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SCIENTIFIC ARTICLE

Association of clonidine and ropivacaine in brachial plexus block for shoulder arthroscopy

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KEYWORDS
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Abstract
Background and objectives: Arthroscopy for shoulder disorders is associated with severe and difficult to control pain, postoperatively. The addition of clonidine to local anesthetics for peripheral nerve block has become increasingly common, thanks to the potential ability of this drug to reduce the mass of local anesthetic required and to prolonging analgesia postoperatively. The present study aimed to evaluate the success of brachial plexus block for arthroscopic rotator cuff surgery using local anesthetic with or without clonidine.
Method: 53 patients of both genders, between 18 and 70 years old, American Society of Anesthesiologists I or II, who were scheduled to undergo arthroscopic shoulder surgery were selected. Patients were then randomized into two groups. The verbal numerical pain scale and the presence of motor block were obtained in the post-anesthetic recovery room and 6, 12, 18 and 24 h postoperatively.
Results: The association of clonidine (0.15 mg) to a solution of 0.33% ropivacaine (30 mL) in brachial plexus block for shoulder arthroscopy has not diminished the visual numeric pain scale values, nor the need for opioid rescue postoperatively. There was a lower incidence of nausea/vomiting postoperatively and a significant motor block time prolongation in the group of patients who received clonidine as adjuvant.
Conclusions: The use of brachial plexus block with local anesthetic for analgesic postoperative control is well established in the literature. The addition of clonidine in the dose proposed for prolongation of the analgesic effect and reduction of opioid rescue proved unhelpful.
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PALAVRAS-CHAVE
Anestésicos locais;
Clonidina;
Artroscopia;
Dor pós-operatória

Associação de clonidina e ropivacaína no bloqueio de plexo braquial para artroscopia de ombro

Resumo
Justificativa e objetivos: A artroscopia para afecções do ombro associa-se a dor de forte intensidade no pós-operatório, de difícil manejo. A adição de clonidina ao anestésico local em bloqueios periféricos tornou-se progressivamente maior graças à potencial habilidade dessa droga de reduzir a massa de anestésicos locais necessários e prolongar a analgesia no pós-operatório. O presente estudo teve como objetivo avaliar o sucesso do bloqueio de plexo braquial para a cirurgia artroscópica de manguito rotador com o uso de anestésico local associado ou não à clonidina.
Método: Foram selecionados 53 pacientes de ambos os sexos, entre 18 e 70 anos, ASA I ou II, que seriam submetidos à cirurgia de ombro por artroscopia. Os pacientes foram então randomizados em dois grupos. A escala numérica verbal de dor e a presença de bloqueio motor eram obtidas na sala de recuperação pós-anestésica (SRPA) com seis, 12, 18 e 24 horas de pós-operatório.
Resultados: A associação de clonidina (0,15 mg) à solução de ropivacaína 0,33% (30 mL) no bloqueio de plexo braquial para artroscopia de ombro não diminuiu os valores da escala visual numérica de dor, nem a necessidade de resgate com opioides no pós-operatório. Houve uma menor incidência de náuseas e vômitos no pós-operatório (NVPO) e aumento considerável do tempo de bloqueio motor no grupo de pacientes que recebeu clonidina como adjuvante.
Conclusões: O uso do bloqueio de plexo braquial com anestésico local para controle analgésico pós-operatório está consolidado na literatura. A adição de clonidina na dose proposta para prolongamento do efeito analgésico e redução de resgate com opioides mostrou-se pouco útil.
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Introduction

Brachial plexus blocks are indicated for anesthesia and analgesia in endoscopic procedures of the upper limb, shoulder, and clavicle. This anesthetic technique enables surgical procedures with short hospital stay (no overnight stay) or anesthesia for procedures on an outpatient basis, with consequent cost reduction. Its analgesic efficacy and low incidence of side effects are important characteristics. When long acting local anesthetics are used, even at a single dose, analgesia time ranges between 10 and 18 h. Brachial plexus block allows painless manipulation in physiotherapy, often critical for rehabilitation.

