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Does hydroxychloroquine provide effective pain relief for people with hand osteoarthritis?

Submission date
17/10/2012

Recruitment status
No longer recruiting

Registration date
24/10/2012

Overall study status
Completed

Last Edited
24/01/2023

Condition category
Musculoskeletal Diseases

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

Plain English summary of protocol

Background and study aims
Osteoarthritis (OA) is the most prevalent form of arthritis and is an increasingly common problem in our aging society. In the UK an estimated 8.5 million people are affected by OA, causing an enormous burden to health authorities, as well as considerable pain and disability to these individuals. A recent study by Arthritis Care reported that 81% of people with OA experience constant pain and 72% have important related conditions, such as high blood pressure or depression. Hand OA is generally considered to be less important and less disabling than knee or hip OA, but 8% of the UK population are estimated to be effected by painful hand OA, with a large proportion reporting significant difficulties with common day-to-day tasks, leading to reduced capacity to work and impacting on both quality of life and general health. However, despite the prevalence of hand OA, there are still limited treatment options. Current treatments for hand OA are limited since they have been shown to only work for short periods and are not effective for all patients. In addition, many of these treatments have side effects that restrict their use. Hydroxychloroquine is commonly used to treat inflammatory arthritis, such as rheumatoid arthritis, to great effect. It has very few side effects. Recent studies suggest that inflammation is also important in OA, and that by reducing inflammation pain will also be reduced. We believe that hydroxychloroquine may be an effective treatment for reducing inflammation in hand OA and that this reduction in inflammation will lead to a reduction in pain. The primary aim of this study is to determine whether hydroxychloroquine is effective at relieving pain in people with painful hand OA. The secondary aim of the study is to determine whether hydroxychloroquine is able to slow or stop the damage to joints caused by OA. The third aim of the study is to determine whether people with more arthritis-related inflammation in their hand (detected by ultrasound imaging) respond better to treatment with hydroxychloroquine.

Who can participate?
People with hand OA from across England. Participants must have moderate to severe painful hand OA that is not responding to their current treatment. In addition, they must have evidence of damage to their joints that is typical of OA – which is detected using an X-ray. There are no age restrictions.

What does the study involve?
Participants will be randomly allocated to one of two groups – the first group will take hydroxychloroquine tablets for 12 months and the second group will take a placebo (dummy) tablet for 12 months. Participants and the researchers running the study will not know which group they are allocated to. Both groups will be allowed to continue taking any other medication for their hand OA that they are using at the start of the study. During the 12 months of the study participants will be asked to attend a special clinic three times for about 1 hour (in addition to a screening visit during which eligibility is assessed) and will be asked to fill in a number of questionnaires and complete a number of hand function tests. At the end of the study we will analyse the change in pain scores between the two groups to determine whether hydroxychloroquine is effective at reducing the painful symptoms of hand osteoarthritis. We will also assess whether hydroxychloroquine improves hand function and slows down the structural damage to the hand joints which is associated with OA.

What are the possible benefits and risks of participating?
You may not benefit directly from this study. However, the trial will give us useful information which may be of benefit to others in the future and aid the development of treatment for OA. The main risk involved in taking part is potential side-effects associated with hydroxychloroquine. Hydroxychloroquine has been used for many years and is relatively safe, with side effects being unlikely. In a small minority of people it can be associated with skin rashes, indigestion, diarrhoea, headaches or blurred vision. Very rarely hydroxychloroquine may damage the retina (part of the eye), but it is important to note that damage to the eye is associated with a cumulative dose of more than 500 g, equivalent to taking the trial medication for 3.4 years. In the duration of this study, the total hydroxychloroquine dose will remain well below this level. To minimise any risk of visual complications participants will be asked about visual impairment (not corrected by glasses) and their eyesight (with glasses where appropriate) will be recorded using a standard reading chart. It is standard practice for all patients taking hydroxychloroquine to have regular blood tests. These are to check that there are no changes to your liver or kidney function during the study. This is not because taking hydroxychloroquine will damage your liver or kidney, but because if you develop liver or kidney problems during the study for another reason, we would need to stop your study medication. We will therefore ask participants to have a blood test before the study, and at 6 and 12 months. There is also a very small risk associated with having hand x-rays for the study. Having an X-ray of each hand will expose you to a small amount of radiation (roughly comparable to the amount of background radiation received in the UK every month). Participants will have an X-ray of each hand at the start and end of the study. The lifetime risk of inducing a fatal cancer in a healthy individual with this dose of radiation is low, about 1 in 500,000.

