

# Use of intravenous lidocaine in a patient with refractory chest pain secondary to Takayasu arteritis. Case report

*Uso da lidocaína endovenosa em paciente com dor torácica refratária secundária à arterite de Takayasu. Relato de caso*

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## ABSTRACT

**BACKGROUND AND OBJECTIVES:** Takayasu's arteritis (TA) is a rare form of chronic inflammatory disease involving large vessels, with uncertain etiology, with chest pain as a common and challenging symptom, resulting from inflammation in the aortic root or arch, pulmonary artery or coronary arteries. The objective of this study was to describe the use of intravenous lidocaine to treat severe and refractory chest pain secondary to TA.

**CASE REPORT:** A 33-year-old female patient diagnosed with TA, with severe chest pain that was difficult to manage, was admitted after consulting an emergency department. The pain was unresponsive to traditional treatment after a week of drug adjustments. As a therapeutic option, a Sympathetic Venous Blockade (SVB) with lidocaine was chosen, achieving a reduction in pain from 10 to 3 on the Visual Analog Scale. Infliximab was administered before discharge. The patient was re-evaluated at an outpatient appointment after 30 days.

**CONCLUSION:** This strategy for the treatment of severe chest pain allowed for pain reduction and relief.

**Keywords:** Case report, Chronic pain, Intractable pain, Lidocaine, Local anesthetics, Takayasu arteritis.

## RESUMO

**JUSTIFICATIVA E OBJETIVOS:** A arterite de Takayasu (AT) é uma forma rara de doença inflamatória crônica envolvendo grandes vasos, com etiologia incerta, tendo a dor torácica como um sintoma comum e desafiador, consequente à inflamação na raiz ou arco aórtico, artéria pulmonar ou coronárias. O objetivo deste estudo foi relatar a utilização da lidocaína por via endovenosa na abordagem da dor torácica intensa e refratária secundária à AT.

**RELATO DO CASO:** Paciente do sexo feminino, 33 anos, com diagnóstico de AT, dor torácica intensa de difícil manejo, internada após consulta em serviço de emergência. Dor não responsiva ao tratamento tradicional após uma semana de ajustes em fármacos. Como opção terapêutica, foi escolhido o Bloqueio Simpático Venoso (BSV) com lidocaína, obtendo redução da dor de 10 para 3 na Escala Analógica Visual. Antes da alta hospitalar foi administrado infliximabe. Paciente foi reavaliada em consulta ambulatorial após 30 dias.

**CONCLUSÃO:** Esta estratégia fora tratamento da dor torácica intensa permitiu redução e alívio da dor.

**Descritores:** Anestésicos locais, Arterite de Takayasu, Dor crônica, Dor intratável, Lidocaína, Relato de caso.

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## HIGHLIGHTS

- Patient with a rare disease, Takayasu's arteritis, with symptoms of chest pain that were difficult to manage
- Patient allergic to NSAIDs, considered standard treatment for chest pain. There was a need to use antidepressants, anticonvulsants and strong opioids, but the pain treatment failed;
- Chest pain was relieved with intravenous lidocaine at a dose of 3 mg/kg for 2 hours, daily, until infliximab was used.

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## INTRODUCTION

Takayasu's arteritis (TA) is a form of chronic vasculitis involving mainly large arteries and their main branches<sup>1</sup>. TA can affect the aorta, subclavian artery, renal artery, iliac artery, coronary artery and other blood vessels<sup>1</sup>. Clinical manifestations vary greatly depending on the area, severity and duration of vascular involvement and severe chest pain may be present<sup>1,2</sup>.

The management and treatment of patients with TA is challenging<sup>2</sup>. In general, corticosteroids associated with immunosuppressive therapy are used to induce and maintain remission of the disease activity<sup>2</sup>. Available therapies include methotrexate, mycophenolate or cyclophosphamide and biological therapies such as tumor necrosis factor inhibitors and interleukin-6, demonstrating efficacy and safety in selected cases, especially in-

fliximab<sup>2</sup>. Early diagnosis and treatment are essential to prevent morbidity and mortality<sup>2</sup>.

Intravenous lidocaine has been used to treat refractory pain of various etiologies<sup>3</sup>. Its role as an adjuvant analgesic has already been explored in several clinical studies. The aim of this case report is to describe the use of intravenous lidocaine for the management of severe pain refractory to conventional treatment in a patient with TA and allergic to non-steroid anti-inflammatory drugs (NSAIDs).

