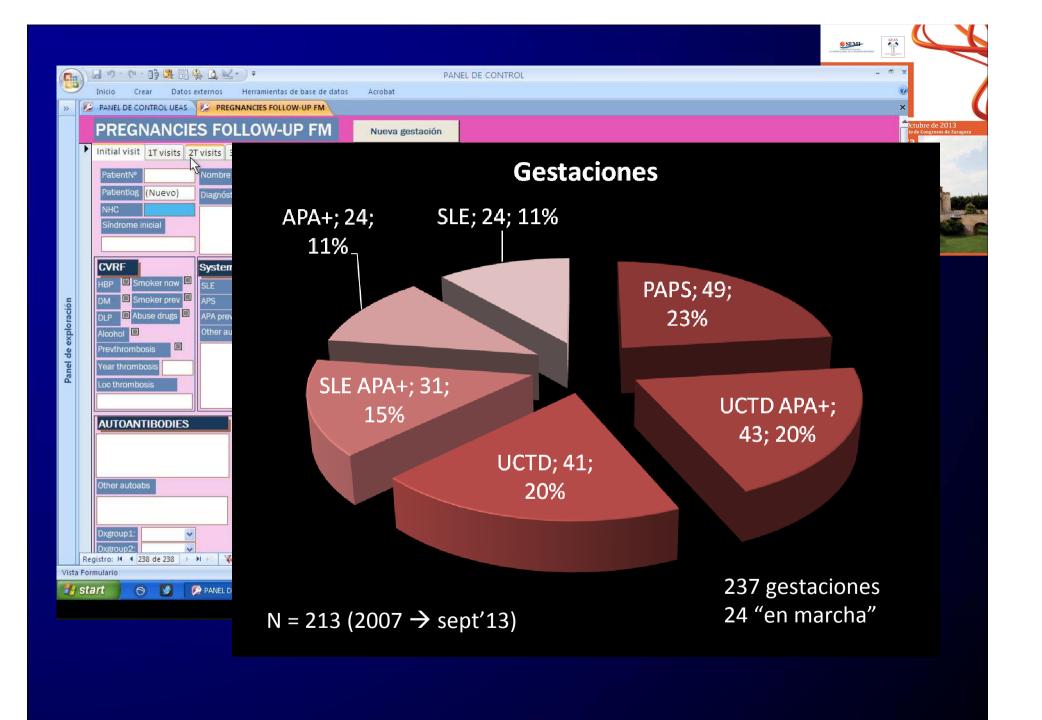
Review

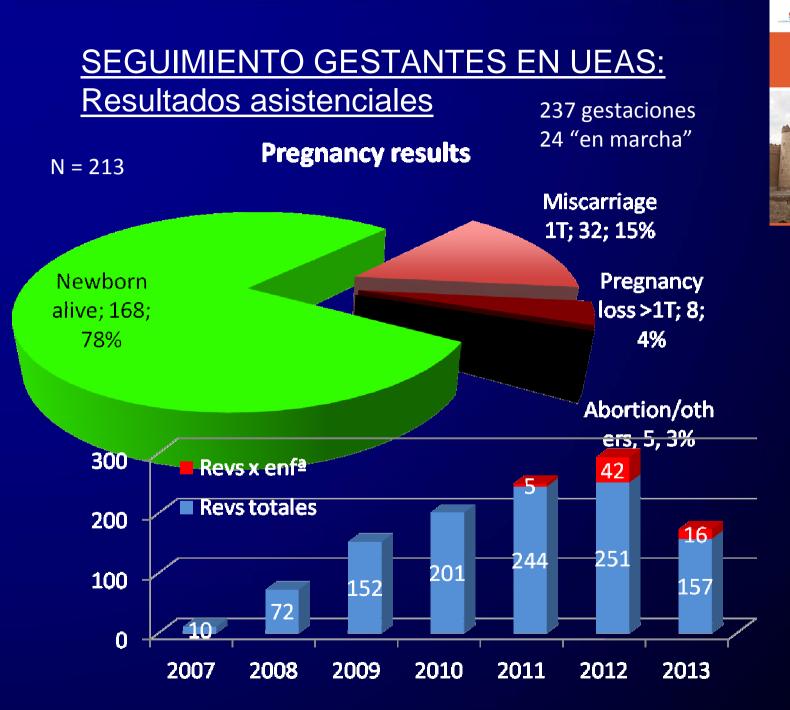
Obstetric antiphospholipid syndrome

Claudio Galarza-Maldonado ^{a,*}, Maria R. Kourilovitch ^a, Oscar M. Pérez-Fernández ^b, Mariana Gaybor ^{a,c,d}, Christian Cordero ^{a,c}, Sonia Cabrera ^a. Nikolai F. Soroka ^e

