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Postoperative pain following hemorrhoid removal surgery using a regional nerve block anesthesia with and without nerve stimulation

Submission date
27/01/2023

Recruitment status
No longer recruiting

Registration date
09/02/2023

Overall study status
Completed

Last Edited
28/03/2023

Condition category
Other

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

Plain English summary of protocol

Background and study aims
Hemorrhoidal disease (HD) is the progressive transformation of normal structures into pathological ones by mechanical, vascular and muscular factors. At least 5% of the general population manifests symptoms related to this pathology and many predisposing factors have been evaluated, although constipation is the most commonly implicated factor. The most frequent symptom is rectal bleeding (rectorrhagia) and having a good clinical history and a thorough physical examination including anoscopy is essential to establish a correct diagnosis. In approximately 80% of the cases, the treatment of hemorrhoidal disease is exclusively medical. In cases refractory to such treatment and in cases of grade III and grade IV hemorrhoids there are numerous options both ambulatory and surgical. The most effective treatment is surgery but it causes a high rate of postoperative pain according to studies at 24h after surgery and is therefore the most feared complication by patients. There are several studies which have found reduced postoperative pain using a regional nerve block with a local anesthetic, local infiltration of anesthetics or the use of fentanyl transdermal patches. The pudendal nerve block with local anesthetic is a well-known and effective alternative for pain control used in some urological, gynecological, prostate and pain medicine procedures.

The ultimate goal of any regional block technique is to deposit the local anesthetic, in sufficient volume and concentration, as close as possible to the nerve or nerves to be blocked. The use of a peripheral nerve stimulator (PNS), or neurostimulator, is a current alternative to other methods of nerve location and identification. This auxiliary method is used to locate the motor component of one or more peripheral nerves through the administration of a direct electric current. The pudendal nerve block guided by anatomical references has been shown to be useful in the control of postoperative pain after hemorrhoidectomy, although the use of the neurostimulator has not been well studied. The main objectives of the study are to compare pain in the immediate postoperative period (24h) after hemorrhoidectomy in patients with pudendal nerve block guided by anatomical landmarks and guided by neurostimulation.

Who can participate?
Adult patients with hemorrhoids refractory to medical treatment

What does the study involve?
Patients with suspected hemorrhoidal pathology were evaluated in the general and digestive surgery office as usual and those with indication for hemorrhoidectomy were included in the surgical waiting list according to the usual criteria, evaluating symptomatology, examination, response to conservative treatment and complementary tests if necessary, as had been done previously. Colonoscopy was performed in those patients older than 40 years with a history of bleeding as recommended by the American College of Surgeons. Once included in the waiting list, patient have a second preoperative consultation performed by the principal investigator or the research team.

What are the possible benefits and risks of participating?
Patients in whom a neurostimulation-guided pudendal nerve block is performed after hemorrhoidectomy present less pain in the postoperative period than those in whom it is guided only by anatomical references. As it is performed according to standard clinical practice, there is no increased risk associated with the study. The expected complications are the same as those that occur during a conventional hemorrhoidectomy with pudendal infiltration.

Where is the study run from?
The Colorectal Surgery Unit of the General and Digestive Surgery Service of the Hospital Nuestra Señora de Candelaria) (Spain)

When is the study starting and how long is it expected to run for?
September 2019 to August 2022

Who is funding the study?
Investigator initiated and funded (Spain)

Who is the main contact?
Ana Soto Sanchez, asotsan@gobiernodecanarias.org (Spain)

Contact information

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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

Clinical trial for the effectiveness of pudendal nerve block with and without neurostimulation for the reduction of posthemorroidectomy pain

Study objectives
Patients in whom a neurostimulation-guided pudendal nerve block is performed after hemorrhoidal surgery have less postoperative pain than those in whom it is guided only by anatomical landmarks.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 17/10/2022, Hospital Nuestra Señora de Candelaria Ethics Committee (Crta. Rosario nº 145 38010 Santa Cruz de Tenerife; +34922602000; ceichunsc.scs@gobiernodecanarias.org), ref: 0VFjn4BZB6y9BQkGc9AivjydYiwp_4wi0

Study design
Randomized single-center triple-blind efficacy study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See trial outputs table

Health condition(s) or problem(s) studied
Postoperative pain in hemorrhoidectomy

Interventions
The present project proposes the performance of a single-center, triple-blind, randomized clinical trial of efficacy, carried out under conditions of routine clinical practice.