Postoperative pain is perhaps the main complication of shoulder arthroscopy involving the rotator cuff.[1] The peripheral nerve block can provide adequate analgesia in early postoperative period for up to 20 h.[2] The success of brachial plexus block depends on the volume of anesthetic used and on the solution concentration. The concentration is the main determinant of motor blockade.[3]

Clonidine, an alpha-agonist with partial action on alpha-2 receptors, has been used for years as a centrally acting antihypertensive. Literature reports on the potential benefits of adding clonidine to local anesthetics are controversial. The addition of clonidine to intermediate or long-acting local anesthetics for peripheral nerve or plexus block prolongs the duration of analgesia and motor block for about 2 h.

The use of this drug in blockades increased progressively due to its ability to reduce the mass of local anesthetic required, as well as to prolong postoperative analgesia.[4] This potentiating effect was also seen when clonidine was added to bupivacaine.[5] Parenteral clonidine, muscle or intravenously administered, did not show the same benefit in peripheral nerve block compared with its local use.[5] Most results found for clonidine shows no adverse effects, such as hypotension or prolonged sedation with its use in regional block.[6,7] The combination of clonidine with bupivacaine, for example, prolonged the analgesic effect of regional blockade for 3–4 h when used in the popliteal fossa in foot and ankle surgeries.[2]

However, Duma et al.[8] reported that clonidine added to long-acting local anesthetic (bupivacaine or levobupivacaine) produced no prolonged analgesic effect on brachial plexus block and increased the variability of patient response to local anesthetics, particularly to blockade latency. Moreover, the optimal dose of clonidine as an adjunct to blockade has not yet been defined.[8] Dose escalation is related to a larger number of adverse effects, mainly related to the drug systemic absorption.

The aim of this study was to evaluate whether the addition of clonidine to a local anesthetic in brachial plexus blockade contributed to the quality of postoperative analgesia in arthroscopic rotator cuff surgery. We evaluated the visual numeric pain scale at the early postoperative period, in the post-anesthesia care unit (PACU), and at the first 24 h after surgery. We also evaluate the need for rescue analgesia with opioids and compared the incidence of residual motor blockade and the length of hospital stay of patients.

Table 1 Anthropometric data, gender distribution, and ASA physical status.

	LA	LA + Cl	*p*
Age (years)	54 ± 10	52 ± 11	0.37
Weight (kg)	77.4 ± 14	78 ± 11	0.89
Sex	M (11), F (13)	M (11), F (15)	0.81
ASA	I (8), II (16)	I (9), II (17)	0.93

Values are expressed as mean ± SD or absolute values.
LA, local anesthetics; LA + Cl, local anesthetic associated with clonidine; ASA, American Society of Anesthesiologists.

Method

This study was approved by the Institutional Ethics Research Committee (HFR-CEP).

Initially, 53 patients of both sexes, aged between 18 and 70 years, classified by the American Society of Anesthesiologists (ASA) as type I or II, scheduled to undergo shoulder arthroscopy (Table 1) were selected. Patients were randomly allocated to two groups. The investigator responsible for postoperative evaluation was blinded to group allocation. All patients signed an informed consent.

Patients with cardiac, respiratory, liver or kidney disease; allergy to local anesthetics and their diluents; neuropathies or cognitive deficits; body mass index higher than 45; and skin infection at the site of blockade, or contralateral hemidiaphragm paralysis were excluded from the study. Smoking was not a criterion for selection of patients in this study design.

The expected effects of using high doses of clonidine, such as sedation and dry mouth, were not evaluated in this study, as patients were under general anesthesia immediately after the blockade. Possible cardiovascular effects of alpha-2 agonist were also not evaluated because the general anesthesia maintenance drugs (sevoflurane and sufentanil) could be confounding factors.

To calculate the sample, we consider a power of 90% and a significance level of 5%, which resulted in a sample size of 23 patients per group.

During anesthesia, patients were monitored with electrocardiogram (DII, V5), pulse oximetry, noninvasive blood pressure, capnography, and inhaled gas analyzer. Premedication was performed with 2 mg intravenous (IV) midazolam. After brachial plexus block, balanced general anesthesia was induced with the following drugs: propofol (3 mg kg^{-1}); sufentanil (0.5 μg kg^{-1}); cisatracurium (0.15 mg kg^{-1}); sevoflurane (1 MAC); dexamethasone (10 mg); ondansetron (4 mg); dipyrone (2000 mg); ketoprofen (100 mg); morphine (used only if required for rescue analgesia, 50 μg kg^{-1}). Local anesthetic solution was diluted with 1% ropivacaine (10 mL) (Cristália Laboratório Farmacêutico) and sterile bidistilled water (20 mL), totaling a volume of 30 mL to be injected.

Postoperatively on the ward, all patients received a fixed dose of IV dipyrone (2000 mg) every 6 h. Morphine (50 μg kg^{-1}) was used as rescue analgesia, whenever necessary.

Protocol 1: Effect of 0.33% ropivacaine on postoperative analgesia in patients undergoing arthroscopic shoulder surgery

Initially, 26 patients were selected for control group. Brachial plexus block was performed with electrical nerve stimulator (Stimuplex DIG; BBraun) and specific needle (Stimuplex A50, BBraun). After proper location of the injection site, 30 mL of 0.33% ropivacaine solution was used. General anesthesia was performed after the blockade.

At the end of surgery, presence of pain was assessed using a verbal numerical pain scale (0: no pain, 10: worst possible pain). During PACU stay, if there was need for rescue with IV morphine at a dose greater than 0.1 mg kg^{-1}, the patient was excluded from the protocol, and plexus block failure was considered.

Verbal numerical pain scale and presence of motor block were obtained in PACU and at six, 12, 18, and 24 h after surgery.

Protocol 2: Effect of 0.33% ropivacaine and clonidine (0.15 mg) on postoperative analgesia in patients undergoing arthroscopic shoulder surgery

Initially, 27 patients were selected for control group. Brachial plexus blockade was performed with electrical nerve stimulator (Stimuplex DIG; BBraun) and specific needle (Stimuplex A50, BBraun). After proper location of the anesthetic injection site, 30 mL of 0.33% ropivacaine solution and 0.15 mg of clonidine (Cristália Laboratório Farmacêutico) were used. Then, the patient underwent general anesthesia.

Verbal numerical pain scale and presence of motor block were obtained in PACU and at six, 12, 18 and 24 h after surgery.

Statistical analysis

For continuous quantitative variables, the values are presented as mean ± standard deviation and comparisons were performed using Student's paired *t*-test (normal variables). For ordinal qualitative variables, the values are presented as median and interquartile range, followed by Wilcoxon test (nonparametric variables) (Software GraphPadPrism 6.0). The statistical significance criterion was set at $p < 0.05$.

Results

In control group, two patients were excluded from analysis (one was lost to postoperative follow-up, one was later considered as ASA III). In clonidine group, one patient was excluded from analysis because we considered that there was a blockade failure (received morphine > 0.1 mg kg^{-1} in PACU).

The anesthesiologist in charge for the case was free to choose the blocking technique. Of the 53 patients originally enrolled, 49 underwent interscalene brachial plexus block and only four patients underwent cervical paravertebral brachial plexus block. There was no difference between the two groups regarding techniques (values omitted). There

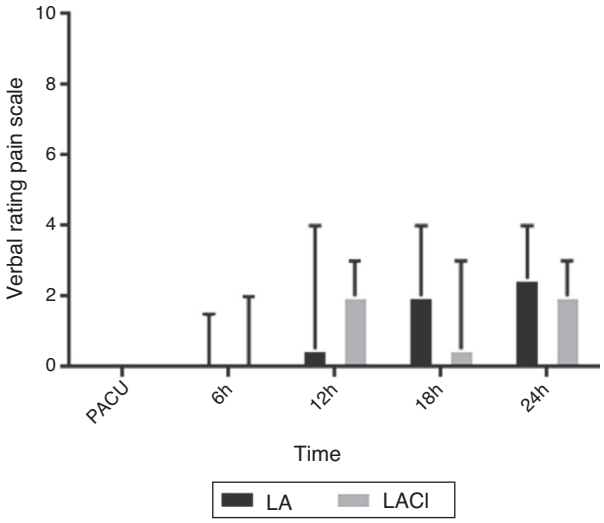

Figure 1 Verbal rating pain scale.

was no complication related to the anesthetic technique in any patient undergoing the experimental protocol.

Brachial plexus block with 0.33% ropivacaine (30 mL) provided satisfactory postoperative analgesia to patients studied at all measured times, as shown in Fig. 1. The visual analog pain scale reached a median value of two after 18 h of surgery, which is consistent with the half-life of ropivacaine. These values do not differ from those usually found in the literature for this type of procedure.[4] Regarding the need for morphine rescue analgesia, the mean number of doses in this group was two (Table 2). Six patients (25%) had postoperative nausea and vomiting (PONV) even after receiving adequate prophylaxis with dexamethasone and ondansetron. The mean duration of motor block in this group after surgery was 1.6 h. The mean hospital stay was 20 h. As almost all patients were discharged before the end of the protocol, it was continued by active search through phone call (20 patients in control group and 22 in clonidine group).

In the second group, brachial plexus block with 0.33% ropivacaine (30 mL) combined with clonidine (0.15 mg) provided satisfactory postoperative analgesia to patients at all measured times, as shown in Fig. 1. The visual analog pain scale was not statistically different from control group at any studied times.

Regarding the need for rescue analgesia with morphine, the mean number of doses in this group was 1.1 (Table 2), also with no statistical difference compared to control group. Regarding PONV, there was incidence in only one patient (3%) despite the standard prophylaxis established. The mean duration of residual motor blockade after the end of surgery was 7.4 h (approximately 4.5 times longer). The mean hospital stay was 18.8 h. A single patient in this group was hospitalized for more than one night, but the reason was not associated with anesthesia.

Table 2 Number of morphine rescue doses, incidence of PONV, and mean time of motor block duration and hospitalization.

	LA	LA + Cl	*p*
Morphine doses (50 μg kg^{-1})	2 ± 2.9	1.1 ± 1.4	0.16
PONV (*n*)	6	1	0.04
Motor block (h)	1.6 ± 2.5	7.4 ± 5.2	0.01
Hospitalization (h)	20.7 ± 6.5	18.8 ± 3	0.24

Values are expressed as mean ± SD.
LA, local anesthetics; LA + Cl, local anesthetic associated with clonidine; PONV, postoperative nausea and vomiting.

Discussion

The combination of clonidine (0.15 mg) to a solution of 0.33% ropivacaine (30 mL) in brachial plexus block for arthroscopic shoulder surgery did not decrease the values of the visual numeric pain scale or the need for postoperative rescue with opioids, a result consistent with other publications that used clonidine, even at doses higher than the one used in this study.[9–11]

Adjuvant drugs are aimed at prolonging analgesia, improve quality or reduce the latency of blocks by local anesthetic. Adrenaline (in a concentration of 1:400,000–1:200,000), clonidine (0.5–1.0 μg kg^{-1}), or opioids (morphine, sufentanil, fentanyl, buprenorphine) may be used, however, with no excessive sedation or hypotension.[12–14]