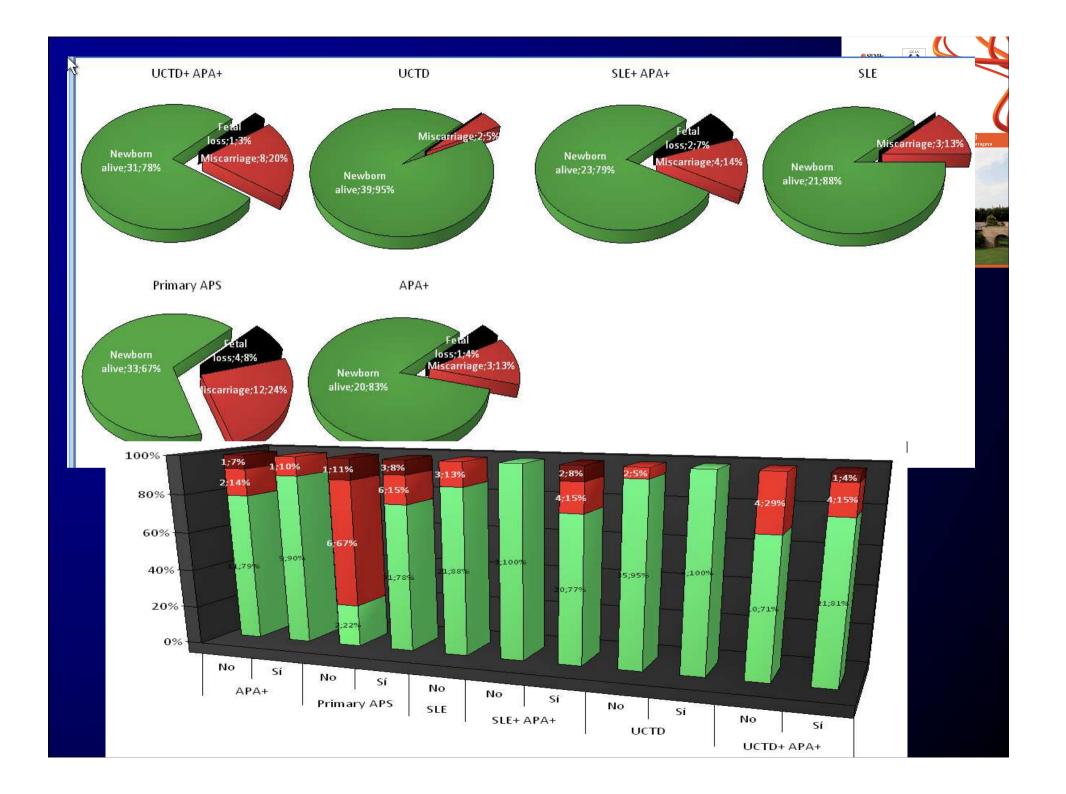
- ^a Unit of Rheumatic and Autoimmune Diseases UNERA, Lupus Center, Mont Sinai Hospital, Cuenca, Ecuador
- b Center for Autoimmune Diseases Research (CREA), School of Medicine and Health Sciences, Universidad del Rosario, Bogotá, Colombia
- ^c Unit of Obstetrics and Gynecology, Mont Sinai Hospital, Cuenca, Ecuador
- d Unit of Obstetrics and Gynecology, Rio Universitary Hospital, Cuenca, Ecuador e National Center of Rheumatic Diseases, Hospital N 9, Minsk, Belarus