## CASE REPORT

Ethical considerations: the information in the clinical case was collected from the patient's medical records after approval by the ethics committee (CAE 62454022.9.0000.0048) and obtaining the Free and Informed Consent Term (FICT).

The patient was a 33-year-old female diagnosed with TA, chronic chest pain and comorbid systemic arterial hypertension and obesity. She was admitted to the emergency department with severe sternal chest pain (Visual Analogue Scale score: 10/10), characterized as sharp and tight, radiating to the left hemithorax and back, without dyspnea, disabling, preventing her from performing daily activities and walking, without improvement with common analgesics and without previous episodes of severe chest pain. Cardiovascular physical examination was unchanged. Tests and examinations for the differential diagnosis of acute coronary syndrome were carried out in the emergency room (normal electrocardiogram and cardiac enzymes).

A chest angiotomography identified a reduction in the caliber of the right main pulmonary arteries and segmental arteries of the right upper lobe and parietal thickening at the level of the aortic arch, suggestive of an ongoing inflammatory process (vasculitis). The patient was followed up on an outpatient basis by a rheumatologist. She described an allergy to dipyron and non-steroidal anti-inflammatory drugs and reported taking prednisone initially 40 mg/day with progressive weaning over 4 months and methotrexate 15 mg/week for 6 months, duloxetine 30 mg, pregabalin 150 mg/day and buprenorphine 5 mg/day. Due to the intensity of the pain, which was difficult to manage, the patient was hospitalized and asked to be monitored by a pain specialist.

## PROCEDURE

Gradual adjustments were made to the doses of the drugs previously used, pregabalin to 225 mg/day, duloxetine to 60 mg, buprenorphine to 10 mg/day and rotation of the latter to morphine, with no improvement in the intensity of pain for a week. Given the refractoriness of the case, which was already using adjuvants with optimized doses, associated with a systematic strong opioid, the decision was made to use Sympathetic Venous Blockade (SVB) with lidocaine, a therapy routinely used at the institution in cases of refractory pain of other etiologies. Immediately after SVB, the patient reported significant relief of chest pain (EAV score: 3/10), lasting up to 48 hours. The Lidocaine infusion was carried out according to the patient's demand, initially on average every two days and then, after a week, daily.

Systemic lidocaine was administered at a dose of 3m/kg, diluted in 250 ml of saline solution, in a continuous infusion pump for 2 hours, under monitoring of vital data. Venous sympathetic blockade is associated with the risk of local anesthetic intoxication and arrhythmias, and attention should be paid to the speed of infusion, the total dose per kg and monitoring of vital data, as well as being prescribed only by an experienced professional in the field and with properly trained nursing staff.

At the same time, the attending team decided to escalate the immunosuppressive treatment to infliximab at a dose of 3mg/kg. After the infliximab was administered, the patient was discharged from the hospital.

During outpatient follow-up, the patient returned with significant improvement in chest pain, still with sporadic episodes of lesser intensity, on maintenance treatment with infliximab and gradual reduction of glucocorticoids.

The patient was also referred to the pain clinic for symptom management and chronic chest pain control, with self-care measures related to lifestyle changes and obesity, as well as the gradual weaning from buprenorphine, pregabalin and duloxetine.

At the 30-day follow-up, the patient maintained good pain control and adherence to the pharmacological and non-pharmacological measures proposed to control the disease.

## DISCUSSION

Takayasu's arteritis is a rare form of chronic inflammatory disease involving large vessels, the aorta and its branches, as well as the subclavian and carotid arteries, with an uncertain etiology<sup>4</sup>. It has a complex clinical course, which has been didactically divided into three stages. The first stage of the disease consists of nonspecific constitutional symptoms such as unrest, fever, night sweats, arthralgia, headache, anorexia and weight loss<sup>5</sup>. The second stage is vascular inflammation, where pain can occur as a result of arterial injury, stenosis, aneurysm and occlusion<sup>5</sup>. This stage can include diminished or absent pulses (mainly in the radial arteries), vascular murmurs, hypertension (involvement of the abdominal aorta), chronic mesenteric ischemia, retinopathy, aortic regurgitation (involvement of the ascending aorta), myocardial infarction, limb claudication (involvement of the distal aorta) and neurological symptoms such as orthostatic hypotension, dizziness, convulsions, transient ischemic attacks, stroke, hemiplegia and paraplegia<sup>6</sup>.

The third stage is characterized by remission of the disease<sup>6-8</sup>. It is important to note that it is not always possible to define all the stages clinically. Although there is a wide variety of symptoms and chest pain is frequent in the description of the disease, there have been no reports in the literature of chest pain of such intensity that is unresponsive to standard treatment of the disease, or reports of pain management in polyallergic patients.

