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Vortioxetine versus other antidepressants in the treatment of Burning Mouth Syndrome

Submission date
21/05/2020

Recruitment status
No longer recruiting

Registration date
25/05/2020

Overall study status
Completed

Last Edited
16/08/2021

Condition category
Digestive System

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

Plain English summary of protocol

Background and study aims
Burning Mouth Syndrome (BMS) is a condition that causes a painful, burning or tingling sensation in the mouth. There may also be a change in the taste in the mouth or a dry mouth. Episodes of these sensation changes may occur for several hours every day for months or longer. BMS is most common in adults over the age of 60 years. Some causes of BMS include reactions to medication or dental hygiene products, the hormonal changes in menopause, allergies, thyroid problems, acid reflux, diabetes, thrush, and sometimes the cause is unknown. It is thought that antidepressants have been shown to be effective in the treatment of patients with BMS.

This study aims to compare how effective and well-tolerated the antidepressant Vortioxetine is for the treatment of patients with Burning Mouth Syndrome when compared to different antidepressants. The study will look at how well participants' symptoms of BMS respond to the treatments, if any side effects occur and how acceptable the treatment is. The study aims to determine which should be considered the first choice in the treatment of BMS.

Who can participate?
Adult patients with Burning Mouth Syndrome.

What does the study involve?
Participants will be randomly allocated to receive one of 5 antidepressant medications for 12 weeks to treat their Burning Mouth Syndrome. At the start of the study and after 2, 4, 6, and 12 months participants will be invited to an appointment where the health of their mouth will be evaluated by they will be invited to complete some questionnaires about their symptoms.

What are the possible benefits and risks of participating?
Side effects that may occur with the use of these medications include nausea, abdominal pain, dry mouth, dizziness, drowsiness, weight gain, increased appetite, sexual dysfunction, and vivid dreams. Participants will be encouraged to inform the investigators if these occur or other reactions occur and, if needed, the therapy will be discontinued.

Where is the study run from?
Federico II University of Naples (Italy)

When is the study starting and how long is it expected to run for?
September 2018 to February 2020

Who is funding the study?
This study is investigator-initiated and funded

Who is the main contact?
Dr Daniela Adamo
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
Which is the best? Vortioxetine versus other antidepressants in the treatment of Burning Mouth Syndrome: an open-label randomized active-controlled 12-month trial

Acronym
VO in BMS

Study objectives
To compare the efficacy and tolerability of Vortioxetine (15 mg/daily) with different antidepressants in the treatment of patients with Burning Mouth Syndrome (BMS)

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 22/01/2019, Ethical Committee of the University of Naples Federico II (Via Pansini 5, Naples, 80100 Italy; +39 817463468), ref: 20/19

Study design
Open-label prospective randomized interventional single-centre study

Primary study design
Interventional

Secondary study design
Randomised parallel 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 participant information sheet

Health condition(s) or problem(s) studied
Burning Mouth Syndrome

Interventions
Age and sex-matched participants will be randomly assigned to 5 study groups in a ratio of 1:1:1:1:1.
1. Vortioxetine (VO) group where patients treated with Vortioxetine (15mg /daily)
2. Paroxetine (P) group where patients treated with Paroxetine (20mg/ daily)
3. Sertraline (S) group which included patients treated with Sertraline (50mg/ daily)
4. Escitalopram (E) group which included patients treated with Escitalopram (10mg/ daily)
5. Duloxetine (D) group which included patients treated with Escitalopram (60mg/ daily)

All of the Antidepressants will be administered at a fixed dose for 12 months, by the multidisciplinary team of physicians. A half dosage will be used for the first week and up-titrated until the therapeutic dosage in the second week of the treatment. The dosage of the ADs is chosen in line with the optimal dosage considered in the treatment of major depression in terms of efficacy, acceptability, and tolerability.

At admission the following information was recorded: age, gender, educational level (in years), marital status, job status, social habits, disease onset (in years), social habits, oral symptoms, systemic diseases, and drug consumption.

The patients were observed for 12 months after enrollment, attending a total of five appointments: baseline (time 0) and after 2 (time 1), 3 (time 2), 6 (time 3), and 12 (time 4) months post-baseline. At each of these appointments, all the patients will be evaluated by a multidisciplinary team composed of an oral medicine specialist and a psychiatrist with a documented experienced in the treatment of chronic orofacial pain.

Each BMS patient will undergo an intra- and extra-oral examination, complete workup (blood tests and electrocardiogram), and a psychiatric evaluation. The neuropsychological evaluation will be completed with the following battery scales:
1. The Visual Analogue Scale (VAS) and the Total Pain Rating Index (T-PRI) from the Short Form of the McGill Pain Questionnaire (SF-MPQ) for the assessment of oral discomfort, intensity, and quality of pain
2. The Hamilton Rating Scale for Anxiety (HAM-A) for the assessment of anxiety
3. The Hamilton Rating Scale for Depression (HAM-D) for the assessment of depression
4. The Clinical Global Impression Severity of Illness (CGI-S) index for the assessment of the severity of the disease at baseline evaluating the patient's level of distress (namely, the intensity or severity of the symptoms) and the impact of the illness on functioning (namely, the effect of the symptoms on functioning in major areas of the patient's life: work, home, school, and relationships)
5. The Clinical Global Impression Improvement scale (CGI-I) for the assessment of the global improvement of the patient after the beginning of the AD (namely, a comparison of the patient' s baseline condition with his/her current condition)
6. The Clinical Global Impression Efficacy Index (CGI-E) for the assessment of the efficacy of the AD (namely, a comparison of the patient's baseline condition with a ratio of the current therapeutic benefit to the severity of AEs)

All these scales will be reviewed for completeness before collection and were administered in their Italian version by a single clinician in order to reduce inter-individual variability of judgment.