Resultados asistenciales RN vivos

RN vivos previos 98 30% Abortos/pér didas fetales 40 19%



Abortos previos 233 70%

Protocolo sgto UEAS-UAR

RN vivos 168 81%

31,5% → 85,5% en gestantes con algún embarazo previo



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|------------------------------|--|----------------------------|---------------------------------|---|-------------------------------|--|---------------------|
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| Hospital | Estambul | Lisboa | Oporto | Florencia | Thailandia | Sudáfrica | Taipei |
| Periodo | 2002-2007 | 1993-2007 | 1993-2007 | 1998-2006 | 1997-2006 | 1998-2007 | 1995-2005 |
| N° y Tipo ptes | 42 LES AL 33% IgG ACL 16.6% IgM ACL 19% | 136 LES 28% AAF+ | 51 LES 21,6% SAF2° | 62 LES 12,9% SAF2° 32,2% AAF+ | 37 LES | 47 LES | 24 LES |
| Abortos/pérdi das fetales | 7,1% | 5,9% | 6% | 17,8% | 27,3% | 33% | 4,2%? |
| RCIU | 14,3% | 14% | | 19,6% | | 14% | 20,8% |
| Preeclampsia | 2,4% | 3,7% | | 14% | | | 12,5% |
| Prematuridad | 23,1% | 28% | 16% | 29,4% | | 39% | 41,6% |
| Brote | | | 42% | | 54,5% | 13% | |

| | | Octo |
|-------------------------------|---|---|
| | HUMS | CRUCES |
| Periodo | Sept'06 -> Sept'13 | 2007-2011 |
| % mujeres con abortos previos | 53.4% | 40% (10% PF) |
| N° y Tipo ptes | 169 ptes, 208 gestaciones 23% PAPS (49) 20% UCTD APA+ (43) 20% UCTD (41) 15% SLE APA+ (31) 11% APA+ (24) 11% SLE (24) | 116 gestaciones: SLE APS Sjögren Systemic sclerosis ANA+, APA+ or Ro+ |
| Abortos/pérdidas fetales | 19% | 13% |
| RCIU | 9,1% | 6.8% |
| Preeclampsia | 3,8% | 1.7% |
| Prematuridad | 5,3% | 12% |
| Trombosis | 0 | 1 |
| Brote | 22% | 23% (pts SLE) |





SEGUIMIENTO GESTANTES Resultados investigación

SYSTEMIC AUTOIMMUNE DISEASES: UEAS

THE "REAL LIFE PRACTICE".

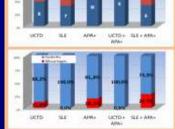
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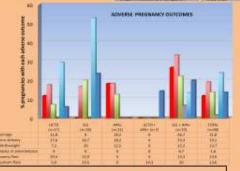




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antiphospholipid antibodies.

Variables related with these outcomes may be previous miscarriages, DNA, Ro and La antibodies and use of aspirin and low-molecular weight heparin













Facultad de Medicina Universidad Zaragoza

A NIEVA II.



ANEXO II:

INFORME / EVALUACIÓN DEL DIRECTOR

ALUMNO: D. JAVIER MORENO DÍAZ

TÍTULO DEL TRABAJO: RESULTADOS GESTACIONALES EN PACIENTES CON ENFERMEDADES AUTOINMUNES SISTÉMICAS

Fecha de Presentación / Depósito (Sello):

DIRECTOR (-ES) (Departamento): JOSÉ VELILLA MARCO, LUIS SÁEZ COMET

GESTACIONALES CIENTES CON

S SÁEZ COMET

"Iniciación a la ina" : José Velilla Marco/

Luis Sáez Comet.

10 de Septiembre de 2012.

ÁREAS DE INCERTIDUMBRE

Niveles AAF

Elección del tto

Tto SAF obstétrico refractario

Tromboprofilaxis a largo plazo

SNAPs

Infertilidad y AAF (y tto?)





