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To determine the effectiveness of amitriptyline compared to placebo in the management of moderate to severe HIV related peripheral neuropathy.

Submission date
06/11/2014

Recruitment status
No longer recruiting

Registration date
17/11/2014

Overall study status
Completed

Last Edited
15/05/2015

Condition category
Nervous System Diseases

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

Plain English summary of protocol

Background and study aims
The peripheral nervous system is part of the nervous system that is made up of the nerves and ganglia (group of nerve cells) outside of the brain and spinal cord (the central nervous system). It connects the central nervous system to the limbs and organs of the body. Damage to peripheral nerves, especially the long nerves of the feet and hands, is common in people infected with HIV. This damage may be caused by the virus itself, some of the antiretrioviral drugs used to treat HIV /AIDS, or as a result of opportunistic infections, for example thrush, herpes and tuberculosis. The nerve damage is often painful, can have a detrimental effect on a person's quality of life and has significant socioeconomic effects. Unlike other types of peripheral neuropathy (e.g., the neuropathy that develops in people with diabetes mellitus), there are, as yet, no effective treatments for painful HIV neuropathy. Here, we want to see if amitriptyline, an antidepressant drug that has been shown to relieve pain in other types of neuropathy, can provide pain relief better than that of a placebo (a dummy pill) in patients with painful HIV neuropathy.

Who can participate?
Adult HIV-infected individuals that have been diagnosed with painful HIV-associated sensory neuropathy. Participants must either be on stable antiretroviral therapy or have never been exposed to antiretroviral therapy for HIV infection.

What does the study involve?
HIV-positive patients attending clinics at Chris Hani Baragwanath Hospital, Soweto, South Africa and that can walk are randomly allocated to receive amitriptyline (25 mg) or a placebo for six weeks. The drug/placebo dose is increased every three days over the first two weeks of the treatment until participants achieve pain relief, intolerable side effects, or a maximum dose of 150 mg per day. The trial drug and the placebo are identical in appearance. Participants visit the study centre every three weeks to receive their medication and to record a pain score. At the end of the first six-week period, participants are taken off their assigned medication for a three-week 'washout' period. After this washout period, those participants who receive amitriptyline

before are now given the placebo and vice versa for another 6 weeks. Dose titration and pain assessments will follow the same protocol used in the first six-week period.

What are the possible benefits and risks of participating?
Some participants may achieve meaningful pain relief when receiving amitriptyline, a drug recommended as first-line therapy for other types of painful peripheral neuropathy. However, any positive results of this study will mostly benefit the large population of HIV-infected patients with painful peripheral neuropathy, for which there are no proven treatments. Risks of participating in the trial include side-effects of the medication, typically sedation, dry mouth and difficulty urinating.

Where is the study run from?
Nthabiseng HIV Clinic and the Centre for Palliative Care, Chris Hani Baragwanath Hospital, Soweto, (South Africa)

When is the study starting and how long is it expected to run for?
April 2009 to April 2010

Who is funding the study?
The Diana Princess of Wales Memorial Fund (UK)

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
Double blind randomised controlled trial to assess the effectiveness of amitriptyline compared to placebo in the management of moderate to severe HIV related peripheral neuropathy.

Study objectives
Amitriptyline is superior to placebo in the management of moderate to severe HIV related peripheral neuropathy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Human Research Ethics Committee, University of the Witwatersrand, South Africa, 16/09/2014, ref: M080709

Study design
Placebo-controlled double-blind crossover group randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Pharmacological management of painful neuropathy

Interventions
All study participants will receive amitriptyline (titrated to efficacy, side effects or a maximum dose of 150 mg daily) or inert placebo in random order for 6 weeks, with a three-week washout period between interventions.

Intervention Type
Drug

Phase

Not Applicable

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

Primary outcome measure
Self-reported pain intensity, assessed on an 11-point numerical pain rating scale.

Secondary outcome measures
1. Pain interference on activities of daily living, assessed using the pain interference sub-scale of the Brief Pain Inventory
2. Physical symptoms, psychological, emotional and spiritual, and information and support needs, assessed using the African Palliative Care Outcomes Scale (APOS)

Primary and secondary outcomes were measured at baseline, three and six weeks for each of the two intervention periods. Across the duration of the study, that represents measurements at 0, 3, 6, 9, 12, and 15 weeks on each participant.

Overall study start date
01/04/2009

Completion date
30/04/2010

Eligibility

Key inclusion criteria
1. Confirmed and documented HIV positive status, either on Arv therapy or not on ARV therapy
2. Diagnosed with moderate to severe peripheral neuropathy using the BPNS and DN4 screening tools and scoring >/= 4 on an 11 point Likert scale visual analogue scale
3. Age above 18 on the date of recruitment
4. Ability to mentally and physically understand to make informed choice to participate in the study

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
124

Key exclusion criteria

All conditions which are likely to cause confounding will be excluded from the study, together with
conditions which are likely to cause drug interactions.
1. Severe pain from DSN caused by ARV drugs which warrants a change in regime
2. Already taking amitriptyline drug, or has taken the drugs at least three weeks prior
3. Limb amputation
4. Kaposi sarcoma of the lower limbs
5. Current post-herpetic neuralgia or herpes zoster
6. Pregnancy or intention to fall pregnant
7. TB treatment
8. Malignancy not related to HIV
9. Major psychiatric disorders including mania or epilepsy
10. Clinically significant renal failure
11. Diabetic neuropathy
12. Clinically significant liver failure or past history as defined by encephalopathy, oedema and jaundice
13. Patient in extreme pain or exhausted
14. Participating on another trial or study
15. MAOI, other tricyclic antidepressants or anti-epileptic drugs
16. Recent myocardial infarction, arrhythmias, heart block
17. History of urinary retention, urinary hesitancy or closed angle glaucoma

Date of first enrolment
01/04/2009

Date of final enrolment
30/04/2010

Locations

Countries of recruitment
South Africa

Study participating centre
86, 14th Street
Johannesburg
South Africa
2193

Sponsor information

Organisation
Diana Princess of Wales Memorial Fund (UK)

Sponsor details

The Royal Foundation of The Duke and Duchess of Cambridge and Prince Harry
Kensington Palace
Palace Green
London
United Kingdom
W8 4PU

Sponsor type
Charity

Funder(s)

Funder type
Charity

Funder Name
Diana Princess of Wales Memorial Fund (UK)

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	14/05/2015		Yes	No