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Circadian variations in cytokines and the effect of timed release tablet prednisone in rheumatoid arthritis

Submission date
16/08/2007

Recruitment status
No longer recruiting

Registration date
04/10/2007

Overall study status
Completed

Last Edited
18/01/2012

Condition category
Musculoskeletal Diseases

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

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
ME/2005/2073

Study information

Scientific Title

Study objectives
Rheumatoid Arthritis (RA) is a systemic, inflammatory condition causing joint pain and swelling, disability, and psychological distress.

To document overnight variations of serum pro-inflammatory and anti-inflammatory cytokines in 12 volunteers with rheumatoid arthritis on one night before and one night during treatment with a Timed Release Tablet (TRT) containing 5 mg prednisone, and to relate blood cytokine levels to biogenic amines and the hormones of the hypothalamic-pituitary-adrenal axis.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval received from the North Somerset and South Bristol Research Ethics Committee (REC) on the 28th November 2005 (ref: 054/Q2006/185).

Study design
Non-randomised, non-controlled interventional single centre study of patients before and after two weeks treatment with night time prednisone

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Rheumatoid Arthritis (RA)

Interventions
The study uses a delayed (timed) release formulation of prednisone which will release the full dose of the active drug during sleep after a lag time of 4 hours, allowing the patient to take the medication at a convenient point in time, namely at 22:00 hours +/- 30 minutes.

Intervention: Timed-Release Tablet (TRT) prednisone 5 mg, one tablet taken at 22.00 each evening for 12 - 16 nights (depending on the convenience of the final study night for the patient). There is no study follow-up after the end of medication.

Intervention Type
Drug

Phase
Not Specified

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

Primary outcome(s)
Changes in overnight pattern of plasma cortisol and interleukin-6 concentrations, determined at baseline and two weeks.

Key secondary outcome(s))
Standard assessment tools will be used to assess the state of the patient's arthritis. These assessments will be:
1. Swollen and tender joint counts
2. Pain (visual analogue scale)
3. Morning stiffness (minutes)
4. Patient's opinion of condition
5. Clinician's opinion of condition
6. Health Assessment Questionnaire
7. The Multidimensional Assessment of Fatigue scale
8. Hospital Anxiety and Depression Scale

The secondary outcome measures are determined at baseline and two weeks.

Completion date
14/06/2008

Eligibility

Key inclusion criteria
1. Have rheumatoid arthritis by the criteria of the American College of Rheumatology
2. Are over 50 but less than 80 years old
3. Have active disease as evidenced by:
3.1. Three or more swollen joints
3.2. Three or more tender joints
3.3. Morning stiffness at least 45 minutes
3.4. Pain at least 30 mm on a 100 mm Visual Analogue Scale (VAS)
3.5. Erythrocyte Sedimentation Rate (ESR) at least 29 mm in first hour or C-Reactive Protein (CRP) at least 15 mg/L
4. Stable Disease-Modifying Anti-Rheumatic Drug (DMARD) therapy (or no therapy) for at least 28 days
5. Stable Non-Steroidal Anti-Inflammatory Drug (NSAID)/analgesic therapy for at least seven days

It is anticipated that the ratio of female to male patients will be approximately 2:1, in accordance with the pattern of disease occurrence. To be safe, we will invite women of childbearing potential to take part in the study only if they are using contraception.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Senior

Sex
All

Key exclusion criteria

1. Pregnancy and lactation
2. Participation in a clinical trial within the past 30 days
3. Presence of contraindication of corticosteroids
4. Known hypersensitivity to prednisone/prednisolone
5. Parenteral treatment with corticosteroids or crystalloid injection into joints within the past three months
6. Other diseases which require corticoid treatments
7. Inflammatory diseases, such as Irritable Bowel Disease (IBD), Colitis, Crohn's Disease, Asthma
8. Other auto-immune diseases
9. Cancer
10. Infections, treatment with antibiotics within the past six weeks
11. Requirement of non-permitted concomitant medication
12. Consumption of benzodiazepines, antidepressants, antipsychotic drugs, antihistaminic drugs
13. Tumour Necrotising Factor - alpha (TNFα) inhibitors
14. Working shift employee
15. Jet lag
16. Significant renal disease (creatinine greater than 150 µmol/L)
17. Significant hepatic impairment

Date of first enrolment
15/06/2006

Date of final enrolment
14/06/2008

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Academic Rheumatology Unit
Bristol
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Sponsor information

Organisation
United Bristol Healthcare NHS Trust (UK)

ROR
https://ror.org/04nm1cv11

Funder(s)

Funder type
Industry

Funder Name
Nitec Pharma AG (Switzerland)

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	01/04/2010		Yes	No