• AL+ débil

Motivo de Consulta:

TEP v AL+. Tto con ACO

Olga, 37^a, gestante 15sem

2 abortos 8sem

2 AL+ débil, ACL-, AB2-

3^a Gestación 15sem: AAS 100 → HBPM 2-3D → amniocentesis → AAS 100

26sem: prolapso cordon, CIR, rotura prematura bolsa → cesárea → feto muerto 740 g

Temas no clares



Zaragoza

SAF OBSTÉTRICO REFRACTARIO

From bloodjournal.hematologylibrary.org at UNIVERSIDAD DE ZARAGOZA on September 13, 2011. For personal use only. THROMBOSIS AND HEMOSTASIS

Brief report

First-trimester low-dose prednisolone in refractory antiphospholipid antibody-related pregnancy loss

*Kate Bramham.1 *Mari Thomas.2 Catherine Nelson-Piercy.3 Munther Khamashta,4 and Beverley J. Hunt5

"Maternal and Fetal Research Unit, King's College London, London, United Kingdom; "Department of Haematology, Guy's and St Thomas" National Health Service (NHS) Foundation Trust, London, United Kingdom: *Obstetric Medicine, Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom: *Lupus Research Unit, King's College London, London, United Kingdom; and "Thromboels and Haemostasis and Lupus Unit, Guy's and St. Thomas' NHS Foundation Trust, London, United Kingdom

The objective of this study was to assess pregnancy outcome in women with a history of refractory antiphospholipid antibody-associated pregnancy loss(es) who were treated with early low-dose prednisolone in addition to aspirin and heparin. Eighteen women with antiphospholipid antibodies who had refractory pregnancy loss(es) were given prednisolone (10 mg) from the time of their positive pregnancy test to 14 weeks' ges-

tation. Before low-dose prednisolone was given as treatment, 4 (4%) of 97 pregnancies had resulted in live births. Among 23 pregnancies supplemented with prednisolone, 9 women had 14 live births (61%), including 8 uncomplicated pregnancies. The remainder were complicated by preterm delivery, preeclampsia. and/or small-for-gestational-age infants. There were 8 first-trimester miscarriages and 1 ectopic pregnancy. There were no

fetal deaths after 10 weeks' gestation and no evidence of maternal morbidity. The addition of first-trimester low-dose prednisolone to conventional treatment is worthy of further assessment in the management of refractory antiphospholipid antibody-related pregnancy loss(es), although complications remain elevated. (Blood. 2011;117(25):6948-6951)

Clinical and Experimental Rheumatology 2011; 29: 551-554.

Adjusted prophylactic doses of nadroparin plus low dose aspirin therapy in obstetric antiphospholipid syndrome. A prospective cohort management study

A. Ruffatti¹, M.T. Gervasi², M. Favaro¹, A.T. Ruffatti², A. Hoxha¹, L. Punzi¹

¹Rheumatology Unit, Department of 'linical and Experimental Medicine, Iniversity of Padua, Padua, Italy: Obstetrics and Gynecology Unit. Iniversity-Hospital of Padua, Padua,

melia Ruffatti, MD, PhD Iaria T. Gervasi, MD faria Favaro, MD lessandra T. Ruffatti, MD riela Hoxha, MD eonardo Punzi, MD, PhD

lease address correspondence to: melia Ruffatti, MD. eumatologia. oliclinico Universitario. ia Giustiniani 2. 5128 Padova, Italy, -mail: amelia.ruffatti@unipd.it eprints will not be available from the

eceived on September 30, 2010; accepted v revised form on February 11, 2011. Copyright CLINICAL AND XPERIMENTAL RHEUMATOLOGY 2011.

Key words: nadroparin, neonatal utcome, obstetric antiphospholipid vndrome, pregnancy outcome

ABSTRACT

Objective. Current guidelines for the treatment of patients with obstetric antiphospholipid syndrome (APS) recommend low dose aspirin (LDA) and prophylactic doses of low molecular weight heparin (LMWH). Most clinicians use a fixed dosage of LMWH in pregnant APS women despite the fact that there are no clinical trials establishing that fixed doses are more efficacious than adjusted ones in preventing pregnancy complications. The efficacy and safety of adjusted single daily doses of LMWH (nadroparin) combined with LDA have thus been evaluated in 33 consecutive pregnancies in women with diagnosed obstetric APS.

Methods. LMWH doses were augmented as the pregnancies progressed and maternal/foetal weight increased. 70-80-90 U/Kg doses ranging between 3800 and 6650 U were administered daily during the first, second and third trimesters, respectively. LDA (100 mg/ day) was also prescribed.

