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Atorvastatin and endothelial function in systemic lupus erythematosus (SLE) patients

Submission date	Recruitment status	[ ] Prospectively registered
12/06/2009	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
21/07/2009	Completed	[X] Results
Last Edited	**Condition category**	[ ] Individual participant data
21/07/2009	Musculoskeletal Diseases	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
FAPESP Grant No.: 2003/06738-0

Study information

Scientific Title
Evaluation of the atorvastatin effect on endothelial-dependent vasodilation in patients with systemic lupus erythematosus: an 8-week controlled trial

Study objectives

1. That atorvastatin therapy improves endothelium-dependent arterial dilation in systemic lupus erythematosus (SLE) patients with and without conventional risk factors for atherosclerotic disease
2. That atorvastatin therapy reduces the plasma levels of non-traditional laboratory markers for atherosclerosis in SLE patients

Ethics approval required
Old ethics approval format

Ethics approval(s)
Local Medical Ethics Committee (Comitê de Ética em Pesquisa da Universidade Federal de Minas Gerais) approved on the 5th November 2003 (ref: ETIC 285/03)

Study design
Interventional single-centre non-randomised unblinded temporal series study with a parallel control group

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Systemic lupus erythematosus (SLE)

Interventions
Patients were divided in two groups:
1. The intervention group consisted of 64 patients who received atorvastatin 20 mg/day during 8 weeks. Thirty-three patients in the intervention group had hypertension, dyslipidaemia and/or obesity, while the remaining 31 did not have any conventional risk factors for CHD.
2. The control group comprised 24 SLE patients followed in the same period without atorvastatin (no treatment)

To reinforce and check adherence to the protocol, phone calls or personal contacts were performed 30 days after the beginning the study and atorvastatin tablets were counted at the end of the study. At baseline and at the end of the 8-week period, all 88 participants underwent complete clinical examination, brachial artery ultrasound and blood sampling for laboratory analysis.

Total duration of treatment: 8 weeks
Total duration of follow-up: 8 weeks

Definitions:
1. Family history of CHD: presence of clinical CHD or sudden death in first-degree relatives at ages before 55 years old and 65 years old for men and women, respectively
2. Hypertension: blood pressure higher than 140 mmHg/90 mmHg or current use of antihypertensive medications
3. Obesity: body mass index (BMI) over 30 kg/m^2 and/or presence of abdominal obesity, considered as abdominal circumference above 88 cm
4. Diabetes mellitus: fasting plasma glucose higher than 126 mg/dl or use of oral hypoglycaemic

agents or insulin
5. Dyslipidaemia: high density lipoprotein (HDL) cholesterol serum levels less than 40 mg/dl or low density lipoproteins (LDL) cholesterol serum levels greater than 130 mg/dl or total cholesterol serum levels greater than 200 mg/dl or triglyceride serum levels greater than 200 mg /dl
6. Menopause: amenorrhoea for more than one year or use of hormonal replacement therapy

SLE disease activity and damage were measured using SLEDAI (Systemic Lupus Erythematosus Disease Activity Index) and SLICC (The Systemic Lupus International Collaborating Clinics /American College of Rheumatology Damage Index for Systemic Lupus Erythematosus), respectively.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Atorvastatin

Primary outcome(s)
1. Resting diameter (mm)
2. Resting flow (ml/min)
3. Hyperaemia flow (mL/min)
4. Flow-mediated dilation (%)
5. Glyceryl-trinitrate induced dilation (%)

Measured at baseline and 8 weeks.

Vascular studies were performed at room temperature (25 - 28°C) using high-resolution ultrasound equipment, vascular colour echo-Doppler with flow mapping (ACUSON, Mountain View - California, USA) and multiple-frequency linear 7 MHz transducer. All patients were evaluated between 8:00 and 10:00 am after 12 hours overnight fast. Antihypertensive medication was stopped 24 hours before the study. All exams were performed by the same examiner and with the guidelines for ultrasound assessment of endothelial-dependent flow-mediated dilation of the brachial artery. Recorded images were later analysed by the examiner without any information on the patient's identification.

Key secondary outcome(s))
1. Total cholesterol (mg/dl)
2. LDL-cholesterol (mg/dl)
3. HDL-cholesterol (mg/dl)
4. Triglycerides (mg/dl)
5. Creatine phosphokinase (CPK)
6. Homocysteine (µmol/L)
7. Lipoprotein-a (mg/dL)
8. Endothelin-1 (pg/ml)
9. Cytokines and receptors (tumour necrosis factor-alpha, sTNFR1 and sTNFR2)
10. Chemokines (CL2, CCL3 and CXCL9) serum levels
11. Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score

12. Anti-DNA antibodies (0 = absent, 1 = present)
13. Anti-oxidised LDL antibodies (0 = absent, 1 = present) and anti-lipoprotein lipase antibodies (0 = absent, 1 = present)
14. Anticardiolipin antibodies (GPL or MPL)

Measured at baseline and 8 weeks.

Laboratory exams were performed according to standard routine techniques. Anti-dsDNA antibodies were detected by indirect immunofluorescence in Crithidia luciliae. Homocysteine and lipoprotein-a serum levels were measured by liquid chromatography (reference range less than 15 µmol/L) and immunonephelometry (Dade Behring, reference range less than 30 mg/dl), respectively. The concentration of cytokines, chemokines, endotelin-1, anti-DNA antibodies, anti-oxidised LDL antibodies, and anti-lipoprotein lipase antibodies, anticardiolipin antibodies were determined by enzyme immunoassay. Anticardiolipin antibodies were considered positive when higher than 20 GPL or 11 MPL.

Completion date
23/02/2006

Eligibility

Key inclusion criteria
1. Female
2. SLE according to the American College of Rheumatology revised classification criteria
3. Disease diagnosis equal or greater than 1 year
4. Aged above 18 years old
5. Regular menstruation

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Female

Key exclusion criteria
1. Current or past use of hypolipidemic drugs in the last six months
2. Menopausal women
3. Diabetes mellitus
4. Serum creatinine above 1.2 mg/dl
5. Pregnancy
6. Smoking status (last 12 months)

7. Family history of coronary heart disease (CHD)
8. Skeletal myopathic disease and/or elevated creatinine phosphokinase
9. Hepatic disease
10. Ciclosporin use

Date of first enrolment
21/07/2004

Date of final enrolment
23/02/2006

Locations

Countries of recruitment
Brazil

Study participating centre
Pasteur Avenue, 135/1403
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Sponsor information

Organisation
State of São Paulo Research Foundation (FAPESP) (Brazil)

ROR
https://ror.org/02ddkpn78

Funder(s)

Funder type
University/education

Funder Name
Federal University of Minas Gerais (Brazil) - Rheumatology Division; Board of Education, Research and Extension (DEPE) (ref: 078/03)

Funder Name

Federal University of São Paulo-Escola Paulista de Medicina (Brazil) - Rheumatology Division

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/10/2007		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes