COMPARISON BETWEEN ROPIVACAINE 1.5 MG ML\(^{-1}\) PLUS FENTANYL 2 MG ML\(^{-1}\) AND ROPIVACAINE 1.5 MG ML\(^{-1}\) PLUS CLONIDINE 1 MG ML\(^{-1}\) AS ANALGESIC SOLUTION AFTER ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION: A RANDOMIZED CLINICAL TRIAL*

KALAKONAS APOSTOLOS, KOTSOVOLIS GEORGIOS, CHALKEIDIS OMIROS AND TRIANTAFYLLOU CHRISTOS

Abstract

Background: Ropivacaine is commonly used as local anesthetic for postoperative analgesia through an epidural catheter. Data show that several adjuvants influence the analgesic effect of local anesthetic potency.

Objective: The aim of the study was to compare fentanyl and clonidine as adjuvants to 1.5 mg ml\(^{-1}\) ropivacaine in terms of motor blockade, pain relief and side effects.

Methods: In this single center, randomized, clinical trial, 52 patients scheduled for arthroscopic anterior cruciate ligament reconstruction were randomly allocated in two groups. At twenty-six patients a solution with ropivacaine 1.5 mg ml\(^{-1}\) plus fentanyl 2 μg ml\(^{-1}\) (group F) was administered through patient controlled epidural analgesia (PCEA) as postoperative analgesia and ropivacaine 1.5 mg ml\(^{-1}\) plus clonidine 1 μg ml\(^{-1}\) (group C) was administered to the remaining twenty-six patients. The VAS score, the Bromage scale and total solution consumption were documented and compared between the two groups for 24 hours after the end of the operation.

Results: The mean patient control consumption of the solution was higher at group C respect group F (p = 0.007). At the 8th hour after the operation we register a statistical significant difference at the mean VAS score between the two groups (p<0.05) with clonidine group achieving a higher score. At the 8th and 12th hour clonidine group register a lower Bromage score than fentanyl group (p<0.005 and p = 0.002).

Conclusion: Ropivacaine 1.5 mg ml\(^{-1}\) plus fentanyl 2 μg ml\(^{-1}\) administered through PCEA compared with ropivacaine 1.5 mg ml\(^{-1}\) plus clonidine 1 μg ml\(^{-1}\) h guarantee higher quality analgesia after ACL reconstruction.

Keywords: Ropivacaine, fentanyl, clonidine, anterior cruciate ligament.

Conflict of interest: The study has been supported solely from the departmental sources.

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Introduction

Placement of an epidural catheter allows to provide better postoperative analgesia for abdominal and lower extremity surgery respect parenteral opioid administration. Several studies comparing PCEA over conventional epidural continuous infusion have found several benefits, including better analgesia and superior patient satisfaction.

Ropivacaine and bupivacaine are the most common local anesthetics administrated for epidural analgesia. Usually adding adjuvants such opioids, α₂-adrenergic agonist, neostigmine, ketamine reduce side effects of local anesthetics and increase the analgesic propriety of the mixture.

The aim of this study was to compare motor blockade, pain relief, drug consumption and side effects during patient controlled epidural analgesia (PCEA) with ropivacaine 1.5 mg ml⁻¹ plus fentanyl 2 μg ml⁻¹ versus ropivacaine 1.5 mg ml⁻¹ plus clonidine 1 μg ml⁻¹.

Methods

After thorough explanation of the parameters of the study 52 ASA 1-2 patients agreed to sign the consent form and participate in our study. These patients were scheduled for arthroscopic anterior cruciate ligament (ACL) reconstruction. After the admission of the patient in the operating room, adequate monitoring for each patient was commenced. To all patients 2.8 ml of heavy bupivacaine 5 mg ml⁻¹ was administrated intrathecally for surgical anesthesia. We used a kit of combined spinal epidural anesthesia and an epidural catheter was advanced 3 cm into the epidural space for postoperative analgesia. The puncture level was L₄-L₅ or L₃-L₄. All the patients were operated by the same surgeon. The epidural infusion was started in the recovery room. Every patient was randomized (sealed and opaque envelopes) in one of the two groups. 26 patients for fentanyl (F) and 26 patients for clonidine (C). The study solution was prepared by an anaesthesia nurse, who was not involved in the treatment of the patients. In group F the epidural mixture consisted of ropivacaine 1.5 mg ml⁻¹ plus 2 μg ml⁻¹ fentanyl and in group C was ropivacaine 1,5 mg ml⁻¹ plus 1 μg ml⁻¹ clonidine. The infusion rate postoperatively was 5 ml h⁻¹ for either solutions regulated by an electronic pump.

All the patients were instructed to self administrate epidural bolus doses of 5 ml on demand using the same pump. The lockout interval was 20 min. An investigator blinded to the identity of the solution visited every patient 2, 4, 8, 12, 24 hours after the operation. At every visit he examined the motor blockade using the Bromage scale (modified Bromage’s score: 0 = no motor block, 1 = hip blocked, 2 = hip and knee blocked, 3 = hip, knee and ankle blocked) and pain using VAS score. Solution consumption, urination, hypotension, nausea and vomiting were also recorded. If any patient wasn’t content from the analgesic regimen (suffered pain VAS>6) automatically was excluded from the trial and another pain rescue regimen was started additionally.

Statistical analysis was performed using the SPSS 15.0. Continuous variable were evaluated with t-test. The Mann-Whitney test was used if data were not normally distributed. A p value less than 0.05 was considered statistically significant.