Moreover, a sleep quality assessment will be performed by means of an analysis of specific items of the HAMD at baseline and after 2, 4, 6, and 12 months of treatment. In addition, the time taken to fall asleep, the number of hours of sleep nightly, and the occurrence of awakenings will be evaluated through a structured interview with the participants at baseline and after 2, 4, 6, and 12 months of treatment.

The safety profile of the antidepressants will be evaluated at each appointment. The patients will be asked to report the occurrence of specific adverse events associated with each antidepressant. Any adverse events will be recorded at each appointment and only in case of serious and long-lasting AEs was the therapy discontinued. The cases without any improvement after six months will be considered as non-responders to the intervention and the therapy will be changed. These participants will then be excluded from the study.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Vortioxetine, paroxetine, sertraline, escitalopram, duloxetine

Primary outcome measure
1. Efficacy of Vortioxetine and other antidepressants, measured using:
1.1. Intra- and extra-oral examination baseline and after 2, 3, 6, and 12 months
1.2. The Visual Analogue Scale (VAS) at baseline and after 2, 4, 6, and 12 months
1.3. The Total Pain Rating Index (T-PRI) at baseline and after 2, 4, 6, and 12 months
1.4. The Hamilton Rating Scale for Anxiety (HAM-A) at baseline and after 2, 4, 6, and 12 months
1.5. The Hamilton Rating Scale for Depression (HAM-D) at baseline and after 2, 4, 6, and 12 months
1.6. The Clinical Global Impression Improvement scale (CGI-I) at 6 and 12 months
1.7. The Clinical Global Impression Efficacy Index (CGI-E) at 6 and 12 months
Calculated as the percentage of patients who showed a remission or a response, at 6 months and 12 months. Clinical remission to treatment was defined as: the absence of any oral symptoms, or occasional and very limited oral symptoms, at the time with VAS score between 0 and 2 and T-PRI score between 0 and 5; HAM-A and HAM-D scores ≤ 7; and CGI-I and CGI-E scores of 1. Clinical response to treatment was defined as: an improvement in the oral symptoms, which were still present with a reduction of the scores of VAS and T-PRI of > 50%; a reduction of the scores of the HAM-A and HAM-D by > 50%, or HAM-A and HAM-D scores ≤ 7; and CGI-I score between 1 and 2 and CGI-E scores between 1 and 2 or between 5 and 6.
2. Occurrence of specific adverse events for Vortioxetine and other antidepressants measured as a percentage of patients who reported AEs over the trial period, at 2, 4, 6, and 12 months

Secondary outcome measures
1. Drop out measured as the percentage of patients who left the trial early due to any reason up to the end of the study duration, recorded at the time of drop out by 12 months
2. Drop out due to adverse events (tolerability) measured as the percentage of patients who left the trial early due to adverse events, recorded at the time of drop out by 12 months

Overall study start date
01/09/2018

Completion date
28/02/2020

Eligibility

Key inclusion criteria
1. Aged ≥18 years
2. Continuous symptoms of oral burning or pain persisting for at least two hours per day, lasting for longer than three months, with no paroxysms and not following any unilateral nerve trajectory
3. No clinical mucosal alterations
4. Normal blood test findings (including blood count, blood glucose, serum iron, ferritin and transferrin, folic acid and vitamin B12 levels)
5. Body Mass Index (BMI) of <30
6. No previous treatment with systemic psychotropic drugs

Participant type(s)

Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
150 (30 for each group)

Total final enrolment
150

Key exclusion criteria
1. Pregnant or breastfeeding
2. Suffering from diseases that could be recognized as a causative factor of BMS
3. Unable to understand the questionnaires
4. History of a psychiatric disorder or suffering from a degenerative and progressive neurological disease
5. Undergoing treatment with a psychotropic drug
6. Previously treated with an antidepressant
7. History of alcohol or substance abuse

Date of first enrolment
01/02/2019

Date of final enrolment
01/02/2020

Locations

Countries of recruitment
Italy

Study participating centre
Federico II University of Naples
Via Sergio Pansini, 5
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Sponsor information

Organisation
University of Naples Federico II

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Sponsor type
Hospital/treatment centre

Website
http://www.unina.it/index.jsp

ROR
https://ror.org/05290cv24

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Publication and dissemination plan
Planned publication in an international journal

Intention to publish date
20/09/2020

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from dott. Daniela Adamo, at danielaadamo.it@gmail.com, in the form of an Excel file. All participants provided their written informed consent.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/05/2021	16/08/2021	Yes	No