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Is neuromodulation with botulinum toxin type A an alternative treatment for chronic anal fissure?

Submission date
14/02/2024

Recruitment status
No longer recruiting

Registration date
16/02/2024

Overall study status
Completed

Last Edited
02/10/2024

Condition category
Digestive System

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

Plain English summary of protocol

Background and study aims
An anal fissure (AF) is a tear in the skin of the anal canal and is the most common cause of pain during defecation. Whereas acute AF is usually superficial and tends to spontaneously resolve, chronic AF lasts for more than 6 weeks and is characterized by exposed internal anal sphincter (IAS) muscle, anal papilla and a skin tag or pile. Botulinum toxin type A (BT) local injection is considered when topical treatment fails. BT reduces anal sphincter tone at rest and reduces pain. The effects begin 3 to 4 days after injection and fade gradually during the third or fourth month. Therefore, the main aim of this study was to evaluate the healing rate of AF with incobotulinumtoxinA (incoBoNT/A) at 2 years.

Who can participate?
Patients older than 18 years with a clinical AF diagnosis for over 2 months who had not responded to previous treatments of dietary and behavioral changes, painkillers, and local treatment with diltiazem or trinitrate glyceryl

What does the study involve?
Patients were treated with local incoBoNT/A injection with a follow-up of 24 months. Healing and improvement rates, pain perception, incontinence, quality of life and safety were assessed.

What are the possible benefits and risks of participating?
The possible benefits are healing, clinical improvement and pain reduction. The risks are the possible adverse effects associated with the use of botulinum toxin, such as constipation with increased pain after bowel movements, hyperemia (increased blood flow), inflammatory polyps (growths), subfissural fistulas (abnormal opening in the skin near the anus), thrombosis (blood clots) and haematoma (collection of blood).

Where is the study run from?
Nuestra Señora del Prado Hospital (Spain)

When is the study starting and how long is it expected to run for?
February 2017 to June 2023

Who is funding the study?
The data analysis and medical writing were supported by unrestricted funding from Merz Pharmaceuticals GmbH (Germany)

Who is the main contact?
Dra. A. Teresa Calderón Duque, ttcd01@gmail.com

Contact information

Type(s)
Public, Scientific, Principal Investigator

Contact name
Dr Teresa Calderón

ORCID ID
http://orcid.org/0000-0001-7428-0314

Contact details
Nuestra Señora del Prado Hospital
Talavera de la Reina, Toledo
Spain
45600
+34 (0)652928109
teresac@sescam.jccm.es

Additional identifiers

EudraCT/CTIS number
2017-001216-11

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
FISAN-BOT-2017-01

Study information

Scientific Title
Utility of botulinum toxin type A in the treatment of chronic anal fissure

Study objectives
To assess the cure rate of chronic anal fissure with botulinum toxin at 2-year follow-up.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 21/04/2017, Clinical Research Ethics Committee of the Talavera de la Reina Integrated Health Area (Hospital Nuestra Señora del Prado. Ctra. Nacional V, km 114, Talavera de la Reina, Toledo, 45600, Spain; +34 (0)925803600 (Ext: 86 316); varroyo@sescam.org), ref: 11/2017

Study design
Prospective open-label single-arm single-center study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Chronic anal fissure

Interventions
Patients were treated with local incoBoNT/A injection to heal anal fissure with a follow-up of 24 months at the Hospital Nuestra Señora del Prado (Talavera de la Reina, Spain)

A vial of 50 U of BT free from complexing proteins (IncoBoNT/A; Xeomin®, Merz Pharmaceuticals GmbH) was diluted in 1.25 ml normal saline, and three syringes were filled with 0.4 ml each (16 U). Patients were placed in the lithotomy position and pretreated with topical local anesthesia (prilocaine/lidocaine cream 25 mg/g each). A total of 48 U incoBoNT/A was injected per patient at three sites (16 U each): both laterals and the posterior intersphincteric groove. After injection, patients were discharged after verifying that there were no complications.

Intervention Type
Procedure/Surgery

Primary outcome measure
Healing rate at 2 years. Healing was defined as scarred AF and without symptoms; improvement was considered when the fissure persisted without symptoms; failure presented persistent fissure and symptoms. Patients who required a surgical approach were considered as a failure. Healing/improvement was assessed at 1 week, 1 month, 3 months, 6 months, 1 year, and 2 years post-injection.

Secondary outcome measures
1. Anal manometry assessment of the internal anal sphincter (IAS) to measure anal resting pressure, voluntary squeeze pressure and pressure during the Valsalva maneuver. IAS pressures were measured using the THD® Anopress system (mmHg) at baseline and at 1 and 3 months post-injection.
2. Pain perception was measured using a pain visual analog scale (VAS) (scoring between 0 [no pain] and 10 [severe pain]) at baseline, 1 month, 3 months, 6 months, 1 year, and 2 years post-injection. Pain perception was also measured at 1 week.
3. Incontinence was measured using the Wexner score (scoring between 0 [no incontinence] and 20 [total incontinence]) at baseline, 1 month, 3 months, 6 months, 1 year, and 2 years post-injection
4. Quality of life was assessed with the SF-36 questionnaire (scoring between 0 [worst health status] and 100 [best health status]) at baseline and 3 months post-injection

Overall study start date
01/02/2017

Completion date
01/06/2023

Eligibility

Key inclusion criteria
1. Aged over 18 years
2. Clinical anal fissure diagnosis for over 2 months that had not responded to previous treatments consisting of dietary and behavioral modifications, analgesics, and local treatment with calcium channel blocker (diltiazem 2%) or nitrates (trinitrate glyceryl 0.4%)

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
55

Total final enrolment
49

Key exclusion criteria
1. Non-idiopathic anal fissures
2. Previously untreated patients

3. BT contraindication such as miastenia gravis, Eaton-Lambert syndrome, pregnancy, and acetylcholine deficiency

Date of first enrolment
28/09/2017

Date of final enrolment
07/03/2022

Locations

Countries of recruitment
Spain

Study participating centre
Hospital Nuestra Señora del Prado
Ctra. Nacional V, km 114
Talavera de la Reina, Toledo
Spain
45600

Sponsor information

Organisation
Hospital General Nuestra Señora del Prado

Sponsor details
-
Talavera de la Reina, Toledo
Spain
45600
+34 (0)925803600
ttcd01@gmail.com

Sponsor type
Hospital/treatment centre

Website
http://www.areasaludtalavera.es/

ROR
https://ror.org/00k5pj069

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Funder Name
Merz Pharmaceuticals GmbH

Results and Publications

Publication and dissemination plan
Once they have the results of the study, the researchers intend to publish an article with the results and present them at national congresses.

Intention to publish date
01/06/2024

Individual participant data (IPD) sharing plan
The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request (Teresa Calderón Duque, ttcd01@gmail.com).
The type of data that will be shared: All the individual participant data collected during the trial, after deidentification.
Dates of availability: Immediately after publication.
Whether consent from participants was required and obtained: All study participants provided informed consent.
Comments on data anonymization: Information concerning the identity of patients will be kept confidential for all purposes. The identity of the patients will not be disclosed or divulged. Patient data collected in the investigator's brochure during the study should be documented in an anonymous and dissociated manner, linked to a code (case number) so that only the investigator can associate such data with an identified or identifiable clinical history. In the data collection forms, patients will be identified by a numerical code. The database generated by the study will not contain any identification of the patient, other than the numerical code by which it will not be possible to reveal the patient's identity.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		30/09/2024	02/10/2024	Yes	No