ISRCTN15330757 https://doi.org/10.1186/ISRCTN15330757

A randomised, crossover, double blind comparison of the analgesic effect and patient tolerability of nabilone and dihydrocodeine in chronic neuropathic pain

Submission date
23/07/2007

Registration date
12/09/2007

Last Edited
18/01/2008

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Signs and Symptoms

[_] 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

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
CL0014 Version 5

Study information

Scientific Title

Study objectives
To compare the efficacy and tolerability of nabilone with dihydrocodeine when used in the treatment of neuropathic pain based upon the following null hypotheses:
1. The analgesic activity of nabilone is not different from that of dihydrocodeine when used in the treatment of neuropathic pain over a six-week period
2. The patient tolerability of nabilone is not different from that of dihydrocodeine when used in the treatment of neuropathic pain over a six-week period
3. The antidepressant effect of nabilone is not different from that of dihydrocodeine when used in the treatment of neuropathic pain over a six-week period
4. Anxiety reducing effects of nabilone are not different from dihydrocodeine when used in the treatment of neuropathic pain over a six-week period

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval received from:
1. South Tees Local Research Ethics Committee on the 20th April 2001 (ref: 00/53)
2. West Ethics Committee Glasgow on the 23rd November 2001 (ref: 01/95)
3. Newcastle and North Tyneside Joint Ethics Committee on the 20th June 2001 (ref: 2000/137)

Study design
Randomised, double blind, crossover trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Mixed neuropathic pain

Interventions

The medication was given in identical tablets either containing 240 µg nabilone or 30 mg dihydrocodeine. The dose schedule was one capsule in the first week, two capsules in the third week, four capsules in the third and fourth week and then eight capsules in week five and six. After a two week washout the treatment was crossed over. If there were side effects the dose was not increased further. During the washout rescue medication in the form of eight tablets 30 /500 codeine with paracetamol was permitted. So each treatment arm was six weeks with a two week washout after six weeks and in the end. Patients with benefit went then into the open label trial (see ISRCTN38408594: A one year open label assessment of the use of nabilone in the treatment of chronic neuropathic pain). Visual Analogue Scale (VAS) scores and hours slept were recorded in a diary daily and then averaged per week. Only pain scores for the last two weeks were used for the analyses.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Nabilone, dihydrocodeine

Primary outcome measure
Mean pain score as measured by VAS 0 - 10 for the last two weeks on treatment.

Secondary outcome measures
1. Sleep was measured as hours slept and if the sleep was interrupted or not in the diary
2. Depression and anxiety were measured with the Hospital Anxiety and Depression Score (HAD) at baseline and after each treatment period
3. Quality of life was measured with the 36-item Short Form questionnaire (SF-36) at baseline and after each treatment period
4. Six psychometric tests were performed at baseline and after each treatment period on a Apple Newton device
5. Side effects were assessed every two weeks with a eight-point questionnaire rating the severity of the side effects on a five point scale plus a field for open comments

Overall study start date
01/07/2001

Completion date
15/11/2002

Eligibility

Key inclusion criteria
1. Patients entering the study will be recruited following written informed consent from pain clinics at participating centres
2. Patients will be in the age range 18 - 90 years with a diagnosis of neuropathic pain made according to the criteria set out below
3. Patients may be taking stable dose regimens of paracetamol, anticonvulsants, antidepressants, opioids or Non-Steroidal Anti-Inflammatory Srugs (NSAIDs)

4. Patients taking excluded medications (see exclusion criteria below) may enter the study after a two week period without these medications

Diagnosis of neuropathic pain:
The term "neuropathic pain" is loosely applied to a variety of heterogeneous conditions and strict diagnostic criteria are difficult to apply. However, for the purposes of this study, the diagnosis will be made on the basis of the following:
1. Pain secondary to an identifiable injury or disease process where damage to the central or peripheral nervous system is suspected
2. Pain persisting for more than three months in the absence of any continuing nociceptive stimulus
3. Pain that is documented as responding poorly to either opioid analgesics or NSAIDs
4. Pain associated with at least two of the following signs/symptoms:
4.1. Abnormal sensation on clinical examination, including sensory loss, paraesthesia, dysaesthesia
4.2. Mechanical allodynia (static or dynamic)
4.3. Pain of a burning character
4.4. Pain of a stabbing or lancinating character
4.5. Signs of sympathetic dysfunction (discolouration, abnormal vasomotor activity, skin trophic changes)

Many conditions may present with neuropathic pain. However, in some conditions the distinction between primary nociceptive and neuropathic pain is extremely difficult. An important example of this is in mechanical low back pain where radiation of pain into the legs is commonly reported in the absence of identifiable nerve injury. Given this diagnostic difficulty, for the purpose of this study, patients with lumbar radiculopathy will not be recruited to the study.

The Central Post-Stroke Pain Syndrome seems to have features that are significantly different to other types of neuropathic pain. For this reason, patients with this syndrome will not be included in this study.

Participant type(s)
Patient

Age group
Not Specified

Sex
Not Specified

Target number of participants
100

Key exclusion criteria
Patients may not enter the study if they have a history of any of the following conditions:
1. Epilepsy
2. Liver disease
3. Psychosis
4. Bipolar disorder
5. Substance misuse

6. Renal failure
7. Adverse reactions to either dihydrocodeine or nabilone
8. Pregnant women, lactating women or women of childbearing potential not using effective methods of contraception
9. Patients involved in ongoing legal action against a third party in which financial compensation is being sought for personal injury alleged to be the cause of the presenting condition

Excluded medications:
Patients may not take the following medications during the study:
1. Dihydrocodeine
2. Antipsychotic drugs
3. Benzodiazepine drugs (excepting stable doses of night-time sedatives)
4. Monoamine oxidase inhibitors

Patients taking dihydrocodeine may enter the study after a washout period of two weeks. Analgesia during this time will be provided with co-proxamol. Patients taking cannabinoid preparations of any kind may not be included in the study.

Date of first enrolment
01/07/2001

Date of final enrolment
15/11/2002

Locations

Countries of recruitment
Australia

United Kingdom

Study participating centre
Pain Management Unit
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Australia
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Sponsor information

Organisation
Cambridge Laboratories Ltd (UK)

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Sponsor type
Industry

Website
http://www.camb-labs.com/index.html

ROR
https://ror.org/001zd1d95

Funder(s)

Funder type
Industry

Funder Name
Cambridge Laboratories Ltd (UK) - supported by a grant

Funder Name
The sponsors/funders had no role in study design, data collection, data analysis, data interpretation, or writing of the report

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	26/01/2008		Yes	No