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Genetic predisposition of patients with vestibulodynia (chronic pain around the opening of the vagina): a case-control study

Submission date
10/07/2023

Recruitment status
No longer recruiting

Registration date
29/07/2023

Overall study status
Completed

Last Edited
24/07/2023

Condition category
Urological and Genital Diseases

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

Plain English summary of protocol

Background and study aims
Vulvodynia is a highly prevalent form of chronic genital pain in women, to such an extent that prevalence studies estimate ranges from 10% to 28% in reproductive-aged women. Localized provoked vulvodynia at the vestibule, known as vestibulodynia (VBD), is the most common manifestation of the disease (about 80%). Women with VBD often describe vulvar pain as burning, stinging, irritation, rawness, and dyspareunia (difficult or painful intercourse). VBD represents a summation and overlapping of various trigger factors (infections, hormonal disturbances, allergies, genetic aspects, psychological vulnerability, and others) with weight and predominance varying from patient to patient. The study aims to develop a specific test to identify earlier the most susceptible subjects to develop VBD and build a preventive strategy to avoid the development and/or chronicity of the disease. Further, data will be obtained to cluster patients to tailor the most appropriate treatment.

Who can participate?
Adult patients with VBD aged 18 to 45 years old compared with a healthy control group

What does the study involve?
Outcomes include features and correlations in VBD patients in comparison with the control group using:
1. Shallow whole genome sequencing of DNA obtained from a blood sample
2. Vestibular microbiome asset obtained from a vestibular sample

What are the possible benefits and risks of participating?
Participants may benefit from the future development of a specific test to identify the most susceptible subjects earlier and from the preventive strategy to avoid the development and/or chronicity of the disease. Patients will also benefit from being clustered into groups for the most appropriate treatment. There are no risks of participating in the study. The vestibular sample is related to vaginal secretion for microbiome analysis and is not a biopsy.

Where is the study run from?
Lower Genital Tract Disease Unit, Vittore Buzzi Hospital (Italy)

When is the study starting and how long is it expected to run for?
March 2023 to September 2023

Who is funding the study?
Associazione Italiana Vulvodinia, a non-profit Italian association whose mission is to improve the health and quality of life of women experiencing vulvodynia and chronic vulvar pain (Italy)

Who is the main contact?
Prof Filippo Murina, filippo.murina@unimi.it

Contact information

Type(s)
Principal investigator

Contact name
Prof Filippo Murina

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Additional identifiers

Protocol serial number
SDSM-2022-01.1

Study information

Scientific Title
Genomic evaluation of patients with vestibulodynia: a case-control study

Acronym
VeGA Study (Vestibulodynia-Genomic-Assessing)

Study objectives

The Research Hypothesis for the present study is to prospectively compare four main parameters that we consider essential in developing vestibulodynia (VBD):
1. Increased sensitivity to pain
2. Inflammatory state
3. Hormonal asset
4. Microbiological pattern
Our aim is to develop a specific test to identify the most susceptible subjects who develop VBD earlier and build a preventive strategy to avoid the development and/or chronicity of the disease. Furthermore, an objective is to collect data in order to cluster patients and customize the most suitable treatment for each individual.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 03/05/2023, V. Buzzi Hospital (Via Castelvetro 24, Milan, 20124, Italy; +39 (0) 257995420; info@asst-fbf-sacco.it), ref: 112/VT/2023

Primary study design
Observational

Study design
Case-control study

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Localized provoked vulvodynia at the vestibule, known as vestibulodynia (VBD)

Interventions
This is a case-control study in women with vestibulodynia (VBD). All women aged 18 years and before menopause, (cessation of menstruation for 12 months) with VBD that will present to our unit on lower genital tract disease will be invited to participate. The control group will include healthy fertile asymptomatic women without any vulvovaginal conditions that will attend the study hospital for cervical cancer screening programs. It is expected this investigator-initiated research study will be completed approximately 6 months following initial approval by the Institutional Ethical Board.

The study team will analyze DNA obtained from a blood sample of patients with VBD compared with a healthy control group, using the technique of Shallow Genome Sequencing (SGS), which is a new and high-throughput technology to achieve genome-wide single nucleotide polymorphisms (SNPs) genetic variation accurately.

