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Efficacy of paraspinal anesthetic block in patients with chronic pelvic pain refractory to drug therapy: a randomized clinical trial

Eficácia do bloqueio anestésico paraespinal em pacientes com dor pélvica crônica refratária a terapia medicamentosa: um ensaio clínico randomizado

Original Article

Keywords

Pelvic pain
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Palavras-chave

Dor pélvica
Nervos periféricos
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Abstract

PURPOSE: To determine whether paraspinal block reduces pain scores compared to placebo in women with chronic pelvic pain refractory to drug therapy. **METHODS:** Subjects with chronic pelvic pain due to benign conditions and refractory to drug therapy were invited to participate in a randomized, double blind, superiority trial at a tertiary reference center. Subjects were randomly allocated to receive paraspinal anesthetic block with 1% lidocaine without epinephrine or placebo (control). Lidocaine was injected along the spinal process of the painful segment in the supra- and interspinal ligaments using a 25G X 2" needle. Placebo consisted of introduction of the needle in the same segment without injecting any substance. The main outcome measured was the pain score based on a visual analog scale at T0 (baseline), T1 (within 15 min after the procedure) and T2 (one week after the procedure). Data were statistically analyzed by ANOVA and the 95% confidence interval (95%CI). **RESULTS:** Mean age was similar for both groups, i.e., 51.2 (paraspinal anesthetic block) and 51.8 years (control). A blind examiner measured the degree of pain according to the visual analog scale from 0 (no pain) to 10 (worst pain imaginable). Based on the visual analog scale, the mean pain scores of the paraspinal anesthetic block group at T0, T1 and T2 were 5.50 (SD=2.92; 95%CI 3.84–7.15), 2.72 (SD=2.10; 95%CI 1.53–3.90), and 4.36 (SD=2.37; 95%CI 1.89–6.82), respectively. The difference between T0 and T1 was statistically significant, with p=0.03. **CONCLUSIONS:** Paraspinal anesthetic block had a small effect on visual analog scale pain score immediately after the injections, but no sustained benefit after one week. Further studies are needed to determine the efficacy of paraspinal anesthetic block with different lidocaine doses for the treatment of visceral pain of other causes. ClinicalTrials.gov Identifier: NCT01635205

Resumo

OBJETIVO: Avaliar se o bloqueio paraespinal reduz os escores de dor quando comparado com placebo em mulheres com dor pélvica crônica refratária a terapia medicamentosa. **MÉTODOS:** As pacientes com dor pélvica crônica de origem benigna que eram refratárias a terapia medicamentosa foram convidadas a participar nesse estudo de superioridade, randomizado, duplo-cego, em um centro de referência terciário. As pacientes foram alocadas randomicamente para receber o bloqueio anestésico paraespinal com lidocaína 1% sem epinefrina ou placebo (controle). A lidocaína foi injetada ao longo do processo espinhal do segmento doloroso, nos ligamentos supra e interespinal, usando uma agulha de 25G X 2". O placebo consistia na introdução da agulha no mesmo segmento sem injetar qualquer substância. O desfecho principal foi a medida dos escores de dor, baseado numa escala análogo visual nos tempos T0 (basal), T1 (dentro de 15 minutos depois do procedimento) e T2 (uma semana depois do procedimento). A análise estatística realizada utilizou ANOVA e o intervalo de confiança de 95% (IC95%). **RESULTADOS:** A média de idade das pacientes foi similar: 51,2 (bloqueio anestésico paraespinal) e 51,8 anos (controle). Um examinador, cego quando ao tratamento, mediu o grau de dor de acordo com a escala análogo visual de 0 (sem dor) a 10 (pior dor imaginável). De acordo com a escala análogo visual, a média dos escores para o grupo bloqueio anestésico paraespinal em T0, T1 e T2 foi 5,50 (DP=2,92; IC95% 3,84–7,90), 2,72 (DP=2,10; IC95% 1,53–3,90) e 4,36 (DP=2,37; IC95% 1,89–6,82), respectivamente. A diferença entre T0 e T1 foi estatisticamente significativano grupo bloqueio anestésico paraespinal, com p=0,03. **CONCLUSÕES:** O bloqueio anestésico paraespinal tem um pequeno efeito na redução da dor(escala análogo visual) imediatamente após a injeção, mas esse benefício não permanece após uma semana. Outros estudos são necessário para avaliar a eficácia do bloqueio anestésico paraespinal usando outras doses de anestésicos no tratamento da dor visceral por outras causas. ClinicalTrials.gov Identifier: NCT01635205

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Conflict of interests: none.

