Estudo Comparativo entre Clonidina Associada à Bupivacaína e Bupivacaína Isolada em Bloqueio de Plexo Cervical para Endarterectomia de Carótida *

A Comparative Study between Bupivacaine and Clonidine Associated with Bupivacaine in Cervical Plexus Block for Carotid Endarterectomy

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RESUMO


MÉTODO: Foram avaliados 30 pacientes de forma aleatória e duplamente-encoberta divididos em dois grupos: G1 recebeu 1,5 mg·kg⁻¹ de bupivacaína a 0,375% associados a 150 µg de clonidina (2 mL) e G2, 1,5 mg·kg⁻¹ de bupivacaína a 0,375% associados à solução fisiológica (2 mL). Foram avaliados: frequência cardíaca e pressão arterial nos momentos 0 (bloqueio), 30, 60, 90 e 120 minutos; necessidade de complementação anestésica; momento para primeira complementação analgésica; quantidade de analgésico usada e intensidade da dor nos momentos 0 (término da operação), 30, 60, 120, 240 e 360 minutos.

RESULTADOS: A complementação anestésica com lidocaína foi de 3,8 mL no G1 e 3,6 mL no G2 sem diferença estatística significativa. O momento para a primeira complementação foi de 302,6 ± 152,6 minutos no G1, e de 236,6 ± 132,9 minutos no G2, sem diferença significativa. Não houve diferença na dose de dipirona e tramadol usada. Não houve diferença na intensidade da dor entre os grupos.

CONCLUSÃO: A associação de 150 µg de clonidina à bupivacaína em bloqueio de plexo cervical para endarterectomia de carótida não promoveu melhora significativa do efeito analgésico avaliado por intensidade da dor, primeira complementação analgésica e quantidade de analgésico complementar.


SUMMARY
Pinto Neto W, Issy AM, Sakata RK – A Comparative Study between Bupivacaine and Clonidine Associated with Bupivacaine in Cervical Plexus Block for Carotid Endarterectomy.

BACKGROUND AND OBJECTIVES: Neurological evaluation can be done during cervical plexus block for endarterectomy, which also maintains postoperative analgesia. The objective of this study was to compare the analgesic effects of clonidine associated with bupivacaine to those of bupivacaine in cervical plexus block.

METHODS: A randomized double-blind study was undertaken with 30 patients divided in two groups: G1 received 1.5 mg·kg⁻¹ of 0.375% bupivacaine associated with 150 µg of clonidine (2 mL), and G2 received 1.5 mg·kg⁻¹ of 0.375% bupivacaine associated with NS (2 mL). The following parameters were evaluated: heart rate and blood pressure at 0 (block), 30, 60, 90, and 120 minutes; the need for anesthetic supplementation; time until the first analgesic supplementation; amount of analgesic used; and pain severity at 0 (end of the surgery), 30, 60, 120, 240, and 360 minutes.

RESULTS: Group 1 received 3.8 mL of lidocaine for anesthetic supplementation, while G2 received 3.6 mL of lidocaine, but this difference was not statistically significant. In G1, the time until the first supplementation was 302.6 ± 152.6 minutes, and in G2 it was 236.6 ± 132.9 minutes, which was not statistically significant. Differences between the doses of dipirona and tramadol were not observed. Differences in pain severity between both groups were not observed either.

CONCLUSION: The association of 150 µg of clonidine and bupivacaine in cervical plexus block for carotid endarterectomy did not improve significantly the analgesic effects evaluated by pain severity, time until the first analgesic supplementations and amount of supplementary analgesics.

Keywords: ANALGESIC: clonidine; ANESTHETIC TECHNIQUES, Regional: cervical plexus; SURGERY: endarterectomy.
INTRODUCTION

Cervical plexus block for carotid endarterectomy has some advantages, although controversies on the best anesthetic technique still exist. In the regional technique the neurologic evaluation is easier to perform than in general anesthesia. Besides, some studies have shown lower neurologic morbidity associated with cervical plexus block 2,3.