Results. Pregnancy outcome was successful in 97% of the patients studied. who delivered, between the 29th and 41st weeks of gestation (mean 37.4 ± 2.1 SD), 32 infants with a mean birth weight of 3084 g \pm 514 SD. One woman (3%) experienced a spontaneous abortion at the 8th week of gestation.

Conclusion. The high live birth rate, the satisfactory mean gestational age and weight at birth and the absence of major pregnancy/neonatal-associated complications indicate that adjusted, once daily doses of LMWH together with LDA could be an efficacious treatment option for pregnant APS patients with no history of thrombosis.

CASOS SAF REFRACTARIO UEAS

8 PACIENTES:

2 ABORTOS 1T

1 no implantación

1 anembriónica

3 RN VIVOS (1 RNBP 37SEM)

1 GESTACIÓN 27SEM

| тто | DOSIS | TIMING |
|------------|--------------|-----------------------------|
| AAS | 100 mg | PRECONCEPCIONAL GESTACIONAL |
| НВРМ | PROFILÁCTICA | GESTACIONAL POSTPARTO |
| PREDNISONA | 10 mg | HASTA SEM14 |



Tromboprofilaxis primaria tras gestación

Retrospectivo
32 pts SAF obstétrico
AAS postparto → Sgto 50 ± 37m
Tasa trombosis:

3.3/100 pacientes-año

4.6/100 pacientes-año si 2 AAF+

4.5/100 pacientes-año si ANA+

10/100 pacientes-año si LES asociado

Full Text

LUPUS

Thrombotic events during long-term follow-up of obstetric antiphospholipid syndrome patients

Lupus July 2011 20: 861-865, first published on May 5, 2011

Lefèvre G et al

Department of Internal Medicine, National Reference Centre for Systemic Sclerosis, University Hospital, Université Lille Nord de France, Lille, France.

The thrombosis rate was high after obstetric APS diagnosis, even for patients taking aspirin.

Tromboprofilaxis primaria tras gestación

Risk of thromboembolic events after recurrent spontaneous abortion in antiphospholipid syndrome: a case—control study

Maria Angeles Martinez-Zamora, ¹ Sara Peralta, ¹ Montserrat Creus, ¹ Dolors Tassies, ² Juan Carlos Reverter, ² Gerard Espinosa, ³ Ricard Cervera, ³ Francisco Carmona, ¹

Juan Balasch¹



Correspondence to

Juan Balasch, Institut Clínic of Gynecology, Obstetrics and Neonatology, Hospital Clínic, Villarroel, 170, 08 Barcelona, Spain; ibalasch⊘ub.edu

Accepted 3 August 2011 Published Online First 6 September 2011

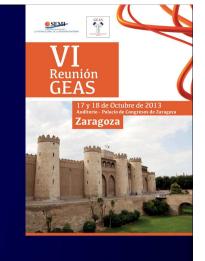
ABSTRACT

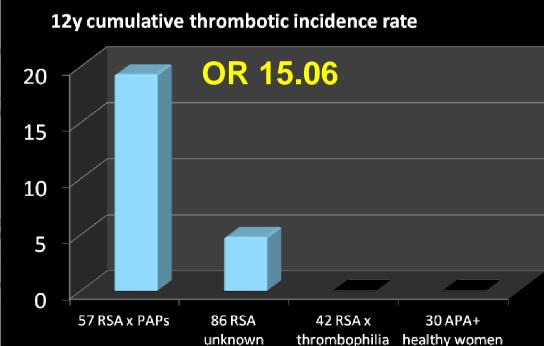
Objective To investigate whether patients having antiphospholipid syndrome (APS) as the only aetiologica factor for recurrent spontaneous abortion (RSA) are at increased risk of thrombosis later in life.

Methods: A case—control study at a tertiary university referral centre. The study group consisted of 57 primary APS and RSA women (APS—RSA group). Control groups included: 86 patients with RSA of unknown aetiology (uRSA group), 42 patients with RSA and thrombophilic genetic defects as the only aetiologic factor for RSA (tRSA group) and 30 antiphospholipid antibody (aPL) positive but otherwise healthy women (aPL group). The main measurement was the thrombosis rate after long-term follow-up.