Results

A total of 2 patients were excluded from the statistical analyses. Reasons for withdrawal are presented in Table 1. There were no significant differences between the two groups in the demographic data. (Table 2) Hypotension and vomiting was rare. The first urination timing between the two groups was statistically insignificant too (Table 3). There was a statistical difference at the mean patient control consumption of the solution. The mean patient control consumption of the solution was higher at group C respect group F (p = 0.007) (Table 3). The pump indication during the 24 hours was statistical different except the 4th hour (p<0, 05). In fact at the 2nd hour group F consumed more solution than group C. At the rest measuring hours (8th, 12th, 24th) group C consumed more (Fig. 1). At the 8th hour after the operation we register a statistical significant difference at the mean VAS score between the two groups (p<0, 05) with group C achieving a higher score (Fig. 2). At the 8th and 12th hour group C register a lower Bromage score than group F (p<0.005 and p = 0.002 respectively) (Table 4).
COMPARISON BETWEEN ROPIVACAINE 1.5 MG ML⁻¹ PLUS FENTANYL 2 MG ML⁻¹ AND ROPIVACAINE 1.5 MG ML⁻¹ PLUS CLONIDINE 1 MG ML⁻¹ AS ANALGESIC SOLUTION AFTER ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION: A RANDOMIZED CLINICAL TRIAL

Table 1
Reason for withdrawal

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Reason for withdrawal</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group F</td>
<td>Insufficient analgesia</td>
<td>Replace with a more dense epidural solution</td>
</tr>
<tr>
<td>Group C</td>
<td>Technical problem</td>
<td>Epidural catheter dislocation</td>
</tr>
</tbody>
</table>

Values in parentheses indicate standard deviation.

Table 2
Demographic characteristics

<table>
<thead>
<tr>
<th>Groups</th>
<th>Age</th>
<th>Weight</th>
<th>Height</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl</td>
<td>27,4 (4,28)</td>
<td>85,04 (8,43)</td>
<td>180 (5,66)</td>
<td>26,24 (2,4)</td>
</tr>
<tr>
<td>Clonidine</td>
<td>28,76 (4,43)</td>
<td>81,88 (7,68)</td>
<td>178,76 (5,87)</td>
<td>25,59 (1,73)</td>
</tr>
</tbody>
</table>

Values in parentheses indicate standard deviation.

Table 3
Patient controlled local anesthetic consumption, time of first urination and cases of hypotension and vomiting

<table>
<thead>
<tr>
<th>Groups</th>
<th>PCEA</th>
<th>Hypotension</th>
<th>Vomit</th>
<th>Urination</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes/No</td>
<td>Yes/No 2h/4h 8h/12h 24h</td>
<td>Yes/No</td>
<td></td>
</tr>
<tr>
<td>Fentanyl</td>
<td>13,40 (14,629)</td>
<td>25/0 25/0 11/6 3/4 1/1</td>
<td>0/0</td>
<td></td>
</tr>
<tr>
<td>Clonidine</td>
<td>27,80 (26,22)</td>
<td>22/24 6/7 11/11 0/0</td>
<td>0/0</td>
<td></td>
</tr>
</tbody>
</table>

- Values in PCEA column indicate the extra mean patient-controlled local anesthetic consumption in addition to the base dose (5 ml h⁻¹) and values in parentheses indicate standard deviation.
- Values in other columns indicate frequency.
* Statistical difference between the groups.

Discussion

Epidural analgesia is more effective for postoperative pain relief respect other regiments. But pain relief isn’t the only goal for a successful postoperative outcome. Other variants such as early mobilization and fewer side effects from the analgesic regiment are some aspects. With this study we compare two analgesic solutions trying to achieve excellent pain relief without any motor blockade and no side effects. Ropivacaine is an amide local anesthetic with a high pKa (8.1). At the same concentration ropivacaine produce less motor block than bupivacaine.

Opioids used epidurally, and especially fentanyl, as adjuvant to local anesthetics reduce the dose and side effects of both drugs and achieve better analgesia. Opioids mediate their analgesic effect by acting at their receptors in the substantia gelatinosa of the spinal cord. These results have been underlined by Berti et al where a combination of ropivacaine and opioid were
administered epiduraly for postoperative analgesia after anterior cruciate ligament repair⁸.

Clonidine is another drug that is frequently used as adjuvant to local anesthetics for epidural analgesia and significantly enhances the duration of analgesia of epidurally administered ropivacaine⁹. This α₂ agonist mediates its analgesic effect by activating postsynaptic α2 receptors in the gelatinous substance of the spinal cord, mimicking the activation of descending inhibitory pathways¹⁰,¹¹,¹². De Kock et al have used clonidine as the sole agent administrated epidurally for postoperative analgesia¹³.

Several studies had already proposed different concentration for epidural ropivacaine. When used alone 2 mg ml⁻¹ seems to be the optimal concentration¹⁴,¹⁵,¹⁶. But sometimes with excessive motor block. Although Tetsuya et al propose 0.5 mg ml⁻¹ as the favorable concentration in order to reduce local anesthetics side effect, in our study we conclude that even in higher concentration up to 1.5 mg ml⁻¹ ropivacaine was also free of side effects¹⁷.

Concentration of 1 μg ml⁻¹ clonidine and 2 μg ml⁻¹ fentanyl as adjuvant in epidural solutions seems to be free of side effects too¹⁸,¹⁹,²⁰.

We register a higher consume from Group C than Group F. Sides effects at both groups were statistically insignificant. Patient comfort was higher at Group F than Group C if we evaluate the VAS score. Even if at Group C the legs sensibility and mobility return earlier the greatest patient’s fear is pain. There are no similar studies with such low ropivacaine concentration after ACL reconstruction operation in order to compare the postoperative analgesia and patient comfort.

In conclusion, we consider that ropivacaine 1.5 mg ml⁻¹ plus fentanyl 2 μg ml⁻¹ administred through PCEA is safe, without side effects and can provide excellent postoperative analgesia after ACL reconstruction.

Acknowledgement

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