In a study, regional block was associated with lower mortality, perioperative ischemia, and myocardial infarction rates 1. Adequate pain relief provided by the regional block can explain the results achieved by those authors, since adequate postoperative analgesia promotes a reduction in the rate of complications.

Several drugs can be used in the treatment of postoperative pain by reducing or blocking pain transmission. Drug associations can offer better results than a single agent. Local anesthetics can be administered isolatedly or associated with another drug 4,5.

Clonidine is a α2-adrenergic agonist used in subarachnoid 6-11, epidural 12, and brachial plexus 13-15 blocks. It exerts its action in the peripheral nervous system by decreasing the secretion of noradrenaline and the inhibiting depolarization of nociceptive neurons in primary afferent nerve endings by binding to α2-receptors, subtypes A and C 16. In the central nervous system, it inhibits neuronal transmission in different areas of the brain, such as: the nucleus of the solitary tract and lateral reticular nucleus of the ventrolateral spinal cord. Studies suggest that clonidine reduces the release of glutamate and noradrenaline, inhibits the opening of calcium channels, and activates the opening of potassium channels 17,18. It also has synergistic effects with local anesthetics, blocking conduction in A-delta and C fibers. It can reduce, indirectly, the absorption of local anesthetics 19.

Although it is effective in regional blocks, studies on the use of clonidine in cervical plexus blocks are rare 10,21. The objective of this study was to compare the effects of bupivacaine and bupivacaine associated with clonidine in cervical plexus block in patients undergoing carotid endarterectomy, evaluating the need of anesthetic supplementation, severity of postoperative pain, and postoperative analgesic consumption.

METHODS

After approval by the Ethics on Research Committee and signing of an informed consent, 30 adult patients undergoing
carotid endarterectomy, randomly divided in two groups, participated in this double-blind study. Patients with contraindications for the blockade (local infection, coagulation disorders) and hypersensitivity to the drugs used were excluded. Patients were divided in two groups by drawing numbers placed in envelopes. Drugs for the blockade were prepared in advance and delivered to the anesthesiologist. Patients were evaluated by a different investigator. Both physicians and patients were not aware of which group they belonged to until the end of the study.

In the operating room, patients were monitored with a cardioscope on D1 and CM5 derivations, digital pulse oximeter, and non-invasive blood pressure. Teflon catheters, 18G or 20G, were used for venipunctures in the upper limb opposite to the site of surgery.

All patients received 10 mg of intravenous diazepam five minutes before the blockade. Patients in group 1 (n = 15) received 1.5 mg.kg⁻¹ of 0.375% bupivacaine without vasoconstrictor associated with 150 µg of clonidine (1 mL), in the deep cervical plexus block, and 10 mL of 0.375% bupivacaine without vasoconstrictor, in the superficial cervical plexus block. Patients in group 2 (n = 15) received 1.5 mg.kg⁻¹ of 0.375% bupivacaine without vasoconstrictor associated with NS (1 mL), in the deep cervical plexus block, and 10 mL of 0.375% bupivacaine without vasoconstrictor, in the superficial cervical plexus block.

For deep cervical plexus block patients were placed in horizontal dorsal decubitus with discrete cervical extension and the head rotated to the contralateral side of the blockade. After cleaning the area, the thyroid cartilage was identified and a horizontal line was drawn in the lateral direction to the point of the posterior sternocleidomastoid muscle and between the anterior and middle scalene muscles – after palpating the transverse process of the fourth cervical vertebra and introducing a 30 x 8-mm needle, perpendicular to the skin, until it touched the muscle; retrieving it by 2-mm mark. Aspiration was done initially and after the injection of every 3 mL of anesthetic to check for the absence of CSF and blood.

Superficial cervical block was done by identifying the external jugular vein and the posterior border of the sternocleidomastoid muscle. The anesthetic was injected at the junction of those two structures at depth of approximately 3 cm. The need of anesthetic supplementation with 1% lidocaine without vasoconstrictor was assessed when the patient presented pain to the surgical stimulus. Hemodynamic parameters (heart rate, systolic, mean, and diastolic pressures) were evaluated at 0 (block), 30, 60, 90, and 120 minutes.