Introduction

Chronic pelvic pain (CPP) is defined as a noncyclical pain lasting for more than six months that leads to lower physical performance and quality of life in women. This condition has a great impact in people's quality of life and it is a burden to the health care system. The prevalence of CPP ranges between 5.7 and 26.6%¹. CPP affects 14.7% of U.S. women² and 19% of adults in Europe³. Slightly higher rates are found in the UK (24%)⁴ and in New Zealand (25.4%)⁵.

Chronic pain is known to cause peripheral nerve hypersensitization⁶. Physical examination reveals signs of root sensitization along the painful nerve segment. Such signs can be detected using a pinch-and-roll technique, which consists of pulling the skin and the subcutaneous tissue by means of digital clamping and manual sliding until finding an area with signs of nerve root sensitization, i.e., increased sensitivity and edema⁷. Signs of root sensitization on physical examination suggest that the peripheral nerve segments may play a role in the maintenance of pain. Prolonged stimulation of α -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPA) changes the resting polarization state of the membrane, and, as a result, the magnesium ions that plug the neighboring N-methyl-D-aspartate receptor (NMDA) are removed. This process primes NMDA for glutamate activation, thus triggering a cascade of events leading to central nervous system hypersensitization ("central windup")^{8,9}. A hyperactive state of one segment reacting to a source of irritation that is constantly stimulating the dorsal ganglia translates into pain and hyperalgesia⁶.

Various treatments are available for CPP¹⁰⁻¹². To ensure the progress is made in treating chronic pain, therapy that targets the mechanisms of hypersensitivity must be used to try to alleviate symptoms. The dorsal horn is a major target for future treatment of chronic pain¹³. Paraspinal anesthetic block (PAB) of nerve roots has been reported to control or evaluate chronic pain by some authors^{14,15}. This technique has been described in case reports to treat root sensitization pain in patients with epicondylitis¹⁶ and in a case report related to renal colic¹⁷. Actually, there are few studies evaluating those patients with pain refractory to the usual approaches¹⁸. Such intervention has not been studied in the treatment of CPP, as shown in a PubMed search (paraspinal AND anesthesia AND chronic pelvic pain women, July 16, 2014), in which no hit was found.

The objective of the present study was to evaluate whether paraspinal anesthetic block reduces the verbal analog scale (VAS) pain scores in patients with CPP refractory to drug therapy.

Methods

Trial design

We conducted a randomized, double-blind, superiority trial of a community population recruited from December 2011 to May 2013 at Hospital de Clínicas de Porto Alegre (HCPA). This study was approved by the Ethics Committee of HCPA (11-0082) and registered at ClinicalTrials.gov (NCT01635205).

Participants

Women aged more than 18 years old attending the outpatient chronic pain clinic at Hospital de Clínicas de Porto Alegre were invited to participate in the study. Inclusion criteria included: complaints of chronic pelvic pain according to American College of Obstetricians and Gynecologists (ACOG)¹⁹, i.e., pain that was localized in the anatomical pelvis, anterior abdominal wall, umbilicus or below the umbilicus, lumbosacral back, or the buttocks, lasting for at least six months, severe enough to cause functional disability or lead to medical care, of benign etiology and refractory to drug therapy. Patients younger than 18 years old, those who had improvement or resolution of their pain after using medication, those who had pain related to oncologic conditions and those allergic to lidocaine were excluded from the study. All patients had been submitted to a full gynecologic evaluation, including laparoscopy, before entering the study.

Interventions

After signing the informed consent, subjects were allocated to the intervention group or to the placebo group. Before the procedure, the paravertebral region between T10 and L2 was tested using the pinch-and-roll technique in order to detect the presence of edema and the increased local sensitization. Patients in the intervention group underwent paraspinal anesthetic block of the spinal on the segment showing the most obvious signs of peripheral sensitization. The paraspinal anesthetic block was performed as described by Fischer¹⁴ along the spinal process and in the supraspinal and interspinal ligaments, using a 25G X 2" needle and 1% lidocaine without epinephrine. The procedure was performed with the patient in lateral decubitus position on the unaffected side. First, the position of the vertebral spine apophysis was found by digital palpation. Next, a manual maneuver using the index and middle finger identified the paravertebral region on the muscles located along the apophysis. These muscles were compressed upwards (using upward pressure) to facilitate the injection of 1 mL of 1% lidocaine. Injection was first conducted in the sagittal plane up to the vertebral lamina, medially to the paravertebral muscles, where there is no needle resistance, and the anesthetic can spread along the

dorsal sensory branches. Then, the needle was pulled back to the subcutaneous tissue and placed cranially so that its end was 3 mm away from the initial point of injection. The procedure was repeated once more in the cranial direction. Next, the same steps were performed in the caudal direction. Finally, the supraspinal and interspinal ligaments were also injected with 1 mL of 1% lidocaine. All steps described above were performed using a single skin puncture by changing the position of the needle at each step. Of note, lidocaine was not administered using the intramuscular route; instead, it was injected through the virtual gap created by the pressure of the paravertebral muscles using digital traction, making the injection painless. In the placebo group, the same procedure was performed with the needle without injecting any substance.

Patients in both groups did not discontinue the drugs used before entering the study.

Outcome

Pain scores were the main measured outcome. Pain scores were measured by Visual Analog Scales as previously published²⁰. Briefly, a 100 mm straight line with anchors placed at both poles (0 cm indicating no pain and 10 cm indicating the worst possible pain) was presented to the subject. Subjects were asked to place a mark somewhere along the line where best describe their current pain. Measurements were made within 5 minutes before procedure (T0), within 15 minutes (T1) and one week after the procedure (T2).

Sample size

Sample was calculated according to the literature for a superiority trial²¹, using the following parameters: an alpha error of 5%, power of 80 and a 40% reduction of the average pain in the experimental group compared to control, i.e., from 6 to 3.6. The standard deviation was 2, based on pilot project with 10 cases. The figured yielded a minimum sample size of 11 cases per group.

Randomization

Sequence generation of randomized numbers was made by specific program (<http://www.randomization.com>) using blocks of four. Allocation sequence was kept in sequential sealed coded envelopes and away from the investigators who performed the interview until implementation of the procedure. Other examiner, blinded to the allocation arm, measured baseline pain score before the procedure (T0). Another researcher (KFR) performed the procedure, either the PAB technique or the dry needle puncture. Subjects were blind to which group they were assigned to. A third examiner (not KFR), blinded to the allocation arm, measured the degree of pain according T1 and T2.

Statistical methods

Statistical analysis used ANOVA to compare mean pain scores over different time periods within the same arm. Student t-test was used to compare pain scores between arms at the same time periods. If data did not have a Gaussian distribution, Kruskal-Wallis and Mann-Whitney U test were used instead for statistical analysis. The data were calculated by intention-to-treat (ITT). In the intention-to-treat analysis, previous pain scores were repeated on subsequent time periods in subjects that were lost to follow-up. For instance, if in T0 pain score was 6 and subject refuses to be submitted to the procedure after allocation, pain scores on T1 and T2 would be 6.

Results

Thirty-eight subjects were evaluated to participate in the study between December 1, 2011 and May 31, 2013. From these, 12 were excluded and 26 met inclusion criteria and were randomized. Exclusions were due to lack of inclusion criteria (n=5), decline to participate (n=3) and other reasons (n=4). All subjects allocated to paraspinal block (n=13) or control (n=13) received the intervention, but one case in the paraspinal block. Two subjects, one from each arm of treatment, were lost on follow-up. Mean age in both groups was around 51 years old, and the majority of the pain etiology was unknown, 62 and 54% in the PAB and control groups, respectively. Detailed characteristics of the study population are depicted in Table 1. At T1, mean initial pain score was 5.5 in both groups. Those allocated to the Fischer technique had a significant reduction in their mean pain score, either by intention-to-treat (2.8 ± 2.1) or per protocol (PP) (2.7 ± 2.1) at T1, while in the control group these differences were not observed (Table 2). No significant difference was observed when mean pain scores were compared between groups at the same period, either by ITT or PP analysis (Table 2 - columns).

No significant difference in side effects was observed between groups. In the PAB group, pain at the site of the procedure was present in 33% of the cases; further details are depicted in Table 3.

Table 1. Characteristics of the patients included

	Paraspinal block (n=13)	Control (n=13)	p-value
Age – mean±SD	51.2±14.8	51.8±16.7	0.9*
Pain etiology – n (%)			
Unknown	8 (62)	7 (54)	
Endometriosis	2 (15)	2 (15)	0.2**
Scar adhesions	3 (23)	4 (31)	

*Student Test; ** χ^2 test; SD: Standard Deviation.