Where is the study run from?
University of Leeds, Leeds Institute of Rheumatic Musculoskeletal Medicine, Chapel Allerton Hospital (UK)

When is the study starting and how long is it expected to run for?
The study is expected to start in September 2012 and will run for about two and a half years. The trial will recruit participants for about a year and a half.

Who is funding the study?
Arthritis Research UK

Who is the main contact?
Dr Sarah Kingsbury
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Contact information

Type(s)
Scientific

Contact name
Prof Professor Philip Conaghan

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Additional identifiers

Protocol serial number
RR10/9390

Study information

Scientific Title
Hydroxychloroquine Effectiveness in Reducing symptoms of hand Osteoarthritis: a randomised, double-blind, placebo-controlled trial

Acronym
HERO

Study objectives
Recent studies indicate that synovitis (inflammation in the joints) is prevalent in osteoarthritis (OA) and is associated with pain in knee and hand OA. Hydroxychloroquine is used in routine practice at treating synovitis in inflammatory arthritides such as rheumatoid arthritis, is widely used anecdotally as a treatment for OA and has been shown to be effective at reducing pain. Hydroxychloroquine has an excellent safety profile, with toxicity generally associated with sustained periods of use that due to the natural history of hand OA are unlikely to be an issue. We propose that treating patients with moderate to severe OA hand symptoms with hydroxychloroquine will be a practical and safe treatment to reduce synovitis and therefore reduce pain.

The trial will aim to address the following questions:
1. Is hydroxychloroquine an effective analgesic treatment for OA?
2. Is hydroxychloroquine cost effective?
3. What is the time course for symptomatic relief with hydroxychloroquine?
4. Does hydroxychloroquine treatment provide any long term structural benefit?

Ethics approval required
Old ethics approval format

Ethics approval(s)
Leeds (East) Research Ethics Committee, 01/05/2012, ref: 12/YH/0151

Study design
Interventional randomised double-blind placebo-controlled multi-centre trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Hand osteoarthritis

Interventions
Patients will be randomised in a 1:1 ratio to one of two groups:

Hydroxychloroquine used in combination with drugs licensed for use in pain management of OA; with choice of drugs and doses determined by clinicians for individual participants.

Placebo group used in combination with drugs licensed for use in pain management of OA; with choice of drugs and doses determined by clinicians for individual participants.

Dosage will be as follows:
1. Participants with an ideal body weight of 30 - 45 kg will be prescribed one capsule with 200 mg hydroxychloroquine (or placebo) as a daily single dose (mean daily dose of 200 mg)
2. Participants with an ideal body weight of 46 - 61 kg will be prescribed one capsule with 200 mg HCQ (or placebo) as a single dose on day 1 and two capsules with 200 mg HCQ (or placebo) as single dose on day 2 (mean daily dose of 300 mg)
3. Participants with an ideal body weight of ≥ 62 kg will be prescribed two capsules with 200 mg HCQ (or placebo) as a single dose (mean daily dose of 400 mg)

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome(s)
Average overall hand pain severity over the past 2 weeks (0-10 numerical rating scale) at 6 months.

Key secondary outcome(s))

Structural assessment at baseline and 12 months:
Bilateral hand X-ray

Self-reported questionnaires at baseline, 3, 6 and 12 months:
1. AUSCAN (pain, stiffness and function) 5-point likert scale
2. 11-point Numerical Rating Scales (NRS) and VAS scales for
3. Average overall hand pain severity/pain in the most painful joint over the past 2 weeks/2 days*
4. NRS scales for
5. Global disease activity/average thumb pain/average pain in other joints over the past 2 days
6. Satisfaction with hand function over the past 2 days
7. Hand pain/aching/stiffness over the last month (no days-all days)

Self-reported questionnaires at baseline, 6 and 12 months:
1. Quality of life using SF12v2 and OAQoL
2. EuroQol EQ-5D
3. HADS

Self-report measures at 3, 6 and 12 months:
1. Global* improvement in hand problem
2. Global* improvement in hand pain
3. Global* improvement in ability to use hands
*A 6-point likert scale: completely better, much better, better, no change, worse, much worse

Baseline measures:
1. Pain elsewhere (pain manikin)
2. Duration of hand pain over the past 12 months (<7 days, 1-4 weeks, >1 month, <3 months, >3 months)
3. Onset of hand pain (last 12 months, 1-5 years, 5-10 years, 10 years or more)
4. Ultrasound synovitis score