After the surgery patients were transferred to the recovery room where they remained until they reached an Aldrete-Kroulic index equal or greater than eight.

Pain severity was evaluated by the visual analogue scale (0 to 10) at 0 (end of the procedure), 30, 60, 120, 240, and 360 minutes. The time between the blockade and the need for the first analgesic supplementation was recorded, as well as the total dose of supplementary analgesic. Intravenous dypiron (1 g) was used for supplementary analgesia and if the patient did not have adequate pain relief, 100 mg of intravenous tramadol were administered. Adequate pain relief was defined as pain ≤ 4. Possible side effects were also recorded.

Parametric and non-parametric tests were used for the statistical analysis, considering the nature of the parameters analyzed. Menusurations with mean central tendencies and dispersion (standard deviation) were used. It was determined a level of statistical significance of p ≤ 0.05. Fisher’s exact test was used to analyze gender; the Mann-Whitney test was used to analyze age and body mass index; and the Student t test was used for weight and height. The Mann-Whitney test was used to analyze the duration of the surgery, hemodynamic parameters, time until the first analgesic supplementation, pain severity, and volume of anesthetic supplementation. Fisher’s exact test was used to analyze the need for anesthetic and analgesic supplementation. Calculations were undertaken with the hypothesis of a reduction in analgesic consumption of at least 20% in the clonidine/bupivacaine group. Statistical calculations indicated that a group with 15 patients would provide a 95% chance of detecting this difference with a level o significance of 0.05.

RESULTS

Both groups were similar regarding the demographic data (gender, age, weight, height, and body mass index), which is shown in table I. The physical status of the patients was as follows: ASA I (G1 = 26.6% and G2 = 0%), ASA II (G1 = 33.4% and G2 = 20%), and ASA III (G1 = 40% and G2 = 80%). Significant differences between the mean surgery duration in G1 (179.5 minutes) and G2 (142.6 minutes) were not seen (Mann-Whitney test, p = 0.421).

As for anesthetic supplementation with 1% lidocaine, G1 received 3.8 mL and G2 3.6 mL, which did not show a statistically significant difference (Mann-Whitney test, p= 0.8270);

### Table I – Demographic Data

<table>
<thead>
<tr>
<th></th>
<th>G1</th>
<th>G2</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (M/F)</td>
<td>10 / 5</td>
<td>6 / 9</td>
<td>0.2723 *</td>
</tr>
<tr>
<td>Age (years)</td>
<td>64.7 ± 8.5</td>
<td>66.2 ± 9.9</td>
<td>0.9174 **</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>64.9 ± 12.3</td>
<td>64.9 ± 12.3</td>
<td>0.3148 #</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>164.4 ± 8.1</td>
<td>164.4 ± 8.1</td>
<td>0.8119 *</td>
</tr>
<tr>
<td>BMI (kg.m⁻²)</td>
<td>23.9 ± 3.6</td>
<td>25.6 ± 3.5</td>
<td>0.2372 **</td>
</tr>
</tbody>
</table>

Results expressed as Mean ± SD

*Fisher’s Exact test; ** Mann-Whitney test; #Student t test
G1 – clonidine; G2 – bupivacaine; p ≤ 0.05; BMI – body mass index
A COMPARATIVE STUDY BETWEEN BUPIVACAINE AND CLONIDINE ASSOCIATED WITH BUPIVACAINE IN CERVICAL PLEXUS BLOCK FOR CAROTID ENDARTERECTOMY

in G1, 13 (86.6%) patients needed anesthetic supplementation, while in G2 11 (73.3%) patients required supplementation, which also did not show a statistically significant difference (Fisher’s exact test, p = 1.0000).

