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Benefits of The Addition of Lidocaine to Botulinum Toxin in The Treatment of Myofascial Syndrome

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ABSTRACT

Background: *One of the main alternatives to treat myofascial pain syndrome (MPS) is botulinum toxin A (BT-A), which acts in the synaptic membrane at the neuromuscular junction, inhibiting the release of acetylcholine, producing muscle relaxation and pain relief, although in many cases its effect is not evident until several days have elapsed.*

Aim: *To test whether we could get a shortening in the reduction of VAS time and a life quality improvement adding local anesthetics (LA) to BT-A dose.*

Methods: *The study design was prospective, controlled, longitudinal and randomized in which we have assessed the evolution of 20 patients randomly divided into two groups. The first group was given IncobotulinumtoxinA (IncoBT-A, T group). The second group was treated with IncoBT-A and an additional dose of 2% lidocaine (TL group). Both groups had previously responded positively to a test with lidocaine 2% infiltration of the affected muscle.*

Results: *There was statistically significant difference between groups TL and IncoBT-A in the VAS assessment on the third day, just as in the Lattinen Index. No significant differences in the other reviews were stated. There was a significant difference in VAS reduction and Lattinen Index improvement at the beginning and end of the study in both groups.*

Conclusion: *IncoBT-A presents an alternative to the management of this condition when conservative therapy has failed. Local anesthetics cause a predictable, short and reversible muscle relaxation caused by blocking nerve conduction in nerve endings, while BT-A acts on the neuronal endings of the motor plate, preventing the release of acetylcholine. Their actions are carried out in different places and with different characteristics. The action of local anesthetics is almost instantaneous and short lasting, while the BT-A action is delayed and long lasting, so both can be complementary and agonists in their final effect.*

Keywords

Myofascial syndrome, botulinum toxin, incobotulinumtoxinA, lidocaine.

Introduction

Musculoskeletal processes are the most frequent cause of pain and of temporary or permanent disability. At least, 30% of the population have locomotor system symptoms with a high prevalence of pain due to muscular origin. The pelvic girdle pain is undoubtedly the most frequent muscular pain. Between 70% and 85% of the adult population suffer back pain at some time in life. The annual prevalence is between 15% and 45%, most of the cases benign and self-limiting episodes, though recurrent, and being the most frequent chronic pain cause in medical visit after headache

[1-3].

This back pain meets the characteristics of chronic myofascial syndrome very often. Some authors consider that up to 80% of chronic low back pain seen at the Pain Units is a pelvic girdle myofascial pain [4-6]. The myofascial syndrome is a clinical picture of recent description [7] generally underdiagnosed and, therefore, undertreated. In general, the prevalence of this syndrome varies from 20-30% of the patients seen in Rheumatology Clinic and in Primary Care consultation, respectively, to 85-93% of patients who come to Pain Units [8-11]. It could be defined as all musculoskeletal non-inflammatory pain, located in a muscle or group of muscles which is refractory to pharmacological treatments and / or the application of physical therapy methods, accompanied by stiffness and autonomic symptoms, as an expression of peripheral nervous system pathologic changes, along with the presence of triggering points [12-14].

It must have three basic components: a) a palpable band in the affected muscle; b) a triggering point; c) a characteristic pattern of referred pain. The palpable band may not be seen by the eye examination; it is a segmental spasm of a small portion of the muscle being only noted if an adequate exploration is undertaken, such as sliding the finger pads along the muscle to taking advantage of the mobility of the subcutaneous cellular tissue that surrounds it. The trigger point is a focus of irritability in the muscle when deformed by pressure, stretching or by contracture what causes referred local pain and occasionally autonomic phenomena.

Trigger points can be classified in: a) active, being painful without stimulation, always sensitive and felt by the patient as a point of constant pain; b) latent or satellites, causing dysfunction when certain maneuvers are performed and only painful on palpation.

They can also be classified in primary ones in the case there is no other disease or underlying cause to be found or can be secondary to pathologies such as nerve entrapments or radiculopathies. The third component is referred pain. It is a kind of pain originated in a trigger point but felt at a distance. The distribution of the referred pain does not coincide with the total distribution of a peripheral nerve or root though it can mimic the pain caused by nervous compression or entrapment. It does not present motor or neurological deficit either [1,3,11,15-21].

There is a large number of theories about the physiopathology of myofascial syndrome, none of them yet completely checked. Nevertheless, authors agree that there are a number of factors that can predispose to the appearance of trigger points: repeated microtrauma, acute traumatisms, inadequate and sustained postures, overuse, mechanical factors such as scoliosis or shortening of limbs, physical factors such as sudden cooling of the body or partial body areas, physical exhaustion, psychological factors such as stress, depression or sleep disturbances, nutritional deficiencies of vitamin B group or minerals (Ca, Fe, K and Mg), obesity and / or endocrine diseases such as hypothyroidism, hormonal changes or menopause [13,22-24].