Clinical measures (baseline, 6 and 12 months):
1. Grip strength (JAMAR)
2. Joint count

Removed as of 05/09/2016:
Severity rating of participant nominated main functional problem over the past 2 days

Completion date
30/03/2015

Eligibility

Key inclusion criteria
1. Patient-reported inadequate response/toxicity to their existing medication (to include paracetamol, oral NSAID or opioid)
2. Moderately severe symptoms (≥4/10 on a 0-10 visual analogue scale) at screening
3. Symptoms for more than half of days in the last 3 months
4. Fulfil the American College of Rheumatology criteria for OA
5. Radiograph of the hands in the past 5 years with changes consistent with OA
6. No change in the average weekly dose of analgesics (including NSAIDs) for at least 4 weeks
7. Has used chondroitin or glucosamine for at least 4 months with no change to the average

weekly dose, is not using or is willing to stop using if recently started
8. Be able to adhere to the study visit schedule and other protocol requirements
9. Capable of giving informed consent and the consent must be obtained prior to any screening procedures

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
248

Key exclusion criteria
Current exclusion criteria as of 25/08/2016:
1. Presence of inflammatory arthritis (e.g. gout, reactive arthritis, rheumatoid arthritis, psoriatic arthritis, seronegative spondylarthropathy, Lyme disease) or fibromyalgia
2. Evidence of psoriasis
3. OA of the 1st CMC joint and no symptomatic OA in other hand joints
4. Oral, IM, IA, or IV steroids or other anti-synovial agents during the last 2 months
5. Any new hand OA treatment in the previous 2 months, including physiotherapy and provision of new hand splint
6. Planned hand surgery in the next 6 months
7.Sensitivity, anaphylaxis or allergy to hydroxychloroquine or any other 4-aminoquinoline compound
8. Unexplained visual impairment that is not corrected by glasses or presence of any eye problems
9. Pregnant or lactating
10. Use of any investigational (unlicensed) drug within 1 month prior to screening or within 5 half-lives of the investigational agent, whichever is longer
11. Evidence of serious uncontrolled concomitant medical condition, including cardiovascular, nervous system, pulmonary, renal, hepatic, endocrine, GI disease or epilepsy, which in the opinion of the investigator makes them unsuitable for the study
12. Uncontrolled disease states, such as moderate/severe asthma or inflammatory bowel disease, where flares are commonly treated with oral or parenteral corticosteroids
13 .Melanoma or non-skin cancer in the past 3 years
14. IA hyaluronans to the hand joints within the last 6/12
15. Intolerance to lactose
16. Significant haematological or biochemical abnormality
16.1. Haemoglobin < 8.5 g/dL
16.2. WCC < 3.5 x 109/L
16.3. Neutrophils < 1.5 x 109/L

16.4. Platelets < 100 x 109/L
16.5. ALT > 2 times ULN for the laboratory conducting the test
16.6. Creatinine > 1.5 times ULN for the laboratory conducting the test

Previous exclusion criteria:
1. Presence of inflammatory arthritis (e.g. gout, reactive arthritis, rheumatoid arthritis, psoriatic arthritis, seronegative spondylarthropathy, Lyme disease)
2. Evidence of plaque psoriasis
3. OA of the 1st CMC joint and no symptomatic OA in other hand joints
4. Oral, IM, IA, or IV steroids during the last 2 months
5. Any new hand OA treatment in the previous 2 months, including physiotherapy and provision of new hand splint
6. Planned hand surgery in the next 6 months
7. Sensitivity, anaphylaxis or allergy to hydroxychloroquine or any other 4-aminoquinoline compound
8. Unexplained visual impairment that is not corrected by glasses or presence of any eye problems
9. Pregnant or lactating
10. Use of any investigational (unlicensed) drug within 1 month prior to screening or within 5 half-lives of the investigational agent, whichever is longer
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Date of first enrolment
01/09/2012

Date of final enrolment
30/03/2015

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Chapel Allerton Hospital
Leeds
United Kingdom
LS7 4SA

Sponsor information

Organisation
University of Leeds (UK)

ROR
https://ror.org/024mrxd33

Funder(s)

Funder type
Charity

Funder Name
Arthritis Research UK (UK) ref: 19545

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Not provided at time of registration

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	20/03/2018		Yes	No
Results article	Cost-effectiveness	17/08/2021	24/01/2023	Yes	No
Protocol article	protocol	02/03/2013		Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes