COVER PAGE

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Study Protocol (ID: POF-LEV-2019-01): a retrospective clinical registry of peripheral nerve block

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TITLE

Registry of peripheral nerve blocks in Traumatology Anesthesia at the Miguel Servet University Hospital.

PROMOTER

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BACKGROUND

Within anesthesia, there are several modalities such as general anesthesia or locoregional anesthesia. General anesthesia refers to the use of intravenous or inhaled drugs to achieve hypnosis, anesthesia and analgesia of the patient to be operated on. However, the action of general anesthesia is systemic and entails numerous side effects such as nausea, vomiting, postoperative delirium, etc. Therefore, it is a technique that involves more interactions and complications with the patient's comorbidity and treatment (1).

Locoregional anesthesia is one of the anesthetic subspecialties that has prospered the most in recent decades, especially with the development of ultrasound as a nerve localization technique. This anesthetic modality began as early as the 19th century and includes central neuroaxial blocks as well as peripheral nerve blocks. These allow surgery to be performed with adequate analgesic, anesthetic and motor control of the surgical site with the advantage that the patient is conscious. It can be used as a single anesthetic technique or combined with general anesthesia to reduce analgesic requirements and its systemic side effects.

Neuroaxial blockade refers to the administration of local anesthetics (LA) in the vicinity of the spinal cord, either within the cerebrospinal fluid at the subarachnoid level or at the epidural level, to produce a sensory and/or motor blockade (1,2).

On the other hand, peripheral nerve blockade (PNB) consists of administering AL around the peripheral nerves or nerve plexus, external to the spinal column. According to the 10th International Classification of Diseases (ICD-10), this procedure is classified with the code 3E0T3CZ as: Block, Nerve, injection of anesthesia (3,4). They can be adapted to surgical needs and used for perioperative anesthesia or analgesia and for chronic painful processes. To perform them, knowledge of nerve anatomy including the brachial and lumbosacral nerve plexuses as well as the major peripheral nerves such as the median, musculocutaneous, ulnar and radial nerves in the upper extremity or the femoral, femorocutaneous, obturator, sciatic, sciaticopopliteal nerves in the lower extremity is required.

The most commonly used peripheral nerve blocks in anesthetic practice are the brachial plexus block with interscalene approach or with supraclavicular, infraclavicular or axillary approach for shoulder and upper extremity surgery. For lower extremity surgeries, the femoral, femorocutaneous, obturator, sciatic or sciatic-popliteal nerve block is used (2,5).

In recent times, the use of PNBs has increased because it has demonstrated an improvement in analgesic control according to the visual analog scale (VAS), a decrease in postoperative analgesia, postoperative nausea and vomiting, a shorter stay in the postanesthesia recovery unit and an increase in patient satisfaction (1,5-9).

Contraindications for peripheral nerve blocks are few and general, such as patient rejection, hemodynamic instability, local infection at the puncture site or allergy to the LA to be used. Possible complications of these techniques are peripheral nerve injury such as neuropraxia, axonotmesis or neurotmesis, vascular complications such as neuronal ischemia or hematoma, or neuronal, cardiovascular or systemic toxicity due to the use of LA (2).

In some countries there are national registries of anesthetic results; however, to date there are no published data of a registry of locoregional anesthesia techniques in Spain (5,10). Therefore, the benefit of this work is estimated to be very high with respect to the risk involved, since it involves the same risks of the usual anesthetic practice with the aim of reviewing this same clinical practice to evaluate its safety and to be able to compare it with international standards.

Therefore, this work will try to make the first description of the mode of use and complications of locoregional anesthesia carried out in a tertiary hospital with an anesthesia unit specialized in this type of techniques in our country. The purpose is to evaluate the current management and the evolution of our usual clinical practice in locoregional anesthesia.

INTERVENTION FRUG

The investigational drugs in the study have been provided by the Pharmacy Service of the HUMS since they are medications used in the usual clinical practice of the ARTD Service.

TRADE NAME:

- Chirocane® 1.25 mg/ml Injectable and infusion solution.

- Chirocane® 2.5 mg/ml Solution for Injection and infusion.

- Chirocane® 5 mg/ml solution for injection and infusion.

- Mepivacaine Braun 1% Solution for Injection EFG.

- Mepivacaine Braun 2% Solution for Injection EFG.

- Bupivacaine Hyperbaric B. Braun 1.25 mg / ml solution for injection.

- Bupivacaine Hyperbaric B. Braun 2.5 mg / ml solution for injection.

- Bupivacaine Hyperbaric B. Braun 5 mg / ml solution for injection.

- Lidocaine B. Braun 20 mg / ml solution for injection.

ACTIVE INGREDIENT:

- Levobupivacaine 1.25 mg/ml Solution for Injection and for infusion.

- Levobupivacaine 2.5 mg/ml solution for injection and infusion.