Chest pain is experienced by more than 40% of patients with TA and results from inflammation in the aortic arch or at the level of the root (affected in 35% of patients), pulmonary artery (10-40%) or coronary arteries (<10%)<sup>9</sup>. Headache is a consequence of the involvement of the carotid and vertebral arteries, with decreased cerebral blood flow, affecting 45% of patients.

Hypertension develops in more than half of cases due to a narrowing of the renal artery or narrowing and decreased elasticity of the aorta and branches<sup>10</sup>.

In the context of TA, pain reflects the site of the vascular lesion. In general, pain is described as responsive to NSAIDs. In the case reported, the patient was allergic to NSAIDs and presented intense chest pain radiating to the left inframammary region and back, refractory to the use of simple analgesics, opioids and adjuvants. Despite the therapies already standardized in the literature for the treatment of TA, it was necessary to look for strategies to treat the pain on its own. Lidocaine, an amide-type local anesthetic, has a well-established role both as an anesthetic agent in perioperative therapy and as an analgesic agent used systemically<sup>11</sup>. The intravenous administration of lidocaine causes an increase in acetylcholine in the cerebrospinal fluid, leading to activation of descending pathways, inhibition of glycine receptors and an increase in endogenous opioids<sup>14</sup>.

Another mechanism described to explain the analgesia promoted by the intravenous infusion of lidocaine is the reduction in post-synaptic potentials due to the activation of N-methyl-D-aspartate receptors<sup>15</sup>. Several studies have outlined dosage protocols for lidocaine infusion to treat pain of different etiologies. Although they may vary, most use a bolus administration regimen, followed by infusion for up to 72 hours to maintain therapeutic analgesic effects<sup>16</sup>. In this reported case, the option was for a continuous infusion dose of 1.5mg/kg/h, due to the patient's risk profile. The possibility of systemic toxicity when using a local anesthetic in continuous venous infusion should always be considered. The safety of this treatment has been described by some authors<sup>17,18</sup>. When intravenous lidocaine is administered in a bolus of 1mg/kg associated with an infusion of 2mg/kg/h, plasma levels of lidocaine of around 2µg/mL are obtained, considering that toxic doses are reached at concentrations above 5µg/mL<sup>14</sup>.

The great challenge in this case was to establish an effective and safe analgesia strategy while the patient was waiting for the immunosuppressive treatment of choice. The combination of various drugs, such as antidepressants, anticonvulsants and opioids was considered insufficient from the point of view of pain relief by the patient during her hospitalization. In addition, the patient also reported intolerable adverse effects, such as nausea and unrest. Antidepressants used as adjuvant therapy for neuropathic pain can present a risk of prolonging the QTc interval and can cause gastroparesis<sup>15,16</sup>.

Anticonvulsants, such as pregabalin and gabapentin, are also effective for neuropathic pain, but can cause sedation, peripheral edema and need to be adjusted in dose for renal insufficiency<sup>17,18</sup>.

Opioids act as agonists on mu, delta and kappa opioid receptors to produce analgesia, and undesirable effects include sedation, nausea/vomiting and decreased gastrointestinal motility, leading to constipation<sup>17,18</sup>. In addition to the analgesic properties of SVB described above, lidocaine seems to be able to modulate the inflammatory response, activating macrophages and monocytes, inhibiting the release of cytokines, leukotrienes, histamine and prostaglandins, among other mechanisms of action. It is also believed to reduce polymorphonuclear adhesion, motility and migration, with the release of nitric oxide, free radicals and

lysosomal enzymes<sup>12,13</sup>. In a previously described case report, a patient with scleroderma had prolonged analgesia, with no adverse effects and a reduction in ischemic changes with the use of intravenous lidocaine<sup>13</sup>.

Among the strategies for pain control, the SVB with lidocaine proved to be effective as an adjuvant in the patient's treatment, with no toxicity. There are few studies in the literature on the use of this drug as an option in cases of pain that is difficult to control.

## CONCLUSION

It was concluded that the local anesthetic lidocaine can be considered a potential strategy in the management of immune and inflammatory diseases.

In a condition of chest pain unresponsive to NSAIDs in a patient with TA, the intravenous lidocaine used in this case proved to be a potential strategy for pain management.

## AUTHORS' CONTRIBUTIONS

### Leandro Barros da Silva

Conceptualization, Methodology, Writing - Preparation of the Original, Writing - Revision and Editing

### Barbara Caroline Silva de Siqueira

Writing - Review and Editing, Supervision

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