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Efficacy of memantine in the treatment of fibromyalgia

Submission date	Recruitment status	[X] Prospectively registered
25/06/2012	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
03/08/2012	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
21/01/2019	Musculoskeletal Diseases	

Plain English summary of protocol

Background and study aims
Fibromyalgia is a long-term condition that causes pain all over the body. No effective treatments have been found so far. There is a need to develop of new and more effective treatments for fibromyalgia. New research has highlighted memantine's effectiveness at pain reduction with an extremely low incidence of side effects, even with prolonged use. The aim of this study is to assess the effectiveness of memantine in the treatment of fibromyalgia.

Who can participate?
Patients aged between 18 and 65 with fibromyalgia.

What does the study involve?
Participants are randomly allocated into two groups. One group is treated with memantine and the other group is treated with placebo (dummy) tablets. There are four visits during the study: at the start of the study, month 1, month 3 and month 6. During these visits patients fill in several questionnaires. At the start of the study and month 6 patients undergo brain scans.

What are the possible benefits and risks of participating?
Not provided at time of registration.

Where is the study run from?
Miguel Servet University Hospital & University of Zaragoza (Spain).

When is the study starting and how long is it expected to run for?
September 2012 to May 2013.

Who is funding the study?
Ministry of Health, Social Policy and Equality (Spain).

Who is the main contact?
Dr José Javier García Campayo

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
2011-006244-73

Protocol serial number
EC11-387

Study information

Scientific Title
Efficacy of memantine in the treatment of fibromyalgia: a double-blind randomised controlled trial

Acronym
NAP

Study objectives
Recent studies have demonstrated elevated levels of glutamate in different brain areas such as insula, hippocampus and posterior cingulate cortex in patients with fibromyalgia, suggesting the possibility of using N-Methyl-D-Aspartate Receptor (NMDAR) antagonist such as memantine in the treatment of this disorder. NMDAR antagonists possess significant pain-reducing and neuroprotective properties and are widely used in clinical practice. Dextromethorphan and ketamine have shown particular pain-reducing efficacy in fibromyalgia syndrome (FMS), although their use as longitudinal treatments is limited. New research has highlighted memantines effectiveness in the treatment of complex regional pain syndrome and phantom limb pain, suggesting that its quality of pain reduction is dependent on the type of pain being treated. Memantine exhibited an extremely low incidence of side effects in human clinical trials, and a recent trial extension demonstrated the drugs clinical tolerability even with prolonged use.

No effective treatments for fibromyalgia have been described. This is the first pharmacological treatment for fibromyalgia based on the physiopathology of the disorder. Previous preliminary studies of our group with memantine showed significant improvements in cognitive function, depression and global clinical impression.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Committee in Aragon (CEICA), 06/03/2012

Study design
Unicentric double-blind randomised trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Fibromyalgia

Interventions
Sample size for this study is 60 subjects recruited in the Mental Health Unit-Primary Care Center "Torrero" in Zaragoza. Patients will be randomly assigned to one of this groups:
1. Treatment group. Patients allocated to this group will receive 20 mg memantine daily (2 tablets of 10 mg each)
2. Control group. Patients in this group will receive placebo.

The dose of 20 mg will be reached following this schema:
1st week: 5 mg daily
2nd week: 10 mg daily
3rd week: 15 mg daily
From 4th week up to 24th week: 20 mg daily

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome(s)
Improvement in clinical variables:
1. Pain threshold
2. Pain perception
3. Cognitive state
4. Health status
5. State of anxiety and depression
6. Quality of life and
7. Perceived improvement

Key secondary outcome(s))

Glutamate levels in different brain regions (insula, hippocampus and posterior cingulate cortex) assessed by Magnetic Resonance Spectroscopy (MRS) and by Quantitative Encephalography and Electroencephalic Cordance on a subsample of 30 subjects (15 from the control group and 15 from the treatment group).

Completion date
31/05/2013

Eligibility

Key inclusion criteria
1. Male or female aged between 18 and 65 years
2. Ability to understand Spanish
3. Diagnosis of fibromyalgia carried out by a rheumatologist according to the American College of rheumatology criteria (ACR1990)
4. Ability to read and understand the Patient Information Sheet
5. Signature of Informed Consent Form
6. In the case of women of childbearing age, commitment not to become pregnant during the entire duration of the study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Undergoing drug treatment for fibromyalgia. Patients in current treatment for fibromyalgia will stop treatment and perform a washout period of one week. During that week the patient may take, if necessary, analgesics such as tramadol or paracetamol to minimise the influence of medication on brain imaging.
2. Currently taking memantine or having taken memantine during the 2 months prior to recruitment
3. Another Axis I psychiatric disorder using Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) that might hinder adherence to the protocol (e.g.: dementia, alcohol and/or substance abuse/dependence, schizophrenia, chronic delirium, acute depression)
4. Pregnancy or breast-feeding
5. Hypersensitivity to the active ingredient, memantine, or to the excipients
6. Medical conditions that require special precautions when administering memantine according to the summary of product characteristics:
6.1. Epilepsy

6.2. Circumstances that may cause high urine pH owing to Proteus urinary infection, renal tubular acidosis or vegetarian diet, recent myocardial infarction, congestive heart disease and uncontrolled arterial hypertension
7. Clinically significant and active evidence of liver or kidney disease, haematological, respiratory, endocrine or cardiovascular disease or disorders (patients with controlled diabetes and patients with controlled hypertension and complete or incomplete right bundle branch block can be included in the study)
8. Use of prescription drugs that may cause relevant drug interactions with memantine according to the summary of product characteristics: NMDAR antagonists (amantadine, ketamine, dextromethorphan), L-Dopa, dopamine agonists and cholinergic agonists.
9. Use of non-permitted concomitant medication during the week prior to the first evaluation visit or where the patient is expected to require treatment (with at least one of the drugs not permitted during the study): antidepressants (duloxetine, venlafaxine, mirtazapine, bupropion, SSRI, etc.), analgesics (pregabalin, gabapentin, opiates, etc.)

Date of first enrolment
01/09/2012

Date of final enrolment
31/05/2013

Locations

Countries of recruitment
Spain

Study participating centre
Miguel Servet University Hospital & University of Zaragoza
Zaragoza
Spain
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Sponsor information

Organisation
Aragon Institute of Health Sciences (Instituto Aragonés de Ciencias de la Salud) (IACS) (Spain)

ROR
https://ror.org/05p0enq35

Funder(s)

Funder type

Government

Funder Name
Ministry of Health, Social Policy and Equality (Spain)

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	01/12/2014	21/01/2019	Yes	No
Protocol article	protocol	03/01/2013		Yes	No