- Levobupivacaine 5 mg/ml solution for injection and infusion.

- Mepivacaine 1% Solution for Injection EFG.

- Mepivacaine 2% Solution for Injection EFG.

- Bupivacaine Hyperbaric 1.25 mg / ml solution for injection.

- Bupivacaine Hyperbaric 2.5 mg / ml solution for injection.

- Hyperbaric Bupivacaine 5 mg / ml solution for injection.

- Lidocaine 20 mg / ml solution for injection.

PHARMACEUTICAL FORM: Solution for injection and infusion.

ROUTE OF ADMINISTRATION: Perineural administration through peripheral nerve block needle.

EXCIPIENTS: indicated in AEMPS data sheets (11-18).

All the drugs are authorized for marketing by the AEMPS, and will be administered according to the usual clinical practice of the ARTD Service, COT Service (11-18). They belong to the AL pharmacotherapeutic group (amides) with ATC code N01B B10 (Anatomical, Therapeutic, Chemical classification system). They consist of a colorless, clear solution for injection and infusion, available in 5 to 10 ml polypropylene ampoules (12).

All of them have been administered by an anesthesiologist specialized in the management of locoregional anesthesia and its drugs, according to the dosage established in the technical data sheets of the Spanish Agency of Medicines and Health Products (AEMPS). The therapeutic indication of the intervention studied is surgical anesthesia by PNB in adults (11-18).

All drugs have been administered perineurally by means of a BNP needle since this is the only way of administering a drug in locoregional peripheral nerve anesthesia. During dose administration, patient monitoring was performed and blood puncture prevention measures were taken according to standard clinical practice (12).

OBJECTIVES

The primary objective of this study is to quantify the number and type of peripheral nerve blocks performed in the routine anesthetic practice of the Traumatology Anesthesia Unit of the Miguel Servet University Hospital. Secondary objectives are: to describe to assess the safety of peripheral nerve blocks in the routine anesthetic practice of the Traumatology Anesthesia Unit of the Miguel Servet University Hospital: number, severity and resolution of complications.

DESIGN

This is a descriptive, observational, retrospective, single-center, retrospective study of a population-based sample of all patients who have undergone orthopedic and trauma surgery and who have undergone PNB, according to standard clinical practice, in the Traumatology Anesthesia Unit of the Miguel Servet University Hospital (Zaragoza, Spain).

The source of our population sample is all patients undergoing scheduled or urgent surgery by the COT Department of the HUMS and who underwent perioperative PNB by the ARTD Department's ATU.

The registration of the cases in this study was carried out at HUMS, where the generated database is kept. The data analysis was carried out in a cross-sectional manner with a retrospective follow-up of the sample.

Patient recruitment spans from January 01, 2011 to November 30, 2019. Cases have been recruited by convenience, during the perioperative process of patients in the surgical block of HUMS, up to a total of 13759 BNPs.

Follow-up after medication administration and BNP performance lasts until the present day. It is performed by the clinical evaluation of the services responsible for patient follow-up, see the COT Service, who does not redirect possible complications encountered in the operated patients.

The anesthetic and surgical procedures have been performed, according to standard clinical practice, in the multifunctional surgical block of the HUMS.

In this work, no biological samples were obtained from a care process and no specific test was performed.

During this work, 3 figures were involved: the PI, the ICs and the anesthesiology team. The team of anesthesiologists has been in charge of performing the interventional techniques of the BNP according to the usual clinical practice and which have been collected in the BD. They were also the ones who completed the CRD after performing the PNBs. The ICs have been those who have made the BD from the CRD of all the NIBPs performed. Finally, the PI will be responsible for the processing of the DB data.

This work has been carried out within the usual care activity of the ARTD Service's TCU and this practice has been followed in all cases.

INCLUSION CRITERIA

In order to be included in this study, patients had to meet all the following inclusion criteria:

1. Written informed consent in which the patient agrees to undergo anesthetic procedures: general, locoregional or local anesthesia (general informed consent of the ARTD Service of the HUMS for any anesthetic procedure).

2. To undergo scheduled or urgent surgery by the COT Service.

3.Have a peripheral nerve block technique performed by the Traumatology Anesthesia Unit (ATU) of the ARTD Service of the HUMS.

EXCLUSION CRITERIA

The following exclusion criteria are available, comprising only those patients in whom PNB is contraindicated:

1. Patient refusal of the peripheral nerve block technique.

2.Contraindication to the performance of the peripheral nerve block technique.

3.Allergic to amide-type local anesthetics, opioids or non-steroidal anti-inflammatory drugs.

STATISTICS

Data were collected in Microsoft Excel tables and IBM SPSS Version 22 for Windows [under license from the University of Zaragoza]. For all analyses a statistically significant result is assumed if $p<0.05$. The statistical analysis performed includes a descriptive and inferential analysis.