Results APS–RSA patients had a significantly higher 12-year cumulative thrombotic incidence rate compared with the three comparator groups (19.3% vs 4.8%, 0.09 and 0.0%, respectively (log rank), p<0.001). Patients in the APS–RSA group had 25.6 thrombotic events per 1000 patient-years (95% CI 12.8 to 45.9). The OR of thrombosis in relation to the presence (APS–RSA group or absence (uRSA and tRSA groups) of aPL in patients with RSA was 15.06 (95% CI 3.2 to 70.5).

Conclusions Our data indicate that a history of RSA associated with aPL is a risk factor for subsequent thrombosis in the long term





Tromboprofilaxis primaria tras gestación

Comparative incidence of a first thrombotic event in purely obstetric antiphospholipid syndrome with pregnancy loss: the NOH-APS observational study

Jean-Christophe Gris, ^{1,3} Sylvie Bouvier, ^{1,3} Nicolas Molinari, ⁴ Jean-Philippe Galanaud, ^{2,5} Éva Cochery-Nouvellon, ^{1,2} Érik Mercier, ^{1,3} Pascale Fabbro-Peray, ⁴ Jean-Pierre Balducchi, ⁶ Pierre Marès, ⁷ Isabelle Quéré, ^{2,5} and Michel Dauzat^{2,5}

¹Department of Hematology, University Hospital, Nimes, France; ²Research Team EA2992, Dysfonction ³ 2630 G Nimes, France; ³Laboratory of Hematology, Faculty of Pharmacy and Biological Sciences, Montpellier 1 Biostatistics, Epidemiology and Medical Information, ⁵Department of Vascular Medicine, ⁶Department of Obstetrics, University Hospital, Nimes, France

The incidence of thrombosis in the purely obstetric form of antiphospholipid syndrome is uncertain. We performed a 10-year observational study of 1592 nonthrombotic women who had experienced 3 consecutive spontaneous abortions before the 10th week of gestation or 1 fetal death at or beyond the 10th week of gestation. We compared the frequencies of thrombotic events among women positive for antiphospholipid Abs (n = 517), women carrying the F5 6025 or F2 rs1799963 polymorphism (n = 279),

and women with negative thrombophill screening results (n = 796). The annuarates of deep vein thrombosis (1.46% range, 1.15%-1.82%), pulmonary emborsism (0.43%; range, 0.26%-0.66%), superficial vein thrombosis (0.44%; range, 0.28% 0.68%), and cerebrovascular event (0.32%; range, 0.18%-0.53%) were significantly higher in aPLAbs women than if the other groups despite low-dose aspirit primary prophylaxis. Women carrying 1 of the 2 polymorphisms did not experience more thrombotic events than women which is the service of the serv

10y follow-up of 1592 women

- without thrombosis
- With 3 consecutive abortions or 1 fetal death >10w

BLOOD, 15 MARCH 2012 · VOLUME 119, NUMBER 11

Zaragoza

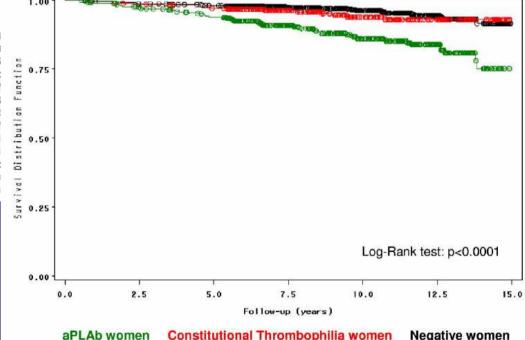


Figure 2. VTE-free survival. Shown are the VTE-free survival rates in initially nonthrombotic women with pregnancy loss (3 unexplained consecutive spontaneous abortions before the 10th week or 1 unexplained fetal death at or beyond the 10th week) with positive aPLAbs, with a positive F5 6025 or F2 rs1799963 polymorphism (constitutional thrombophilia), or with a negative thrombophilia screening (negative).