The pudendal nerve is mixed, 70% of its fibers are somatic and 30% are autonomic. Three branches of the nerve have been described: The perineal branch which is divided into superficial and deep produce the sensory innervation of the lower third of the vagina and urethra, the posterior portion of the skin of the perineum scrotum, labia majora and labia minora. The dorsal branch of the penis/clitoris provides sensory innervation to the erectile tissue of the corpus cavernosum and crus of the penis/clitoris and the skin covering the dorsolateral aspect of the glans penis and penis/clitoris. The inferior rectal branch produces the sensory innervation of the perianal skin, the caudal third of the rectum and the posterior part of the vulva, but it is also the branch that produces the motor innervation of the levator ani muscle and the external sphincter of the anus. However, numerous studies have described a great anatomical variability of this

nerve, which may mean that infiltration according to anatomical references may sometimes be ineffective. In the anatomical descriptions in the literature, it has been seen that the nerve can present as a single trunk (53.3%), as two trunks (36.7%) and as three trunks (6.7%).

Others found the pudendal nerve as one trunk (56.2%), two trunks (31.5%) and three trunks (12.3%). In addition, further anatomical investigations found that in most cases the perineal branch and the rectal branch come from a common trunk. The ultimate goal of any regional block technique is to deposit the local anesthetic, in sufficient volume and concentration, as close as possible to the nerve or nerves to be blocked. The use of a peripheral nerve stimulator (PNS), or neurostimulator, is a current alternative to other methods of nerve location and identification. This auxiliary method is used to locate the motor component of one or more peripheral nerves through the administration of a direct current, whose frequency (Hz), intensity (mA) and duration (msec), depending on the device, are varied by the operator. The electric current flows between the positive and negative electrodes of the circuit. Between them, and under their influence, the nerve is interposed. Depending on the distance at which the electric field is located at the tip of the negative stimulating electrode (represented by a needle insulated with Teflon), the amount of electricity and the stimulation threshold of each nerve, depolarisation and an action potential will be produced or not, which will generate a muscular contraction and movement of different intensity. Thus, the action performed is a motor nerve stimulation which in our case will involve a contraction of the external anal sphincter and the objective is therefore the location of the nerve. The pudendal nerve block guided by anatomical references has been shown to be useful in the control of postoperative pain after hemorrhoidectomy, although the use of the neurostimulator has not been well studied and we believe that it can improve the results.

Randomization
Randomization will be performed by means of a sequence of random numbers generated computerized with the statistical package Stata 13.0. According to this list, patients will be assigned to the pudendal nerve block group guided by anatomical references or guided by neurostimulation. This sequence will be available in the operating room of the center in closed envelopes where the intervention of the patients will be performed so that it can be used by the members of the research team after finishing the surgery.

Masking
The participating subject, the observing researcher and the researcher analyzing the data are unaware of the treatment received.

Study Population
The reference population to which the results of the present study are intended to be applied are all those patients with hemorrhoids refractory to medical treatment, grade III-IV symptomatic hemorrhoids and grade II hemorrhoids that do not respond to conservative procedures (hemorrhoidal ligation/sclerosis) and who meet the criteria for major ambulatory surgery (MOS). Therefore, we intend to take a sample based on the following inclusion and exclusion criteria.

Selection Period
The study will be carried out in the Colorectal Surgery Unit of the General and Digestive Surgery Service of the Hospital Nuestra Señora de Candelaria. Patients with suspected hemorrhoidal pathology will be evaluated in the general and digestive surgery office as usual and those with an indication for hemorrhoidectomy will be included in the surgical waiting list according to the usual criteria, evaluating symptomatology, examination, response to conservative treatment and complementary tests if necessary, as was previously done. Colonoscopy will be performed in

those patients over 40 years of age with a history of bleeding as recommended by the American College of Surgeons.

Once included in the waiting list, they will have a second consultation prior to the procedure. The principal investigator or her research team will inform the patient about the study and offer to participate in it. If the patient accepts, he/she will sign the informed consent form. After this, a standardized clinical history will be taken and the patient will await the date of the intervention after a pre-anesthetic assessment for surgery in AMC.