A descriptive analysis of the data will be performed: the qualitative variables (age, sex, etc.) will be presented by means of the frequency distribution of the percentages of each category and the quantitative variables studied (volume of local anesthetic, concentration of local anesthetic, etc.) will be explored with the Kolmogorov-Smirnov test of conformity (goodness-of-fit test to a normal distribution). Likewise, indicators of central tendency (mean or median) and dispersion (standard deviation or percentiles) will be given.

The degree of association between variables will be examined using graphical (scatterplot) and analytical (simple correlation coefficient) methods. The interpretation of the intensity of the relationship will be performed according to the criteria established by Gerstman (2015) and Martínez-González and et al. (2014) (20,21).

Regarding the bivariate analysis or comparison between two variables (factors), the association between the factors will be investigated by means of hypothesis contrast tests. In case both variables compared are qualitative, by means of a comparison of proportions with chi-square or Fisher's exact test. If one of them is quantitative, a comparison of means will be made by means of Student's t-test, ANOVA, and if they do not follow a normal distribution, the Mann-Whitney U test or the Krustal-Wallis test. Likewise, a bivariate correlation (Pearson's correlation coefficient) will be carried out when both variables are quantitative or, if the application conditions are not met, a Spearman's correlation.

As for the multivariate analysis, to study the relationship of each variable controlling for the possible effect caused by third variables, the analysis will be completed by regression models.

ETHICS

The present study will be carried out in strict accordance with the international ethical recommendations for research in humans contained in the Declaration of Helsinki, Good Clinical Practice guidelines and following the recommendations of the AEMPS regarding post-authorization studies (22,23).

The protocol of this study will be evaluated by the AEMPS and the corresponding Autonomous Community Ethics Committee (CEICA) before proceeding with its performance and subsequent dissemination.

All patients were duly informed by the anesthesiologist in charge of the anesthetic technique to be performed and signed the general informed consent form for the performance of anesthetic techniques of the ARTD Service.

No invasive procedure added to the usual clinical practice of a BNP is performed in this research.

This work is a retrospective observational study so it does not require an insurance policy other than the insurance coverage of HUMS and SALUD for the usual clinical practice.

In this research project, there are no diagnostic tests derived from the research. No genetic analysis or any test that has relevance to the health of the patient's relatives or third parties is performed.

Likewise, no student participation is required.

Participants in this research study will not be compensated financially or with other services, nor will they be reimbursed for the expenses derived from their participation.

PROCESSING OF PERSONAL DATA

The study data come from an anonymous database which does not include any patient identification data. The computer that contains this database is within the HUMS computer system with its corresponding firewall system. Access to this database is restricted to the research team (IP and IC). Each patient has been assigned a study identification code, only the research team has access to this information and is responsible for its safekeeping, all in order to protect patient confidentiality.

In accordance with the Organic Law on Data Protection (Point 5, SAS order 3470/2009), consent is not required for the collection of information in this study, given

the retrospective nature of the analysis. In any case, the exemption of consent does not negatively affect the rights and well-being of the participants as it does not alter the follow-up or the collection of information from routine practice.

This work is carried out during the usual clinical practice of the ARTD Service of the HUMS and therefore does not interfere with the care tasks of the center, nor does it increase the waiting list, nor is any medication prescribed, nor does it involve a distribution of resources that could affect the principle of justice. The patients recruited are part of the usual surgical program of the COT Service of the HUMS, so no advertisement or alternative means of patient recruitment is needed.

PUBLICATION POLICY

The results of this study will be property of the UAT of the ARTD Service who will decide the publication policy.

The conclusions of this research work will derive in a doctoral thesis work of the Doctoral School of the University of Zaragoza, will be presented in congresses and scientific publications but will always be done with pooled data and will never be disclosed anything that could identify you.

As defined in article 42 of RD 1090/2015, the results obtained in the research work will be published, whatever the result, in scientific journals with mention to the CEIm that approved the study. Likewise, the promoter will publish the results report once the research carried out in the CE is concluded, in accordance with article 47 of the aforementioned RD.

GLOSSARY OF ACRONYMS

- AA: Adverse event.

- AAG: Serious Adverse Event.

- AEMPS: Spanish Agency of Medicines and Health Products.

- AL: Local anesthetic.

- ARTD: Anesthesia, Resuscitation and Pain Therapy.

- DB: Database.

- PNB: Peripheral nerve block.

- CEICA: Research Ethics Committee of the Autonomous Community of Aragón.

- IC: Informed Consent.

- COT: Orthopedic Surgery and Traumatology.

- CRD: Data Collection Notebook.

- VAS: Visual Analog Scale.

- HC: Clinical History.

- HUMS: Miguel Servet University Hospital.

- IC: Collaborating Investigator.

- PI: Principal Investigator.

- IV: Intravenous line.

- SI: All units of measurement are expressed according to the International System of Units.

- UAT: Traumatology Anesthesia Unit.

- OV: Oral route.

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