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Vaginal diazepam plus Transcutaneous Electrical Nerve Stimulation: a powerful synergy to treat vestibulodynia

Submission date
13/08/2016

Recruitment status
No longer recruiting

Registration date
24/08/2016

Overall study status
Completed

Last Edited
29/01/2019

Condition category
Urological and Genital Diseases

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

Plain English summary of protocol

Background and study aims
Vulvodynia is a persistent, unexplained pain in the vulva (the skin around the entrance to the vagina). Symptoms include a burning or stinging pain that can be triggered by touch, for example when having sex or using a tampon. It may be focused on part of the vulva or be more widespread, with pain in the buttocks and inner things. It often occurs in women that are otherwise healthy.
Pelvic floor muscle dysfunction (for example, abnormal tightening of the muscles) is present in a significant number of women with vulvodynia. It is possible that there is a link between increased mucosal sensitivity (sensitivity of the inner lining of the vagina) and the underlying muscles leading to compensatory contracture (muscle contraction) and hypertonicity (muscle spasms). This may result in pain. Conversely, underlying pelvic floor muscles dysfunction may lead to mucosal sensitivity. Transcutaneous electrical nerve stimulation (TENS) can be used to treat pain. This treatment involves using a machine to deliver a mild electrical current to the painful area. Diazepam is a drug known to treat muscle spasms. The aim of this study is to combine the use of TENS with diazepam inserted into the vagina to treat vulvodynia.

Who can participate?
Adult women with Vulvodynia.

What does the study involve?
Patients are randomly and assigned into one of two groups. Those in group 1 are given a diazepam vaginal tablet with instructions to insert one a day, before going to sleep, for the next 60 days. They also receive TENS therapy. Those in group 2 are given a dummy tablet with instructions to insert one a day, before going to sleep, for the next 60 days. They also receive TENS therapy. All patients are then assessed to see whether both their pain levels and pelvic floor muscle measurements have improved.

What are the possible benefits and risks of participating?
Possible benefits include pain relief and improvements in pelvic floor muscle dysfunction. No adverse side effects are expected.

Where is the study run from?
V. Buzzi Hospital-Milan (Italy)

When is the study starting and how long is it expected to run for?
March 2016 to September 2016

Who is funding the study?
Italian Vulvodynia Association

Who is the main contact?
Dr Filippo Murina
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
ICP-1345/2016

Study information

Scientific Title
Vaginal diazepam plus Transcutaneous Electrical Nerve Stimulation - a powerful synergy to treat vestibulodynia: a randomized controlled trial

Study objectives
The aim is to investigate the effectiveness of vaginal diazepam in addition to Transcutaneous Electrical Nerve Stimulation (TENS) on the treatment of vestibulodynia (VBD); we believe that the synergy of the effect of the two therapies as a multimodal treatment strategy, would improve both vulvar pain and pelvic floor muscle dysfunction.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Institutional Review Board of V. Buzzi Milan (Italy), 30/10/2015, ref:.N. 1345/2016

Study design
A double-blind placebo-controlled randomised controlled study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Vestibulodynia, localised provoked vulvodynia at the vestibule

Interventions
Patients were randomly and blindly assigned into one of two groups to receive diazepam or placebo vaginal tablet. Identical vaginal tablet containing 5 mg of diazepam or placebo, were received from the manufacturer in separated boxes with the same color and they were random numbered, by staff not participating in the study, in a pharmacy outside the hospital. Investigators were blinded to the randomization code until all data were analyzed. The vaginal tablet containing equal parts of diazepam and placebo (cornstarch) were placed in plastic bags and randomly distribute to patients enrolled in the study. Both diazepam and placebo formulations used an identical lactose monohydrate and cellulose microcrystalline composition, commonly used for vaginal tablet and absorption of the base was previously evaluated optimal.

Before randomization, patients were asked to stop any topical or systemic therapy they were taking.
Treatment instructions were to insert one vaginal tablet daily, before going to sleep, for 60 days. This time of administration was chosen to avoid any theoretical sedative effects from the diazepam.
All patients received TENS therapy in a self-administered domiciliary protocol. A dual channel portable TENS unit (NeuroTrac Continence; VerityMedical, London, UK) was used, which produces a symmetrical biphasic wave and has three customizable mode programs.The stimulationwas delivered through a commercially available plastic vaginal probe (Periprobe VAG2ST Beac, Pavia, Italy), 20 mm in diameter and 110 mm in length, with two gold metallic transversal rings as electrodes. It was inserted into the vagina for 20 mm.

Two customized programs were set according to results from previous studies. The standard protocol for TENS was 15 minutes of 100-Hz frequency and pulse duration of 50 microseconds (first program), followed by 15 minutes of 5-Hz frequency and pulse duration of 100 microseconds (second program). All patients received a supervised trial before using the TENS at home. The trial consisted in 6 to 7 sessions and served to familiarize the patient on use of TENS, while allowing the therapist to check that the patient was using the device properly. In the TENS treatment protocol, the pulse is increased rapidly until the patient reports the onset of any sensation under the electrodes. The intensity is then increased slowly until this sensation

reaches a level described as the maximum tolerable, without experiencing pain. After completing the trial, the patient is consigned their TENS unit after verbal and written instruction, with a recommendation to perform home treatment 3 times each week.

Intervention Type
Mixed

Primary outcome(s)
Pain modification, assessed using VAS and Dispareunya score

Measured from baseline to 60 days

Key secondary outcome(s))
Modification of pelvic floor muscle measurements, via assessment of variation in pelvic floor muscles parameters and vestibular nerve fibers current perception threshold

Completion date
01/09/2016

Eligibility

Key inclusion criteria
1. Diagnosis of Vestibulodynia (VBD)
2. At least 18 years of age
3. Diagnosed with moderate or severe pelvic floor tone hypertonic disfunction

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Female

Key exclusion criteria
1. Allergy to diazepam or any benzodiazepine
2. Currently pregnant
3. Have any contraindication to diazepam

Date of first enrolment
01/03/2016

Date of final enrolment

01/04/2016

Locations

Countries of recruitment
Italy

Jamaica

Study participating centre
V. Buzzi Hospital-Milan
Italy
20124

Sponsor information

Organisation
Italian Vulvodynia Association (Associazione Italiana Vulvodinia)

ROR
https://ror.org/03kj3qm29

Funder(s)

Funder type
Charity

Funder Name
Italian Vulvodynia Association (Associazione Italiana Vulvodinia)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?

Results article	results	01/09/2018	29/01/2019	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes