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Comparison of Intra-articular 0.2% Ropivacaine vs 0.75% Ropivacaine in Postoperative Knee Arthroscopy

Abstract:

All patients with acute lesions assistant to the orthopedic and trauma center of the ABC medical center will be invited to participate in the study. Those that meet the inclusion criteria and later sign an informed consent will be randomized to receive 10 ml of a solution with ropivacaine at 0.75% and 0.2% intraarticular for the first 5 minutes after the end of surgery (closing of surgical wounds). Both the patient, the physician who applies it and the evaluator of outcomes remain blinded to the dose of ropivacaine the patient receives.

Two hours after the end of the surgery, while the patient is in his room, the presence of pain will be evaluated by a visual analog scale (EVA), while the patient is asked to flex and extend his knee. The result will be quantified continuously, to later categorize the pain in none to slight pain (0-3 points) and moderate-severe pain (4-10 points). All the information will be recorded on established forms in the clinical file (general data), that includes the variables of interest for the study, and is reported by the physicians after standardization of all those encharged with collecting information to comply with the conceptual and operative

operationalization of the variables described in the research protocol. In addition to the evaluation of pain, the administration of opiodes to patients for necessary reasons (presence of pain) by the physicians in charge is recorded.

It is hoped that, in patients with knee arthroscopy for acute lesion, there is a difference in the frequency of moderate-severe pain of 30% in the post-operative (frequency of 37.5% in patients with ropivacaine at 2% and frequency of 7.5% in patients with ropivacaine at 7.5%).

Background

Knee arthroscopy is a minor outpatient orthopedic procedure, used primarily to remove loose bodies, for debridement of meniscal tears, debridement and remodeling of cartilage lesions, ligament reconstruction, meniscus transplants, and arthroscopically assisted synovectomy[1].

Estimates made in the United States of America indicated that in 2006, 6.3 million orthopedic surgical procedures were performed in an outpatient context[1], of which 984,999 (95% CI: 895,999 to 1,073,215) corresponded to knee arthroscopies[1]. In Sweden it is estimated that a team consisting of an average of 7 surgeons (from teaching, general and local hospitals) performs 330 (110-2,600) arthroscopies annually[2].

Post-surgical pain after performing knee arthroscopies has been described in 62.5% of patients acutely (4 days after the operation), and in 76.9% of subjects chronically (1 year after surgery). surgery)[3]. In patients with moderate-severe preoperative pain (4-10 points according to the visual analogue scale (VAS)), the presence of acute and chronic pain occurs in 45.6% and 42.7%, respectively, while in those with pain between 0 -3 points, acute and chronic pain occurred in 17.2% and 6.9%, respectively[3].

Global Surgical Recovery has been investigated using the Global Surgical Recovery Index after knee arthroscopy, the evaluation tool consisted of a question “Yes, 100% recovery means that your health “You have returned to the same level you had before the surgery, what percentage of recovery do you have now?” (“if 100% recovery means your health is back to the same level as it was before the surgery, what percentage of recovery are you now?”), with 88.5% of participants responding with values ≤80% in a period of 4 days after surgery and 50.0% values ≤80% one year after surgery[3].

Currently there is no guideline or consensus for the treatment of elective knee arthroscopies[2], [4]. However, when analyzing the responses of a questionnaire sent to various orthopedic units members of the “Swedish Arthroscopy Society”, it was reported that the most common anesthesia technique corresponded to 1) general (83%), 2) local anesthesia without or with minimal sedation was used in 13% of patients, 3) while spinal anesthesia was performed in 4% of patients[2]. In the postoperative period, 1/37 (2.70%) of the units interviewed did not use local intra-articular anesthesia for the treatment of pain, 8/37 (21.62%) used short-term lidocaine or prilocaine (with or without adrenaline), in 20

/37 (54.05%) used long-acting intra-articular bupivacaine, 5/37 (13.51%) used morphine and 3/37 (8.10%) NSAIDs[2].
After the use of the different anesthesia methods, the adverse effect on the articular cartilage has been evaluated, in addition to the favorable analgesia effects for pain management, showing no difference in the harmful effect between the use of general, spinal and analgesia. local[5].
The effect of the use of various analgesics on pain control in procedures similar to knee arthroscopy has previously been studied[6-10].

After arthroscopy that does not include a procedure such as anterior cruciate ligament, tibial tuberosity osteotomy, medial patellofemoral ligament or meniscus surgery, a median opioid consumption corresponding to 11.3 (0-52) pills has been reported[11].

Acute pain (Outcome)

Pain has been defined as an unpleasant emotional experience associated with tissue damage, not just a primary sensation; and like any emotional experience, it is subjective[12], [13]. Only the patient himself knows his pain and how much it hurts, therefore any assessment of pain must include the report of the subject suffering from the pain [13]. The evaluation of acute pain, being a time-limited, unidimensional and short event, is easier to measure, is easily reproducible and is not significantly affected by other variables[13].
It is not possible to extrapolate experimentally produced pain to situations where the pain is caused by a pathological process in the patient, because the patient's psychological state, associated with the pathology, is present[13].

Pain assessment

Subjective measurement is the most frequently used way to measure pain; Unidimensional methods only assess intensity and treat pain as a single or simple dimension[13].
In order to standardize the evaluation of outcomes of experimental studies and the choice of optimal measurement instruments within different contexts of clinical epidemiology, initiatives have emerged, such as the COMET initiative[14], from the English “Core

Outcome Measures in Effectiveness Trials". " and COSMIN (COnsensus-based Standards for the selection of health Measurement INstruments)[15]. After a search to identify the best tool for the evaluation of pain in the present study in the different bases of the standardization initiatives for evaluating outcomes, first in the database of the COMET initiative[16], no results were seen. of valid measurement instruments when performing a general search with the terms "Pain" and Knee (knee), or when searching for the terms "Anesthesia and pain control"[17]. However, in the COSMIN initiative's database of measurement instruments for patient-reported outcomes, a search with the term "knee" (Patient-reported outcome measures for the knee)[18] returned a search result, which describes measurement properties of various instruments used in patients with various knee procedures or conditions[19], including the VAS.

Visual analogue scale

The visual analogue scale (VAS) was described and devised in 1976. It consists of a 10 cm line that continuously represents the pain spectrum[13]. The line can be displayed horizontally or vertically, with right-angled endings at the ends, where the descriptions "No pain" and "The worst pain imaginable" appear (Figure 1) [13]. The patient is free to indicate the intensity of his or her pain sensation on the continuous line, which constitutes the main advantage of the measurement method[13]. In the evaluation of patellofemoral pain, the reliability of the VAS is 0.95-0.96, measuring the ability to identify the change in pain intensity in various periods of time (test-retest)[19].

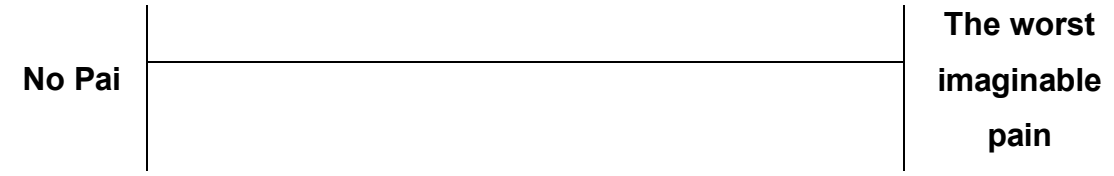

Figure 1. EVisual Analogue Scale (VAS)

Ropivacaine

Ropivacaine is a long-acting amide local anesthetic that began clinical use in 1996.[20] Structurally, it is chemically similar to bupivacaine and mepivacaine, because they are derivatives of "pipecoloxylidide" (name not defined in Spanish), however, ropivacaine,

being the agent with the lowest lipophilic behavior of its peers, is characterized by lower toxicity. systemic when compared with bupivacaine and levobupivacaine[21]–[23].
The possible benefits of ropivacaine have been studied in different contexts: 1) in infiltration anesthesia[20], 2) in peripheral neural blockade (sciatic and femoral nerves)[24], [25]; 3)continuous postoperative analgesia[26]–[29]; 4) intra-articular application[30], [31].

Until now, the efficacy (comparison against placebo or non-active substance) of ropivacaine in the control of pain after knee arthroscopy has not been evaluated. However, the results of the efficacy or efficiency of active substances similar to ropivacaine have been studies [32-41]. Ropivacaine, such as bupivacaine or levobupivacaine in pain control, in different strata of the population that has undergone knee arthroscopy, as well as the adverse effects and limitations of studies previously carried out in the population of interest for this study.

Research question

What is the analgesic effect of the intra-articular administration of 0.2% ropivacaine vs 0.75% ropivacaine in the immediate postoperative period of knee arthroscopy in acute injuries?

Justification

The prevalence of moderate-severe pain in post-knee arthroscopy patients is 71.2%. The prevalence of acute postoperative pain is 37.5% and chronic pain is 37.7%, exceeding the prevalence compared to that of other surgical procedures of different specialties.
This study will provide evidence regarding the effect of an anesthetic on postoperative pain control, as well as the effects on reducing opioid consumption and patient mobilization.
The administration of opioids is part of a common practice in pain management, however it represents a risk for patients due to their adverse effects and high risk of dependence. It is necessary to look for alternatives that reduce opioid consumption in postoperative patients, taking care of the cost-benefit for the patient as well as for health institutions.

The reduction in postoperative pain with the applied strategies that has been observed is up to 30% in the immediate postoperative (1st measurement), 20% at 8 hrs (2nd measurement) and 10% at 24% (3rd measurement).

Objectives

General objective:

- To evaluate the analgesic effect of the intra-articular administration of 0.75% ropivacaine in the immediate postoperative period of knee arthroscopy in acute injuries.

Specific objectives:

- To evaluate the effect of intra-articular administration of 0.75% ropivacaine in reducing opioid consumption in the immediate postoperative period of knee arthroscopy in acute injuries.
- To evaluate the effect of intra-articular administration of 7.5% ropivacaine on mobility in the immediate postoperative period of knee arthroscopy in acute injuries.

Hypothesis

The Intraarticular administration of 0.75% ropivacaine reduces acute pain by 30% in postoperative knee arthroscopy patients in acute injuries.

Methods

All patients with acute knee articular cartilage lesions who attend the Orthopaedic and Trauma Center of the ABC Medical Center will be invited to participate, under the scrutiny of a sole surgical team.

Selection criteria

-Mental health: healthy (not taking any medication)
-Articular cartilage lesion Grade I, II or III by Outerbridge
-Elective knee surgery
-Patients with any of the following diagnoses:
-Simple menisc lesion

-Lesion of a single knee (unilateral)

Exclusion criteria

-Neuromotor diseases (alterations in step, strength or sensitivity)

-History of knee surgery (orthopedic)

-Instability that includes knee ligament lesions

-Addictions

-Mental diseases in medical treatment

-Hepatic diseases

-Allergy to any of the medications used in the study

-Epidural or peridural anesthesia

-Chronic pain in treatment

-Postoperative drain of knee arthroscopy

-Pregnant or lactating

Model description

After confirming that the patients meet the selection criteria, they will be invited to participate in the study. Upon accepting through signed informed consent, the physician in charge of randomization (physician 1) will be informed and the surgery scheduled. The day of the surgery, the physician in charge of randomization will report the maneuver to be received from the anesthesiologist (physician 2) in charge, who will prepare the dose of ropivacaine and give it to a physician blinded to the maneuver (physician 3); this physician will apply the ropivacaine intraarticular to the patient. The level of pain will be evaluated two hours after the end of surgery by a physician blinded to the maneuver the patient has received (physician 4), while the patient is in his room, and the presence of acute-moderate-severe pain (4-10 points) is evaluated by a visual analog scale (EVA) while the patient is requested to flex and extend the knee.

Randomization:

Randomization will be performed by number generator software OxMaR (Oxford Minimization and Randomization).

Blinding:

Blinding will be performed once the patient will agree to participate; the physician in charge of randomization will inform the anesthesiologist of the maneuver that corresponds to the patient programmed for surgery, who will prepare the dose for the patient and hands it to the physician who will apply the maneuver (who is blinded to the maneuver). All patients will receive 10 ml of solution with different doses of ropivacaine, the application vehicles being equal in physical appearance. The physician who will evaluate the outcome will not participate in the randomization, surgery or application of the maneuver, and will remain blinded to the dose the patient receives, as does the patient.

Maneuver

Knee arthroscopy will be carried out by 2 orthopedic surgeons trained in arthroscopic surgery and with minimum experience of 10 years.

The application of ropivacaine will be performed at the end of the surgical procedure, once the arthroscopic portals are sutured, the main surgeon for the infiltration is given, according to the randomization, 10 ml of ropivacaine at 0.2% or 10 ml of ropivacaine at 0.75%, as may be the case, which will be administered with the anesthesized patient by intraarticular via in the knee (in the anatomical level of the upper pole of the ball joint, under the iliotibial band). Once the infiltration is complete, placement of gauze and simple bandage procedes, and once the anesthesiologist indicates, the patient is passed to recovery, where the evaluation of outcomes (no-slight pain / moderate severe pain) will be performed.

Exit from the study:
-Any transoperative event that requires the suspension of surgery.
-Any transoperative event that impedes the application of intraarticular ropivacaine.

The patients in both arms receive 10 ml of intraarticular solution in the knee (at the anatomical point at the level of the upper pole of the ball joint, under the iliotibial band), with different content of ropivacaine; the vehicle for application presents the same physical appearance for all patients and is applied by previously standardized treating physicians.

Sample size
Expecting an absolute difference, an absolute difference of 30% is expected for the presence of moderate-severe pain, considering a level of significance=5% and power=80%. Needed are 68 subjects, 34 for each arm.
Given that the evaluation of outcome is performed 2 hrs. after the application of the maneuver, and due to the low incidence of postoperative anesthetic complications, loss of information is estimated at <1%.