Temas no claros: **SN-APS**



ELR, 32a

2 abortos 1T, tras inseminación artificial Raynaud 10^a evolución Descenso C3, rash malar, discoide? → UCTD? AAF REP -

3ª gestación → pérdida fetal 17sem

4ª gestación → SAF seronegativo? → AAS + HBPM → RN 39sem 3040g

Antiphospholipid syndrome

Seronegative antiphospholipid syndrome

G R V Hughes, M A Khamashta

History repeats itself

doi: 10.1136/ard.2003.006163

Ann Rheum Dis 2003;62:1127.

CONCISE REPORT

Clinical manifestations of antiphospholipid syndrome (APS) with and without antiphospholipid antibodies (the so-called 'seronegative APS')

Jose Luis Rodriguez-Garcia, Maria Laura Bertolaccini, Maria Jose Cuadrado, 12 Giovanni Sanna. 12 Oier Ateka-Barrutia. 1 Munther A Khamashta 1

Rodriguez-Garcia JL, Khamashta MA, Bertolaccini ML, et al. Ann Rheum Dis (2011), doi:10.1136/annrheumdis-2011-200614





G5A4P0:

.- 1ª gestación: pérdida fetal de 23 semanas en 2005, tras amniocentesis en 14sem, con hematoma retrocorial desde semana 11. Cariotipo 46XY. Estudio entonces en Escocia N: oligoamnios tras amniocentesis. Biopsia placenta entonces: 14x8x2.5 cm, peso 144g ("trimmed weight"), con corddón umbilical de 25 cm, con 3 vasos. Membranas adheridas traslúcidas pero posiblemente incompleta. Superficie materna placentaria completa pero con área deprimida central. Coágulo de 9x8x2.5 cm con peso 64g, con contorno similar a la depresión descrita. Sin anormalidades en sección. Confirman hematoma retroplacentario, con depósitos de hemosiderina que sugieren cronicidad.

- .- 2ª gestación: en 2006, aborto de 6 semanas.
- .- 3ª gestación: en 2007, aborto de 8-9 semanas.
- .- 4ª gestación: en 2008, aborto de 7 semanas. Tras este aborto fue enviada a infertilidad donde detectaron AAF positivos.
- .- 5ª gestación (actual, con FUR 13/6/9).

Historia actual

Paciente enviada de ginecología por gestación actual y antecedente de 3 abortos de 1T (y una pérdida fetal de 23sem tras amniocentesis), junto con el hallazgo de anticuerpos antifosfolípido positivos (3 IGM ACL+, 1 AL+ MODERADO).

Refiere naúseas desde que conoce su embarazo actual (FUR 13-6-9). No vómitos.





www.anticoagulacionyembarazo.com











Anticoagulación y Embarazo

Arbol de Consulta para la Anticoagulación durante el Embarazo y Puerperio

Presentación

Tríptico

Dosis

Pruebas Invasivas

Contraindicaciones

Trombofillas

Seguridad

PRESENTACIÓN



La anticoagulación está tomando cada día más relevancia dentro del campo de la obstetricia y está permitiendo llevar a término y sin complicaciones las gestaciones que así lo precisen. Es un tema complejo, sin protocolos estrictos establecidos, por todo esto es importante que el médico y la paciente conozcan bien las indicaciones de profilaxis

antitrombótica. Tomando como referencia los últimos protocolos publicados, hemos desarrollado este programa, descargable desde el icono que se encuentra a la derecha, que guiará al médico de una forma sencilla para poder realizar un informe personalizado sobre el tratamiento recomendado más adecuado para cada paciente.

> Dr. Ricardo Savirón Cornudella. Dra. Ana Cristina Lou Mercadé. Dra. Rosa Cornudella Lacasa