Clonidine antinociceptive mechanisms are controversial, particularly regarding synergy with local anesthetics for peripheral blocks, as peripheral nerve axons have no alpha-2 adrenergic receptors. Despite having originally been used as an antihypertensive and nasal decongestant, clonidine is an alpha-2 adrenergic agonist used as an adjuvant to local anesthetics, particularly in opioid-dependent patients.[15] Nervous conduction delay or blockade through sodium channels may explain the origin of clonidine-induced antinociception. The presence of alpha-2 agonists receptors in peripheral nerves can be decisive in analgesic potentiation, but the results are still controversial.[16,17] Other possible mechanisms may include local vasoconstrictor effect or analgesic effects on the central nervous system.[5] Some authors suggest that inflamed tissues are concomitant with increased sensitivity of A-delta and C pain fibers, which is why the addition of clonidine would be potentially beneficial.[18]

There is a significant interaction of clonidine addition to local anesthetics in ocular blocks (retrobulbar, peribulbar, and subtenon), which leads to akinesia and prolongation of analgesia.[19] Its analgesic potentiation has been described when it was administered in the intrathecal and epidural space (spinal anesthesia), particularly associated with short-acting local anesthetics.[20]

Regarding the ideal drug combination, clonidine appears to have greater adjuvant benefit with intermediate-acting local anesthetics, such as lidocaine and mepivacaine. A systematic literature review evaluated 27 studies, of which 15 had positive and 12 negative results on the addition of clonidine.[16] It seems that there are no side effects at doses up to 0.15 mg. Moreover, clonidine seems to be of greater benefit when added to upper compared to lower limb blocks.[16]

There is evidence in the literature that favors the addition of clonidine to reduce the latency of peripheral nervous block with ropivacaine when this drug is used for anesthesia.[21] However, the results are controversial regarding prolonged postoperative analgesia. Casati et al.[7]

reported that clonidine increased the analgesic effect time of ropivacaine by 20% after lower limb surgery.

In our study, we found a lower incidence of PONV. The smoking variable was not studied, a known protective factor against PONV,[22] which may interfere with the results.

Clonidine, when given orally as premedication, was effective as an adjuvant drug to reduce PONV in ophthalmic pediatric surgery.[23] Similar effect was also seen in otologic surgery[24] and to prevent postoperative nausea and tremors of elderly patients undergoing neuraxial blocks.[25] As a single drug for PONV prophylaxis, its effect is not as evident.[26] Clonidine also showed benefit in reducing PONV when used in the anesthetic induction of patients undergoing mastectomy,[27] without an increase of sedation or the emergence of other significant adverse effects. In the genesis of PONV appears to be an adrenergic autonomic dysfunction component, for which reason the use of clonidine appear to be beneficial.[28]

Clonidine is a medication of lower cost than the antiemetic drugs acting through 5-HT3, such as ondansetron and its similar. However, we believe that its real benefit as a single drug for PONV prophylaxis is small and also that it is not used routinely in most anesthesia services for this purpose. Furthermore, this drug potential antiemetic benefit can be obtained by oral or venous administration without the need to add it to the local anesthetic solution.

There was a considerable increase in motor block duration in patients receiving clonidine as an adjuvant. There is evidence in the literature on prolongation of motor block of bupivacaine and mepivacaine by alpha-2 agonist.[6,29] The question to be posed is about the actual benefit of this prolonged motor block, as the need for rescue with opioids is not reduced. In our opinion, postoperative prolonged motor block only increases patient anxiety, without providing real anesthetic or surgical benefit. This opinion is also shared by other authors.[30] In selected cases, it may even delay the recovery process, when we consider the real possibility of early physiotherapy.

There was no difference regarding patient's hospitalization. Therefore, clonidine did not affect the procedure operating cost.

The use of brachial plexus block with local anesthetic for postoperative analgesic management is consolidated in the literature. However, the addition of clonidine at the dose proposed to prolong the analgesic effect and reduce the rescue with opioids in the present study population proved to be of little benefit for brachial plexus block There are other drugs whose additive utility remains uncertain (tramadol, calcium channel blockers, neostigmine, dexamethasone, hyaluronidase, $NaHCO_3$) and that may be the subject of future studies.

Conflicts of interest

The authors declare no conflicts of interest.

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