Perioperative and Intraoperative
All non-allergic patients will be administered in the operating room:
Paracetamol 1g iv
Dexketoprofen 25mg iv
Ondansetron 8mg
Metoclopramide 10mg
Methylprednisolone 0,5 mg/kg
Amoxicillin 2g iv

Surgery will be performed under general anesthesia with orotracheal intubation or laryngeal mask at the discretion of the anesthesiologist and 2g iv of metamizole will be administered during surgery.

The surgery will be performed in a prone or supine position according to the surgeon's indications and will be performed according to the Ferguson technique leaving the skin half open and suturing with vicryl 3/0 and prior submucosal infiltration of the hemorrhoid to be treated with bupivacaine 0.25 with a vasoconstrictor.

The intervention will be performed by one of the colorectal surgeons belonging to the research team except for Dr Ferrer Vilela who will be in charge of the postoperative follow-up at 24h and 7 days blindly (without knowing the patients assigned to each group). After finishing the surgery, the corresponding envelope will be opened with the assigned randomization:
Group 1: pudendal nerve block guided by anatomical references.
Group 2: pudendal nerve block guided by neurostimulation.

In order to prevent the learning of neurostimulation-guided infiltration from influencing the way of infiltrating by anatomical references, two groups of surgeons are established (in each intervention there will be one surgeon from each group), one who will infiltrate guided by anatomical references and the other who will infiltrate guided by neurostimulation.

Blind infiltration
Dr G Hernández
Dr M.Hernandez

NE-guided infiltration:
Dr Soto
Dr N Diaz
Dr E Perez

Pudendal infiltration in both cases will be performed at the end of surgery with bupivacaine 0.5 with vasoconstrictor 10ml on each side.

Guided by Anatomical References
The key is to locate the ischial tuberosity. This is done with the opposite hand to the one that will perform the injection and sometimes it may be useful to perform a rectal touch to help guide the needle to the ischial tuberosity. Once located (usually at a depth between 2.5 and 3.8 cm of the skin depending on the size of the patient), after aspiration, 5mL of anesthetic solution is injected around the inferior and anterior part of the ischial tuberosity and the other 5mL in the path of withdrawal of the needle.

Guided by Neurostimulation
Train of four (TOF) stimulation is the modality to assess the degree of the blockade. Four stimuli are released at frequencies of 2Hz (2 per second). The ratio between the amplitude of the fourth and the first response in a succession of 4 stimuli (train) (T4:T1 ratio) assesses the degree of the block. The four TOF impulses disappear in inverse order to the degree of depth of the block. The fourth TOF response disappears when 75-80% of the receptors are occupied, the third response disappears at 85% occupancy, the second response disappears at 85-90% occupancy and the first response at 90-95% occupancy. We will start stimulation when we have 4 T1-T4 responses (4 visible jerks in the thumb adductor).
Turn on neurostimulator
Frequency selection 2Hz
Connect the alligator clip cable to the electrode on the skin
Connect the needle to the cable connector
1.0mA average output current
Insert the needle into the puncture site
Advance needle until anal musculature contraction is seen
Reduce current while optimizing needle position to achieve muscle contractions below 0.5 mA and above 0.2 mA to avoid intraneural infiltration
Once achieved without moving the needle infiltrate the 10mL of bupivacaine.
After injection of the dose, a local anesthetic test is the absence of muscle contractions in 5 seconds
Repeat on the contralateral side.
After surgery data related to the procedure will be collected

Based on Aldrete's classification, a scoring system that includes the evaluation of the general condition, pain, fever, therapeutic compliance, bleeding, oral tolerance and coloration of the extremities. Once these aspects have been evaluated, a score is obtained that varies between -8 and 8. Patients with a score between 4 and 8 are considered fit for discharge from the unit.