Table 2. Pain scores at different time periods in subjects with chronic pelvic pain refractory to medical management submitted to the paraspinal anesthetic block or to the dry needle (control)

Group	T0		T1		T2		p-value	
	ITT	PP	ITT	PP	ITT	PP	ITT	PP
PAB	5.5±2.7 (3.7–7.1)	5.5±3 (3.5–7.4)	2.8±2.1 (1.5–4.1)	2.7±2.1 (1.3–4)	4.2±2.3 (2.8–5.6)	4.4±2.4 (2.7–5.9)	0.01*	0.02*
	n=13	n=12	n=13	n=12	n=13	n=11		
Control	5.5±2.9 (3.9–7.1)	5.5±2.7 (3.9–7.1)	4.3±2.8 (2.6–5.9)	4.3±2.8 (2.6–5.9)	3.7±2.7 (2–5.2)	3.6±2.7 (1.8–5.3)	0.07**	0.2***
	n=13	n=13	n=13	n=13	n=13	n=12		
PAB versus Control****	0.9	0.9	0.1	0.1	0.5	0.4		

*ANOVA, Tukey's posthoc test comparing T0 versus T1; **ANOVA, Tukey's post-hoc test comparing T0 versus T1; ***ANOVA; ****Student T-test comparing at each time point (columns); Data are presented as intention-to-treat and per protocol and numbers are mean±SD (95% confidence interval). PAB: Paraspinal Anesthetic Block; ITT: intention-to-treat; PP: per protocol; T0: baseline pain; T1: pain score within 15 min. of the procedure; T2: pain score one week after the procedure.

Table 3. Adverse effects after procedure in those subjects submitted to paraspinal anesthetic block and control group

Adverse effects	PAB (n=12) n (%)	Control (n=13) n (%)	p-value
Pain at the procedure site	4 (33)	1 (8)	0.1*
Headache and pain exacerbation	0	2 (16)	
None	8 (67)	10 (77)	

* χ^2 for trend; PAB: Paraspinal Anesthetic Block.

Discussion

CPP encompasses several conditions causing pain symptoms; therefore, there are several different treatment options. Herein, we verify whether paraspinal anesthetic block reduces the verbal analog scale (VAS) pain scores in patients with CPP refractory to drug therapy. Our results showed a significant reduction in the VAS pain score immediately after the procedure, which is consistent with the study reported by Miranda et al.¹⁶. Similar results were observed either in ITT and PP analysis related to T1 period. The pain-relieving effects of paraspinal block may reflect the blockage of tonic, normally non-painful input to central neurons, which is necessary to maintain their ability to signal pain. Of note, mean pain values are not different between groups in any time period. Possible explanation could be related to the wide confidence interval found in each group. No persistent effect was found according to the VAS one week after the procedure. This finding might be related to the half-life of lidocaine. The half-life of lidocaine is about two hours²² and this effect is unlikely to produce a long standing pain relief, as reported in a case report of renal colic pain¹⁷. Another possibility is that lidocaine does not suppress other factors of nerve root sensitization, e.g., prostaglandins⁶. Actually, some authors found that prostaglandin E2 (PGE2) is increased with lidocaine²³. Furthermore, nerve root cuffs, which are lateral prolongation of dura mater, arachnoid lamina, and pia mater, function as a barrier between the axons and somata in the dorsal

root ganglion and injected drugs²⁴. Nevertheless, lidocaine is also known for crossing the blood-brain barrier, which may lead us to hypothesize that higher drug concentrations or volumes may sustain pain relief for a longer time. Furthermore, the reduction of pelvic pain after paraspinal nerve block, though ephemeral, suggests that modulation of a nociceptive afferent input to the central nervous system maybe a target to treat CPP refractory to oral medications.

The present trial has few limitations. We did not provide different concentrations and volumes of lidocaine for comparison, a compound that crosses. The external validity of our data is limited to women with CPP, excluding visceral pain due to other etiologies. In addition, we acknowledge that chronic pain is a complex condition and other factors that reduce pain thresholds, such as behavioral, physical and emotional aspects of the patient⁶, were not considered. Our results show that the technique presented here does not bring lasting benefits to patients with chronic pain.

However, positive aspects of the study include its design, power calculation, proper randomization and blinding. Our findings are limited to a wide population of women with chronic pelvic pain refractory to oral medication.

In conclusion, the paraspinal blockade technique described herein provides a short relief of CPP compared to baseline pain values. It yields few side effects, but it does not provide a long-lasting effect. Although paraspinal anesthetic block does not offer a long-term pain relief, it shows that local treatment may be a way to manage CPP. The use of combination of different local anesthetic and volumes²⁵ may provide an alternative management of CPP. Only future clinical trial with new dosage and concentrations of lidocaine will provide these answers.

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