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The anti-migraine activity of supplement formulation PEATONIDE® combining palmitoylethanolamide and melatonin

Submission date
25/06/2024

Recruitment status
No longer recruiting

Registration date
06/08/2024

Overall study status
Completed

Last Edited
06/08/2024

Condition category
Nervous System Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Migraine represents a severe neurological condition, causing significant debilitation and pain for about 15% of the global population. As reported by the International Classification of Headache Disorders, episodic migraine manifests as acute headaches occurring on 14 or fewer days per month, while chronic migraines entail experiencing headaches on 15 or more days within a month. Migraine significantly affects the quality of life, ranking among the top 20 causes of disability in the adult population according to the World Health Organization. Despite the considerable impact on quality of life and decline in work performance and productivity, migraine often goes undiagnosed and untreated. Palmitoylethanolamide (PEA) and melatonin are thought to have anti-migraine activity through a synergistic effect leading to a reduction of vasodilation and thus the symptoms associated with migraine. This study aims to determine the effect and safety of treatment with a combination of hydrodispersible PEA and melatonin, as a supplement called PEATONIDE®, once a day in patients with episodic migraine, assessing both the duration and intensity of migraine attacks and the incidence of events and associated disability symptoms.

Who can participate?
Patients including both men and women aged 18 years old and over, with a diagnosis of episodic migraine (with or without aura) for at least one year before recruitment according to IHS-3 criteria and at least two migraine attacks for at least three months before recruitment.

What does the study involve?
Participants in the study will be given a supplement called PEATONIDE®, containing 1200 mg of hydrodispersible PEA and 0.2 mg of melatonin, or a placebo, to be taken orally every evening at bedtime for three months. During the study, participants will be allowed to use only acetaminophen and NSAIDs for acute migraine relief, with no other preventive or acute treatments permitted. Patients will record their migraine experiences in a daily headache diary, noting the number of migraine days per month, days using analgesics, intensity and duration of attacks, level of disability, presence of aura, and associated symptoms such as nausea, vomiting, sensitivity to light (photophobia), and sensitivity to sound (phonophobia). The intensity and

disability of migraine attacks will be rated on a 10-point and a 3-point Likert psychometric scale scale, respectively.

What are the possible benefits and risks of participating?
Possible beneficial effects include the reduction of the number of monthly migraine attacks, the reduction of duration and intensity of migraine attacks, the reduction of the amount of medication for migraine management, and the reduction of the symptoms associated with migraine. Patients will be monitored for vital signs and adverse events to assess tolerability and safety.

Where is the study run from?
National Institute of Biostructures and Biosystems Inter-university Consortium (Istituto Nazionale Biostrutture e Biosistemi Consorzio Interuniversitario; I.N.B.B. Consortium)

When is the study starting and how long is it expected to run for?
February 2023 to April 2024

Who is funding the study?
Erbozeta S.p.A.

Who is the main contact?
Professor Giancarlo Tenore (University of Naples Federico II, Department of Pharmacy), giancarlo.tenore@unina.it

Contact information

Type(s)
Public, Scientific, Principal Investigator

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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
Anti-migraine activity of supplement formulation (PEATONIDE®) based on the synergic combination of palmitoylethanolamide and melatonin

Acronym
AMSPM

Study objectives
Migraine pathophysiology is associated with mast cells, which act as the immediate call-center of the neuroimmune system. They represent both the source and target of several neuropeptides which are involved in migraine inflammatory process (e.g., histamine, serotonin, NO, prostaglandins, and leukotrienes). Therefore, mast cell degranulation inhibitors represent an innovative therapeutic approach for the prevention of migraine attacks. It was well reported that palmitoylethanolamide (PEA) and melatonin could contrast the immune response by down-regulating mast-cell degranulation. Therefore, the combination of the two molecules could increase the potential anti-migraine activity through a synergistic effect leading to a reduction of vasodilation and thus the symptoms associated with migraine.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 20/09/2023, Azienda sanitaria locale Napoli 1 Centro (Via Comunale del Principe, 13/a, Napoli, 80145, Italy; +39 0812541111; comitatoetico@aslnapoli1centro.it), ref: 1644

Study design
Monocentric randomized placebo-controlled two parallel-arm study

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
University/medical school/dental school

Study type(s)
Treatment

Participant information sheet

Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Treatment of migraine attacks in subjects affected by episodic migraine (with or without aura)

Interventions
All included patients are treated with a formulation consisting of 1200 mg of hydrodispersible PEA and 0.2 mg of melatonin (PEATONIDE®) or with a placebo by oral administration taken every evening at bedtime for 3 months. The evaluation of migraine is based on the filling out of a daily headache diary. The headache diaries are administered during the two cycles of 4-week run-in periods and for three monthly cycles of treatment. After the two-month run-in period, the patients are randomly assigned to placebo or treated (PEATONIDE®) groups for the next three cycles. Participants will be randomised by the drawing of envelopes containing randomisation numbers. The random number list will be generated by an investigator with no clinical involvement in the trial.

Data from the second cycle of the 4-week run-in period are averaged and served as baseline values. In the run-in and treatment cycles, the following variables are collected: number of days per month with migraine in the previous month; number of days per month taking any analgesic for migraine in the previous month; intensity, duration and grade of disability of migraine attacks; presence of aura; presence of associated symptoms (nausea, vomiting, photophobia, and phonophobia). The intensity and disability of migraine attacks are rated on a 10-point and a 3-point Likert scale, respectively.

Intervention Type
Supplement

Primary outcome measure
Migraine frequency (days of migraine attacks per month) comparing the two-month run-in with the three-month treatment cycles measured using a headache diary daily

Secondary outcome measures
The following secondary outcome variables are assessed during the two-month run-in and the three-month treatment cycles:
1. The intensity of migraine attacks measured using a 10-point Likert scale for each migraine attack
2. Duration of migraine attacks measured in hours for each migraine attack
3. Grade of disability of migraine attack measured using a 3-point Likert scale for each migraine attack
4. The amount of analgesics used during migraine attacks measured as dose unit for each migraine attack

Overall study start date
27/02/2023

Completion date
16/04/2024

Eligibility

Key inclusion criteria
1. Aged 18 years old and over
2. Diagnosis of episodic migraine (with or without aura) for at least one year before recruitment according to IHS-3 criteria
3. At least two migraine attacks for at least three months before recruitment

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
60

Total final enrolment
60

Key exclusion criteria
1. Inconsistent supplement intake
2. Regular uptake of analgesic drugs for more than 12 days per month
3. Treatment with other supplements, or drugs, potentially having preventive effects on migraine

Date of first enrolment
16/10/2023

Date of final enrolment
16/11/2023

Locations

Countries of recruitment
Italy

Study participating centre
Istituto Nazionale Biostrutture e Biosistemi Consorzio Interuniversitario
Viale Maria Bakunin, 41
Napoli
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Sponsor information

Organisation
Erbozeta S.p.A.

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Sponsor type
Industry

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Funder(s)

Funder type
Industry

Funder Name
Erbozeta S.p.A.

Results and Publications

Publication and dissemination plan
Planned publication in a peer-reviewed journal

Intention to publish date
29/07/2024

Individual participant data (IPD) sharing plan
The datasets generated during the current study will be available upon request from Professor Giancarlo Tenore (University of Naples Federico II, Department of Pharmacy), giancarlo.tenore@unina.it. The data available are files (format Word) containing migraine diaries filled out by patients during the clinical trial. The timing for availability is 2 weeks. Consent from participants was required and obtained.

IPD sharing plan summary

Available on request