Aplicación



Ultima versión 1.06

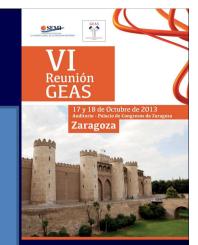
Capturas de la Aplicación

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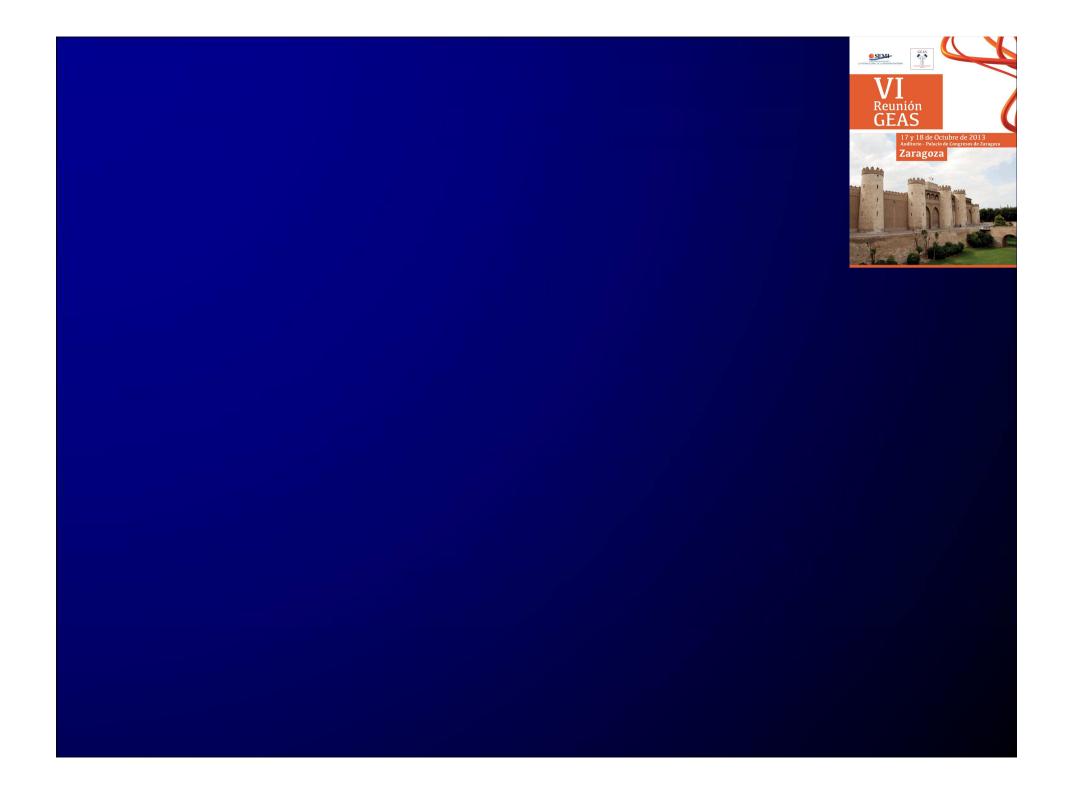
Página auspiciada por

Take-home-messages:

- □Colaboración UAR-UEAS: imprescindible para buenos resultados obstétricos en EAIS
- □Se necesita:
 - □Planificación + Seguimiento coordinado
 - □H^a previa obs y AI, y perfil inmunológico
 - ☐"Política de puertas abiertas"
 - □Teléfono directo
 - ☐Sesiones conjuntas







Factors involved in worse pregnancy prognosis are shown in the next table

| Factor | Р |
|---------------------------|--------|
| Diagnostic Group | 0,029 |
| Lupus Anticoagulant | 0,025 |
| IgM Anticardiolipin | 0,047 |
| Any APA | 0,010 |
| Previous Miscarriage | <0,001 |
| ANA + | 0,044 |
| AAS previous to pregnancy | 0,001 |



CONCLUSIONS

We report worse pregnancy outcomes in patients with APA with a higher rate of miscarriages than in CTD alone.







| | Gestaciones UEAS | DEA Dra. Vicente Iturbe |
|--------------------------|---|--|
| Hospital | HUMS | HUMS |
| Periodo | Sept'06 -> Sept'13 | Ene'04 - Jul'09 |
| N° y Tipo ptes | 169 ptes, 208 gestaciones 23% PAPS (49) 20% UCTD APA+ (43) 20% UCTD (41) 15% SLE APA+ (31) 11% APA+ (24) 11% SLE (24) | 42 ptes, 64 gestaciones: 60% LES (25), 28% AAF+ 17% SAF 19% UCTD 2% ESP 2% Artritis psoriásica |
| Abortos/pérdidas fetales | 19% | 12% |
| RCIU | 9,1% | 22.9% |
| Preeclampsia | 3,8% | 14.3% |
| Prematuridad | 5,3% | 18.4% |
| Brote | 22% | 20% |