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CASE REPORT: THE SUCCESSFUL USE OF HYDROXYZINE FOR ANALGESIA IN A PATIENT WITH LUMBAR SPINAL STENOSIS

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Background: Lumbar spinal stenosis is a chronic condition associated with low back pain that is usually alleviated with traditional pain medications, spinal injections, or surgery. Antihistamines are a drug class that are not usually used for analgesia.

Case Report: We present the case of a 51-year-old woman who presented with low back pain radiating down the right lower extremity. Magnetic resonance imaging of the lumbar spine revealed multilevel degenerative changes, including bilateral foraminal narrowing at L5-S1. Despite conservative treatments, her pain persisted. A trial of 10 mg hydroxyzine 3 times daily led to a 50% reduction in reported pain.

Discussion: Hydroxyzine is an H1 inverse agonist not commonly used for analgesia. Potential mechanisms include antagonizing H1 receptors on lumbar nerve roots and interaction with neural cytokines.

Conclusions: Improvement after the use of antihistamines for lumbar stenosis pain is rare and leads to consideration of its use as a treatment option.

Key words: Antihistamines, lumbar spinal stenosis, hydroxyzine, analgesia, pain medicine, case report

BACKGROUND

Lumbar spinal stenosis is a chronic condition in which narrowing of the spinal canal compresses nerve roots and vascular structures (1). This results in significant low back pain and neurogenic claudication in most cases (2). It is generally caused by degenerative conditions, such as spondylolisthesis, systemic illness, or postsurgical pathology. Clinically, lumbar stenosis presents with pain, numbness, and weakness in the lower back radiating to the buttocks and legs (3). First-line treatment includes lifestyle modifications, physiotherapy, and pain medications, such as acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), and neuropathic agents. Spinal injections and surgical interventions can be considered when a patient is nonresponsive to conservative treatment (1,2).

One medication class that has not been widely recognized for its use in analgesia in lumbar stenosis is antihistamines. Antihistamines are inverse agonists of guanine nucleotide-binding protein-coupled histamine receptors (4). Hydroxyzine is an antihistamine that specifically targets the H1 receptor and is used in the treatment of generalized anxiety disorder and psychoneurosis. While there have been a few studies that have observed the use of antihistamines for analgesia, these have been in combination with other pain medications and further work is needed (5-7). This article presents the first case to our knowledge of the use of hydroxy-

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zine for a patient suffering from lumbar stenosis with neurogenic claudication after being nonresponsive to conservative treatment.

CASE

A 51-year-old woman with a past medical history of lumbar discectomy and prediabetes presented to the pain management clinic with severe atraumatic low back pain for the past 10 years. She said the pain was across her lower back, radiating down the right lower extremity. She described it as a stabbing pain in her back, accompanied by a burning sensation that radiated down her thigh and extended to the bottom of her heel, worsening with prolonged walking or standing. Her pain had not improved with neuropathic agents (such as gabapentin or pregabalin), anti-inflammatories (NSAIDs and acetaminophen), or muscle relaxers (Flexeril, Merck & Co Inc, West Point, PA). Additionally, she participated in multiple courses of physical therapy and had 2 prior lumbar epidural steroid injections, none of which provided relief.

On the physical exam, she had full strength of her bilateral lower extremities with normal sensation to light touch. There was tenderness to palpation over her right and left lumbar paraspinals and right sacroiliac joint. Special test yielded a positive straight leg raise test on the right and a positive flexion abduction external rotation on the right. Magnetic resonance imaging of the lumbar spine revealed bilateral foraminal narrowing at the L5-S1 level, as well as ligamentous hypertrophy from L3-S1 causing spinal stenosis. She was diagnosed with lumbar spinal canal stenosis with neurogenic claudication. A trial of 10 mg of hydroxyzine 3 times a day was started with the goal of reducing her neurogenic claudication and lumbar back pain. On follow-up after 3 months, she reported a decrease of all her pain symptoms by 50% on the Numeric Rating Scale. Informed consent was obtained verbally from the patient to report these findings in the present case report.

DISCUSSION

This case showed the successful management of pain in a patient with lumbar spinal stenosis with neurogenic claudication treated with antihistamines, a drug class not generally used for analgesia. Although some research has been conducted on antihistamines for analgesia, there are still gaps in the literature. One double-blind randomized controlled trial (8) found that dihydropyridine was as effective as pregabalin, an antiepileptic normally used for neuropathic pain. Additionally, phenyltoloxamine has been shown to be an effective adjuvant for acetaminophen and aspirin (7). There have also been a few reported cases (9,10) of antihistamines for pain relief in pegfilgrastim-induced bone pain and trigeminal neuralgia. However, these studies have mostly looked at antihistamines as a part of combination therapy along with other pain medications or have not specifically been indicated for neuropathic pain, such as in spinal stenosis.

Antihistamines are considered in treatment-resistant pain because of the presence of histamine receptors throughout the peripheral and central nervous system (CNS) contributing to pain sensation (11). Histamine has 4 well-known receptors. Hydroxyzine is a potent H1 receptor inverse agonist. Inverse agonists preferentially bind and stabilize receptors in the inactive state causing negative intrinsic activity. This results in a reduction in spontaneous receptor activity (12). Furthermore, the H1 receptor mRNA has been shown to be expressed in up to 20% of lumbar dorsal root ganglion (DRG) neurons (13). This proposes the mechanism that antihistamines, such as hydroxyzine, can stabilize H1 receptors on lumbar nerve roots in the inactive state, leading to diminished pain.

A review on this topic explained that mast cells in the histamine-signaling pathway can interact with nonneuronal glial cells to mediate neuropathic pain (13). Satellite glial cells in the lumbar DRGs can secrete cytokines that mediate chronic neuropathic pain, and antihistamines can inhibit these cytokines. It is also possible that histamine released by mast cells recruits glial cells involved in pain and antihistamines inhibit this pathway (13). This demonstrates an alternate mechanism of antihistamines specifically in neuropathic analgesia.

Prior theories have also proposed that antihistamines interact with opioid systems within the CNS. One series of studies (14) found that morphine administration in H1-receptor knockout mice had better analgesic effects than wild-type mice. This could explain the role of antihistamines in analgesia as an adjuvant to opioids as seen in prior studies. However, the specific mechanism of this interaction, as well as what role antihistamines play individually in this theory, remains unknown.

Further research needs to be done to better understand the role of antihistamines in neuropathic analgesia. Randomized control studies should compare the

use of antihistamines alone to antihistamines with other pain medications to see if it is effective by themselves or play an adjuvant role. There also needs to be work done on more broad, diverse patient populations to understand in which clinical situations antihistamines are best indicated. It would be useful to clinicians to know what types of patients are resistant to other pain medications and would benefit from antihistamines earlier in their treatment regimen.

CONCLUSIONS

This was one of the first case reports to show the effective use of antihistamines alone for analgesia in lumbar spinal stenosis. This shows the possibility of further incorporating antihistamines as a part of the treatment regimen for spinal neuropathic pain. More clinical studies are needed to understand the efficacy and specific clinical indications of antihistamines in spinal stenosis.

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