The time between the blockade and the administration of the first dose of 1 g of intravenous dypirone was 302.6 ± 152.6 minutes in G1, and 236.6 ± 132.9 minutes in G2, and this difference was not statistically significant (Mann-Whitney test, p = 0.7168).

Statistically significant differences between both groups regarding the number of patients who needed analgesic supplementation, both with dypirone (G1 = 20% and G2 = 20%; Fisher’s exact test, p = 1.3487) and tramadol (G1 = 0% and G2 = 13%) after the end of the surgery (Fisher’s exact test, p = 0.4828) were not observed.

Pain severity according to the scores of the visual analogue scale did not show statistically significant differences between both groups at every evaluation time, which can be seen in table II.

Blood pressure and heart rate also did not show statistically significant differences between both groups, and those parameters did not show significant changes at the assessment moments (Table III).

In G1, four patients developed hypertension and 1 patient developed bradycardia during the surgery.

Table III – Blood Pressure and Heart Rate

<table>
<thead>
<tr>
<th></th>
<th>G1 (n = 15)</th>
<th>G2 (n = 15)</th>
<th>p **</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure (BP)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M₀</td>
<td>163.8 ± 17.3</td>
<td>157.3 ± 28.0</td>
<td>0.4937</td>
</tr>
<tr>
<td>M₃₀</td>
<td>147.9 ± 27.7</td>
<td>153.8 ± 36.3</td>
<td>0.6632</td>
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<tr>
<td>M₆₀</td>
<td>145.3 ± 19.5</td>
<td>148.2 ± 27.5</td>
<td>0.7715</td>
</tr>
<tr>
<td>M₉₀</td>
<td>152.5 ± 31.3</td>
<td>147.8 ± 36.0</td>
<td>0.6945</td>
</tr>
<tr>
<td>M₁₂₀</td>
<td>158.2 ± 23.3</td>
<td>154.9 ± 35.8</td>
<td>0.7470</td>
</tr>
<tr>
<td>Diastolic blood pressure (DBP)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M₀</td>
<td>90.8 ± 15.8</td>
<td>87.9 ± 14.2</td>
<td>0.6630</td>
</tr>
<tr>
<td>M₃₀</td>
<td>84.8 ± 18.7</td>
<td>87.9 ± 20.7</td>
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<td>M₆₀</td>
<td>90.2 ± 13.9</td>
<td>89.8 ± 24.9</td>
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<td>M₉₀</td>
<td>92.5 ± 18.1</td>
<td>88.3 ± 23.2</td>
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<td>M₁₂₀</td>
<td>93.2 ± 17.2</td>
<td>89.3 ± 18.1</td>
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<td>Mean arterial pressure (MAP)</td>
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<tr>
<td>M₀</td>
<td>113.4 ± 12.4</td>
<td>115.6 ± 19.3</td>
<td>0.5337</td>
</tr>
<tr>
<td>M₃₀</td>
<td>108.4 ± 23.3</td>
<td>109.2 ± 21.9</td>
<td>0.9174</td>
</tr>
<tr>
<td>M₆₀</td>
<td>112.6 ± 4.0</td>
<td>112.0 ± 18.6</td>
<td>0.9669</td>
</tr>
<tr>
<td>M₉₀</td>
<td>115.8 ± 22.8</td>
<td>115.4 ± 31.3</td>
<td>0.7766</td>
</tr>
<tr>
<td>M₁₂₀</td>
<td>120.6 ± 19.6</td>
<td>115.2 ± 25.9</td>
<td>0.5339</td>
</tr>
<tr>
<td>Heart rate (HR)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M₀</td>
<td>74.3 ± 10.6</td>
<td>83.7 ± 13.2</td>
<td>0.0381</td>
</tr>
<tr>
<td>M₃₀</td>
<td>75.4 ± 14.7</td>
<td>83.1 ± 13.4</td>
<td>0.2998</td>
</tr>
<tr>
<td>M₆₀</td>
<td>76.7 ± 14.6</td>
<td>82.3 ± 14.0</td>
<td>0.2998</td>
</tr>
<tr>
<td>M₉₀</td>
<td>76.0 ± 14.4</td>
<td>80.1 ± 10.4</td>
<td>0.2135</td>
</tr>
<tr>
<td>M₁₂₀</td>
<td>77.2 ± 14.7</td>
<td>79.5 ± 10.5</td>
<td>0.5490</td>
</tr>
</tbody>
</table>

Results expressed as Mean ± SD
G1 – clonidine; G2 – bupivacaine; M₀ – end of the surgery, M₃₀; M₆₀; M₉₀; M₁₂₀ – minutes after the end of the surgery; p ≤ 0.05; Mann-Whitney test

*ANOVA; ** Mann-Whitney test
G1 – clonidine; G2 – bupivacaine; M₀ – block; M₃₀; M₆₀; M₉₀; M₁₂₀ – moments (minutes) after the blockade

DISCUSSION

In the present study the demographic data were similar to that reported in the literature 20,22–25. Those procedures are usually used in patients with systemic disorders.

The best anesthetic technique for carotid endarterectomy still is surrounded by controversies.

For this type of surgery the anesthetic technique used seems to be the most indicated for patients with some any kind of organ involvement, since it causes less respiratory changes and promotes greater hemodynamic stability. The lack of differences in blood pressure with general anesthesia or regional block was reported in one study 26. However, another study reported a greater incidence of hypertension associated with regional block 22. In the present study hypotension requiring treatment was not observed and blood pressure levels were similar to those reported in the literature 22,26.

In regional blocks the neurological system is evaluated continuously during clamping of the carotid; therefore, it decreases the need for derivations 26, i.e., placement of a catheter to reroute blood from the area proximal to the obstruction to distal brain areas which increases the risk of
thrombus formation; this represents another advantage of regional blocks. Besides, the length of hospitalization is significantly lower.

Superficial and deep cervical plexus blocks can be used for carotid endarterectomy; however, combining the blockade of both plexuses promotes anesthesia of better quality. In the present study, superficial and deep cervical plexus blocks were used to reduce the incidence of failures and provide greater muscle relaxation, which brings great benefits for the surgical technique.

Clonidine was administered to determine whether postoperative analgesia was better than with bupivacaine alone. Some studies have demonstrated that intravenous clonidine reduces the need of anesthetic supplementation in cervical plexus blocks. Studies have demonstrated an increase in the duration of the cervical plexus block when the association of clonidine and lidocaine is used. In the present study, clonidine was administered in the deep cervical plexus, since the superficial cervical plexus originates from this structure.

In peripheral blocks, doses of clonidine in the range of 150 to 300 µg are used. In the literature, the volume used in cervical plexus blocks varies from 10 to 30 mL. Volume is important in all blocks, but the toxic dose of the local anesthetic should be observed.

The need of anesthetic supplementation in carotid endarterectomy under cervical plexus block (C2 to C4) is not uncommon, due to the failure of areas innervated by the C2 and C3 nerve roots and more commonly when the carotid sinus is manipulated. This region is innervated by afferent portions of the glossopharyngeal and vagus nerves and the sympathetic trunk, which are not anesthetized in the superficial and deep cervical plexus blocks. In the present study, the supplementation volume was smaller than that reported in the literature, which varies from 5 to 10 mL.

The preference for lidocaine can be explained by its lower toxicity and other authors have used this anesthetic in concentrations ranging from 0.5 and 1% for anesthetic supplementation.

Anti-inflammatory drugs were not used due to the greater possibility of renal damage in elderly patients and those with comorbidities, such as hypertension and diabetes mellitus reported in the literature as well.

Similarly to other studies, the quality of analgesia in the present study was satisfactory. Studies have demonstrated that postoperative analgesia is better in cervical plexus block. Clonidine exerts its actions in the peripheral nervous system by binding pre-synaptic receptors of Aδ and C fibers, decreasing the release of glutamate and noradrenaline from nerve endings, as well as opening calcium channels and inhibiting the depolarization of nociceptive neurons. It is also synergistic with local anesthetics by blocking the conduction of stimuli in Aδ and C fibers, and increasing potassium conductance. This drug can decrease the absorption of local anesthetics due to the vasoconstriction caused by its effects in postsynaptic α2 receptors in the smooth muscle of the blood vessels.

The severity of postoperative pain can be measured by means of easy to use scales. The visual analogue scale is used more often.

In the literature, the incidence of strokes varies from 0.4 to 8%, and the need for carotid derivation from 9 to 20%. The rate of myocardial ischemia reported in the literature varies from 1 to 5.7%, and tachycardia from 6.66 to 35%. The incidence of bradycardia in the present study was also similar to that reported in the literature that varies from 2.5 to 13.5%. Four patients (26.6%) developed hypotension, also similar to that reported by some authors, i.e., 24 to 35%. Hypertension occurred when the carotid was clamped and this is also reported in the literature. In G1, one patient (2.2%) developed sinus bradycardia; this incidence is similar to that reported in the literature, i.e., 2.5 to 13.5%. Those complications did not require treatment. Other complications, such as damage of the vagus and recurrent laryngeal nerves, affecting 1.2 to 35% of the patients and intravascular injection of the local anesthetic are also reported in the literature.

The association of 150 µg of clonidine and bupivacaine in cervical plexus block for carotid endarterectomy did not promote a significant improvement of analgesia, evaluated by pain severity, the first analgesic supplementation, and the amount of analgesic supplementation.

REFERENCES

A COMPARATIVE STUDY BETWEEN BUPIVACAINE AND CLONIDINE ASSOCIATED WITH BUPIVACAINE IN CERVICAL PLEXUS BLOCK FOR CAROTID ENDARTERECTOMY

RESUMEN:
Pinto Neto W, Issy AM, Sakata RK - Estudio Comparativo entre la Clonidina Asociada a la Bupivacaina y la Bupivacaina Aislada en Bloqueo de Plexo Cervical para Endarterectomía de Carótida.

JUSTIFICATIVA Y OBJETIVOS: El bloqueo de plexo cervical permite la evaluación neurológica durante la endarterectomía, además de mantener la analgesia postoperatoria. La clonidina es agonista alfa-2 con un efecto analgésico en diferentes bloqueos. El objetivo de este estudio fue comparar el efecto analgésico de la clonidina con la bupivacaina con relación a la bupivacaina aislada en bloqueo de plexo cervical.

MÉTODO: Se evaluaron 30 pacientes, de forma aleatoria y en doble ciego, divididos en dos grupos: G1 recibió 1,5 mg.kg\textsuperscript{-1} de bupivacaina a 0,375% asociados a 150 µg de clonidina (2 mL) y G2, 1,5 mg.kg\textsuperscript{-1} de bupivacaina a 0,375% asociados a la solución fisiológica (2 mL). Se evaluaron la frecuencia cardíaca y la presión arterial en los momentos 0 (bloqueo), 30, 60, 90 y 120 minutos; la necesidad de complementación anestésica; el momento para la primera complementación analgésica; la cantidad de analgésico usado y la intensidad del dolor en el momento 0 (término de la operación), 30, 60, 120, 240 y 360 minutos.

RESULTADOS: La complementación anestésica con bupivacaina fue de 3,8 mL en el G1 y 3,6 mL en el G2 sin diferencias estadísticas significativas. El momento para la primera complementación fue de 302,6 ± 152,6 minutos en el G1, y de 236,6 ± 132,9 minutos en el G2, sin diferencia significativa. No hubo diferencia en la dosis de dipirona y tramadol usada. No hubo diferencia en la intensidad del dolor entre los grupos.

CONCLUSIÓN: La asociación de 150 µg de clonidina a bupivacaina en el bloqueo de plexo cervical para la endarterectomía de carótida, no generó ninguna mejora significativa del efecto analgésico evaluado por la intensidad del dolor, en la primera complementación analgésica y en la cantidad de analgésico complementario.