Sample size and statistical analysis: Sample size was estimated to establish a difference of 30% in considering the presence of moderate-severe pain among patients treated with different doses of ropivacaine, considering an alpha level of 0.05 and beta of 0.20. Required

were 68 patients divided into two groups of 34 each. Loss of information was expected at <1%, and 2 subjects were added to the sample size, increasing the requirement to 70 subjects in total. For statistical analysis, the statistical program SPSS version 27 will be used (IBM Armonk, New York). Contrast of the incidence of outcomes between the two groups by different doses of ropivacaine will be carried out by X^2 or Fisher exact test, when necessary. Multivariate analyses will be performed by logistic regression analysis, considering a value of $p<0.05$ as significant, and double gradient differences in exposure to different variables between treatment groups were included in multivariate analysis.

In the *intention-to-treat analysis* (ITT), the main and secondary outcomes will be contrasted between the groups, considering the randomization of the different doses of ropivacaine, and in the *per-protocol analysis (PP),* the results of the incidence of moderate-severe pain will be contrasted between groups formed by randomization; however, those that received opioids in the first 2 hours post-surgery will be excluded, in order to know the effect of the use of ropivacaine at 7.5% without the effect of a conjugate maneuver.

Variables to be evaluated

Dependent variable	
Pain (Primary outcome)	**Conceptual definition:** Sensory and emotional experience associated with a present or potential injury or a described one. **Operational definition:** The sensation of painful discomfort at the surgical site (Mild, moderate or severe). **Type of variable:** Dichotomous qualitative. **Measuring instrument:** VAS (0-10 points) **Measurement units:** Mild 0-3 points, moderate-severe 4-10 points.

Opioid use	**Conceptual definition:** Drug whose analgesic action is produced thanks to the interaction with the opioid receptors of the neurons of the central nervous system. **Operational definition:** According to the VAS pain score administration of Tradol dose of 50mg IV. **Type of variable:** Qualitative dichotomous **Measuring instrument:** Information extracted from the patient's file. **Measurement units:** Not use / Use.
Mobility	**Conceptual definition:** Amplitude of joint oscillation within natural limits. **Operational definition:** The active mobility performed by the patient in the postoperative period. **Variable type:** Dichotomous qualitative. **Measuring instrument:** Observation made by the doctor in the postoperative period after the indication of flexion and extension of the leg, elevation and descent of it actively before the doctor. **Measurement units:** Present / absent.
Independent variable	
Ropivacaine 0.75%	**Conceptual definition:** Long-lasting amide-type local anesthetic with lower lipid solubility. **Operational definition:** IA administration to the knee of 10 ml of 0.75% ropivacaine. **Variable type:** Dichotomous qualitative. **Measuring instrument:** Experimental maneuver.

	Measurement units: No / Yes
Ropivacaine 0.2%	**Conceptual definition:** Long-acting amide-type local anesthetic with lower lipid solubility **Operational definition:** IA administration to the knee of 10 ml of 0.2% ropivacaine. **Variable type:** Dichotomous qualitative. **Measuring instrument:** Experimental maneuver. **Measurement units:** No / Yes
Peripheral variables/covariates/Probable confounders /Probable interactors	
Sex	**Conceptual definition:** Organic condition of the individual. **Operational definition:** Identification of the individual as Male or Female. **Type of variable: Dichotomous** qualitative. **Measurement units:** Male / Female.
Age	**Conceptual definition:** Time lived by a person. **Operational definition:** 18-35 years; 36 – 60 years. **Variable type:** qualitative ordinal **Measurement units:** 18-35; 36-60
BMI	**Conceptual definition:** Mathematical reason that associates weight and height. **Operational definition:** 1. normal weight BMI<25 vs 2. overweight BMI≥25

	Variable type: qualitative ordinal **Measurement units:** kg/m ^{2}
Time of evolution	**Conceptual definition:** Duration from the onset of symptoms or their detection **Operational definition:** 1. <4 weeks and 2. >5 weeks **Variable type:** qualitative ordinal **Measurement units:** number of weeks
Physical activity	**Conceptual definition:** Any body movement produced by skeletal muscles that requires energy expenditure **Operational definition:** active *vs* sedentary **Variable type:** dichotomous qualitative **Measurement units:** 0-1
Etiology of surgery	**Conceptual definition:** Cause of the organism before the disease **Operational definition:** traumatic *vs* degenerative **Variable type:** dichotomous qualitative **Measurement units:** 0-1
Duration of Surgery	**Conceptual definition:** Time spent performing interventions inside and outside the human body **Operational definition:** 1. <45 min and 2. ≥ 45 min **Variable type:** qualitative ordinal **Measurement units:** minutes

Type of articular cartilage injury	**Conceptual definition:** Description of the different degrees of chondropathy **Operational definition:** I: 0mm, II: < 0.5mm and III : >0.5mm **Variable type:** qualitative ordinal **Measurement units:** millimeters

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