Evaluation of current perception threshold (CPT) is a technique which quantifies the sensitivity of vestibular nerve fibers. The CPT values will be measured using the Neurometer CPT/C electrodiagnostic neurostimulator (Neurotron, Inc., Baltimore, MD), which emits constant alternating sinusoid waveform current stimuli at frequencies of 2000 Hz (specific for large, myelinated Ab fibers), 250 Hz (specific for Ad fibers), and 5Hz (specific for C fibers), at intensity levels from 0.001 to 9.99mA.

Clinical procedures:
Candidates for enrollment will be screened within 15 days prior to enrollment. Before initiation of any test procedures, Subjects will be fully informed of the study plan, procedures, and risks involved in participating in the study. Each potential Subject will be required to read and indicate her understanding by signing and dating the ICF prior to the initiation of any screening procedures. Screening procedures will consist of the following:
- Physical examination and medical history will be collected
- Evaluation of symptoms: 0–10-point visual scale (VAS) related to dyspareunia and vulvovaginal pain/burning, only in the VBD group
- Vulvoscopy with an evaluation of vestibular cotton swab test
- Taking blood samples for DNA analysis (about 3ml)
- Taking vaginal secretion at the vestibular site for microbiome analysis
- Assessment of vestibular CPT evaluation using the Neurometer CPT/C, electrodiagnostic neurostimulator
- Vestibular mucosa thickness performed by ultrasound measurements (B-Scan) with a 20 MHz validated system (Derma Scan C, Cortex Technology, Denmark), producing cross-sectional images of the skin down to a depth of approximately 15 mm
- Assessment of vaginal EMG measurements, collected at states of rest and during several exercises of the pelvic floor through an EMG device with a vaginal sensor (Myotonus plus©-London-UK)

Intervention Type
Genetic

Primary outcome(s)
1. DNA patterns obtained from a blood sample measured using Shallow Genome Sequencing at baseline
2. Vestibular microbiome asset obtained from a vestibular sample measured using complex analysis using 16sRNA technique at baseline

Key secondary outcome(s)
1. Vulvar vestibule current perception threshold (CPT) values (1=0.01 mA) measured using a G-trode Vaginal/Rectal Electrode (Neurotron, Inc., Baltimore, MD) at baseline
2. Vestibular mucosa thickness measured using ultrasound measurements (B-Scan) with a 20 MHz validated system (Derma Scan C, Cortex Technology, Denmark), producing cross-sectional images of the skin down to a depth of approximately 15 mm at baseline
3. Vaginal electromyography (EMG) measured at rest and during several exercises of the pelvic floor using an EMG device with a vaginal sensor (Myotonus plus©-London-UK) at baseline

Completion date
15/09/2023

Eligibility

Key inclusion criteria
1. Women aged at least 18 years old and before menopause (absence of menstruation for 12 months)
2. Experience moderate to severe pain (minimum of 5/10 on a numerical rating scale in at least 90 % of attempted sexual intercourse) for the VBD group
3. Pain limited to the vestibule during vaginal intercourse and during activities exerting pressure

on the vestibule (tampon insertion, tight jeans or pants, cycling, horseback riding) for VBD group
3. Presence of VBD for at least 3 months and diagnosed according to the standardized gynecological examination protocol by one of our staff gynecologists
4. Have a stable sexual partner (sexual activity should include some attempted vaginal penetrations to evaluate pain intensity)
5. Subject is willing to attempt sexual activity between visits
6. Read and signed informed consent

Participant type(s)
Healthy volunteer, Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
45 Years

Sex
Female

Key exclusion criteria
1. Active vulvovaginal infections at the time of their gynecological examination
2. Genital bleeding of unknown origin
3. Unwillingness to provide informed consent to the trial
4. Women with concomitant vulvar dermatosis or other vulvar disorders
5. Symptoms or signs in the past related to VBD, only for the Control group

Date of first enrolment
15/05/2023

Date of final enrolment
30/08/2023

Locations

Countries of recruitment
Italy

Study participating centre
V.Buzzi Hospital
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Sponsor information

Organisation
Associazione Italiana Vulvodinia Onlus

ROR
https://ror.org/03kj3qm29

Funder(s)

Funder type
Research organisation

Funder Name
Associazione Italiana Vulvodinia

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Prof Filippo Murina, filippo.murina@unimi.it. Overall data and statistical analysis will be available from October 2023. Consent from participants will be required and obtained.

IPD sharing plan summary
Stored in non-publicly available repository, Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file			24/07/2023	No	No