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Effects of addition of low-dose oral daily corticosteroids to the initial anti-rheumatic therapy on radiographic damage and disease activity in patients with early rheumatoid arthritis

Submission date
27/12/2013

Recruitment status
No longer recruiting

Registration date
04/02/2014

Overall study status
Completed

Last Edited
11/03/2015

Condition category
Musculoskeletal Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
Rheumatoid arthritis (RA) is an autoimmune disorder when the body tissue is mistakenly attacked by its own immune system. This causes inflammation of the joints, with destruction of bone around the involved joints. Experts suggest that preventing early joint damage can have huge long-term benefits. Early, aggressive treatment is the key to slowing or stopping RA progression and joint destruction. Corticosteroids (prednisolone) decrease inflammation and reduce the activity of the immune system. Added to other anti-rheumatic medication, low doses of corticosteroids may provide significant relief from pain and stiffness for people with rheumatoid arthritis. Our aim was to find out if addition of low-dose corticosteroids to the usual treatment soon after diagnosing RA may help to stop joint damage, improve inflammatory-related signs and symptoms of RA and improve disease outcomes in the long run. Further, we wanted to study if these effects could be achieved without serious toxicity issues.

Who can participate?
Adult men and women aged 18-80 years with newly diagnosed active RA can participate in this study.

What does the study involve?
Eligible patients were allocated at random to take either prednisolone (corticosteroids) daily or no prednisolone over a period of two years. Other anti-rheumatic drugs were selected by the treating specialist according to current recommendations. Participants were seen at the beginning of the study and at 3, 6, 12, 18, and 24 months for follow up. Disease activity was measured and questionnaires about physical function were completed. X-ray of the hands and feet were obtained at study entry and after 1 and 2 years. Participants were also invited to give blood to a biobank for studies of prediction of RA disease course and complications.

What are the possible benefits and risks of participating?
Taking corticosteroids may reduce the rate of worsening of the disease in the affected joints. This study may help in deciding the best treatment for future patients with early RA. We believe that this study may also help to tailor the treatment to the individual patient's characteristics and needs. Possible side effects as high blood pressure, increased lipid content in blood and heart-related complications were looked for and registered if they occurred at all.

Where is the study run from?
This study took place in six rheumatologic clinics (Helsingborg, Kristianstad, Mölndahl, Spenshult, Kalmar, Huddinge) in southern Sweden.

When is the study starting and how long is it expected to run for?
Participants were recruited between September 1995 and December 1999. However, the study follow-up was extended beyond two years of follow up, as we wanted to look at participants' health over many years to assist future studies about the course, treatments and complications of RA disease.

Who is funding the study?
1. The Swedish Rheumatism Association (Sweden)
2. King Gustav V 80-years foundation (Sweden)
3. The Ugglas Foundation (Sweden)
4. The Börje Dahlins Foundation (Sweden)
5. The Gorthon Foundation in Helsingborg (Sweden)
6. Foundation for assistance to disabled people in Skåne (Stiftelsen för Rörelsehindrade i Skåne) (Sweden)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Effects of addition of low-dose oral daily prednisolone to the initial disease-modifying anti-rheumatic drugs (DMARD) therapy on progression of radiographic damage and disease activity in patients with early rheumatoid arthritis, as well as effects on adverse outcomes and toxicity

Study objectives
To evaluate if low-dose prednisolone, 7.5 mg daily, added to DMARD therapy over the first two years after diagnosis of RA was able to reduce the progression of joint destruction and provide sustained reduction of disease activity with an acceptable level of toxicity/adverse outcome, including effect on bone mineral density.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Lund University, ref: LU 154-95
2. Gothenburg University, ref: Gbg M45-95
3. Karolinska Institutet (Karolinska Institute), ref: KI 153-95
4. Linköping University, ref: Li 123-95

Study design
Comprehensive cohort study incorporating a randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
The patient information sheet was in Swedish only (not available in web format). All patients gave their informed consent.

Health condition(s) or problem(s) studied
Rheumatoid arthritis

Interventions

The patients were recruited from the 6 centres involved in the BARFOT (Better Anti-Rheumatic FarmacOTherapy) Study Group in southern Sweden. The randomization was done as block randomization for each centre according to a central randomization with stratification for sex. At start of the first DMARD the participants had been randomised to either 7.5 mg prednisoone daily, orally (P group), or no prednisolone (NoP group) for the first 2 years. The choice of DMARD was left to the treating physicians, who followed the recommended treatment strategy in Sweden at the time of the study. All patients were given 1000 mg calcium per day.

Study entry: registration only

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
The difference in changes in radiographic damage scores after 2 years
Timepoint(s): Pre- and post-intervention. Clinical assessment at the start of the study and at 3, 6, 12, 18, and 24 months. Radiographic evaluation at baseline and after 1 and 2 years

Secondary outcome measures
1. Remission rates and differences in disease activity and function
2. Adverse events

Overall study start date
01/09/1995

Completion date
01/12/1999

Eligibility

Key inclusion criteria
1. Diagnosis of RA according to the 1987 revised criteria of the American College of Rheumatology (ACR)
2. Age 18-80 years
3. Disease duration of ≤ 1 year
4. Active disease defined as a Disease Activity Score in 28 joints (DAS28) of >3.0
5. Started by the treating rheumatologist on the first DMARD

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
80 Years

Sex
Both

Target number of participants
The planned Sample Size (>160 patients) was achieved. Sample Size: 250.

Key exclusion criteria
1. Earlier treatment with glucocorticoids for RA or other diseases
2. Previous treatment with DMARDs
3. Contraindication for glucocorticoid therapy
4. Previous fragility fractures
5. Patients aged < 65 years with a T-score lower than -2.5 on bone densitometry; and patients aged ≥ 65 years with a Z-score of less than -1

Date of first enrolment
01/09/1995

Date of final enrolment
01/12/1999

Locations

Countries of recruitment
Sweden

Study participating centre
Karolinska University Hospital Huddinge
Stockholm
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Sponsor information

Organisation
Karolinska Institute (Karolinska Institutet) (Sweden)

Sponsor details
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Sponsor type
University/education

ROR
https://ror.org/056d84691

Funder(s)

Funder type
Research organisation

Funder Name
The Swedish Rheumatism Association (Sweden)

Funder Name
King Gustav V 80-years foundation (Sweden)

Funder Name
The Ugglas Foundation (Sweden)

Funder Name
The Börje Dahlins Foundation (Sweden)

Funder Name
The Gorthon Foundation in Helsingborg (Sweden)

Funder Name
Foundation for assistance to disabled people in Skåne (Stiftelsen för Rörelsehindrade i Skåne) (Sweden)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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	01/11/2005		Yes	No
Results article	results	01/11/2008		Yes	No
Results article	results	01/04/2013		Yes	No
Results article	10-year follow-up results	07/04/2014		Yes	No
Results article	results	30/07/2014		Yes	No