Intervention Type
Other

Primary outcome measure
Pain after hemorrhoidectomy measured using a verbal numerical scale one hour after the end of the surgery

Secondary outcome measures
1. Pain after hemorrhoidectomy measured using a telephone survey asking about the degree of pain (verbal numerical scale) 24 hours after the surgery and 7 days after the surgery
2. Need for rescue medication for pain control measured using a telephone survey asking about the need or not for additional medication (aids or others) 24 hours after the surgery and 7 days after the surgery
3. Constipation in posthemorroidectomy pain measured using the Bristol scale at 24 hours after

the surgery and 7 days after the surgery
4. Patients' quality of life measured using the Short Health Scale Haemorrhoidal Disease (SHSHD) score questionnaire and 36-Item Short Form Survey (SF-36) at 24 hours after the surgery and 7 days after the surgery
5. Degree of satisfaction after the procedure measured in the consultation interview by asking the patient to rate the process from 1 to 10, one month after the surgery
6. Adverse events incidence measured using patient medical records. It is the investigator's responsibility to document all adverse events occurring during the clinical trial. At each visit /evaluation, all adverse events observed by either the investigator or one of his clinical collaborators, as well as those spontaneously reported by the subject, should be documented. The investigator will evaluate all adverse events and record them in the adverse events section of the subject's data collection notebook. Adverse events should be recorded at each evaluation visit throughout the study. The nature of each event, time of onset after administration of the drug or medical device, duration, severity and relationship to treatment should be stated. Details of any remedial treatment should be recorded on the appropriate pages of the data collection notebook. Initial symptomatology should be well documented at the screening visit.

Overall study start date
29/09/2019

Completion date
20/08/2022

Eligibility

Key inclusion criteria
1. Hemorrhoids refractory to medical treatment, grade III-IV symptomatic and grade II hemorrhoids that do not respond to conservative procedures (hemorrhoidal ligation/sclerosis) at Nuestra Señora de Candelaria Hospital
2. Outpatient surgery
3. Aged 18 years of age and over
4. Acceptance of the study and signature of the informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
74

Total final enrolment
79

Key exclusion criteria
1. Patients with inflammatory bowel disease
2. Concomitant anal pathology (fissure, fistula, etc)
3. Hemorrhoidal pathology with surgical indication other than the Ferguson technique
4. Chronic pain in treatment with morphine or derivatives
5. Paracetamol and NSAID allergy

Date of first enrolment
01/06/2020

Date of final enrolment
01/08/2022

Locations

Countries of recruitment
Spain

Study participating centre
Hospital Nuestra Señora de Candelaria
Carretera del Rosario 145
Tenerife
Spain
38005

Sponsor information

Organisation
Hospital Universitario Nuestra Señora de Candelaria

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Sponsor type
Hospital/treatment centre

Website
http://www.uihunsc.com/

ROR
https://ror.org/005a3p084

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

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

Intention to publish date
01/09/2023

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publicly available repository

Documentation Collection and Filing
For the collection of data, each patient will be assigned a number, thus avoiding the handling of the patient's personal data.
The information has been collected in a database with a password in the SPSS program.
There will be a documentation file for all the data, which will be kept in its entirety on paper and on computer support for 5 years after the end of the study. This file should contain the following elements:
-Approval by the CEIC of the protocol and informed consent form.
-Copy of the written consent form, and the approved protocol with any amendments if applicable.
-Any correspondence with the CEIC
-Signed acceptance of the protocol.
-Curriculum vitae of the principal investigator.
-Record of signatures of the members of the research team.
-Serious AA communications.

Information to The Subject
The investigator should explain to each subject the nature of the study, its purposes, procedures, expected duration, and the potential risks and benefits related to participation in the study, as well as any inconvenience that this may entail. Each participant should be advised that his or her participation in the study is voluntary and that he or she may leave the study at any time, without this affecting his or her subsequent medical treatment or relationship with the treating physician.

Informed consent will be provided in a standard written form, in language easily understood by the participant. The subject must have sufficient time to read and understand the explanations before dating and signing the informed consent and must receive a copy of the signed document. No subject can be included in the study without having previously given informed consent.

However, the pathology under study and the characteristics of the study patients may make it difficult to provide adequate information, so if the physician considers that a patient is not in a position to receive and understand the information, or if the time to be devoted to it may put him/her at risk, the possibility of requesting consent from his/her family member or legal representative will be considered.

IPD sharing plan summary

Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Informed consent		07/02/2023	No	Yes
Participant information sheet			07/02/2023	No	Yes