The hypothesis in which there is a greater consensus is that trigger point etiology (TP) is attributed to the motor plate dysfunction, where the alpha motoneurons contact with the muscle fibers. The dysfunction should be due to an abnormal depolarization of the motor plate in which there would be a sum of presynaptic (excessive release of acetylcholine), synaptic (defect of the cholinesterase enzyme) and postsynaptic mechanisms (increased activity of the nicotinic acetylcholine receptor). These mechanisms would act synergistically causing on the postsynaptic membrane a rapid and sustained activation of the nicotinic receptors, inducing a potential of muscular action and contraction maintained in resting conditions with persistent shortening of the sarcomeres.

The muscular contraction would cause a local ischemia picture with decreased arterial flow, decreased arrival of oxygen, of calcium and other nutrients which are necessary to induce muscle relaxation. The growing demand for local energy caused by the presynaptic, synaptic and postsynaptic mechanisms, causes a rapid consumption of ATP, which implies a metabolic failure called "energetic crisis". On the other hand, tissue ischemia would induce synthesis and release of algogenic and inflammatory substances, such as: bradykinins, noradrenaline, serotonin, histamine, prostaglandins, leukotrienes, P substance, calcitonine gene related peptide (CGRP), all in an acid medium, activating the muscle nociceptors and increasing the activity in the motor plate with the consequent appearance of pain and thus completing the circle of the called "integrated hypothesis" by Simons [1,25-28].

The first sequel to this peripheral sensitization would be the muscular spasm added to the pain caused by the spontaneous discharges of action potentials. Under normal circumstances this injury recovers with early treatment and the nociceptors return to its normal threshold of sensitivity. For reasons still unknown, local sensitization is expanded towards neighboring nociceptors in some patients and in this way the injury begins to become chronic, the muscle being less elastic, getting shorter and more limited and weaker. The main effect is an increase in excitability of some neighboring nociceptors and even neurons of second and third order, causing central awareness that may be responsible for the referred pain [3,22,29,30].

Currently, there is no a definitive gold standard test for diagnosis. Nor are there laboratory or radiological objectivable data that can guide us in the diagnosis. Only a thorough physical examination and an exhaustive clinical history are the basic elementsto guide us towards the diagnosis. The use of algometers can be helpful as well as the pressure threshold, which is the minimum amount of pressure that induces pain, being considered abnormal if it is less than 2 kg/cm^2 [1,3,31], relating it with a normal control point usually measured in theopposite side. In a review of medical literature, it was observed that the four most frequent diagnostic criteria applied were: painful nodule on the tense band, recognition of pain on the part of the patient, characteristic pattern of referred pain and local response of shaking [32]. The examination of the lumbar spine should be performed by assessing the general mobility of the lower back in all its possible movements, flexo-

extension, rotation and lateralization, which will give us a pattern of limitation that will help us identify the affected muscle or muscles.

The association of more than one muscle in the production of pain is frequent in the lower back. The detailed history of pain, its location and the aggravating mechanisms of it will allow us to reach the identification of the affected muscles. The three muscles of the pelvic girdle that more often cause myofascial pain are: quadratus lumborum, iliopsoas and pyramidal. The quadratus lumborum is a large muscle that presents three fiber bundles: a) iliolumbar: from the iliac crest to the transverse processes L1 to L4; b) iliocostal: from the iliac crest to the twelfth rib; and c) lumbocostal: from the twelfth rib to the transverse processes of the lumbar vertebrae. Its function is the homolateral extension and inclination of the spine, so contributing to forced expiration. It is the main muscle in maintaining the erect position. Its contracture is the most frequent cause of lower back pain wich increases with prolonged standing, coughing and sneezing.

The pain may radiate to the groin, testicles and the sciatic path. Patients present difficulty for turning on the bed, getting up from the chair and from supine decubitus position, calves paresthesias and burning sensation in legs and feet. They also have a big hypersensitivity on the greater trochanter. They walk well on all fours, the pain improving when unloading the weight of the upper body by supporting the back, resting the arms on the table or holding the hips with the hands. First, we will explore the mobility of the lumbar spine finding that the lateral flexion is affected. For the physical examination is extremely important the placement of the patient as the TP of this muscle are difficult to find due to the limited space existing between the last rib and the iliac crest. The exam must be done with the patient in lateral decubitus with the symptomatic side above.

A small cushion should be placed under the hip to increase the distance between the last rib and the iliac crest. The patient should be asked to extend the arm of the affected side above the head to catch the rib edge. This way the top of the body is fixed and the space between rib and the iliac crest increases. The quadratus lumbarum is located in front and outside of the outer edge of the spinal muscular mass. Its fibers can be felt easily perpendicular along the inner part of the iliac crest and also in the angle which is formed by the paravertebral mass and the twelfth rib and in the angle formed by the iliac crest and the paravertebral muscles. The palpation of the TP will cause pain which will radiate towards the greater trochanter and the external side of the thigh or towards the sacroiliac a region and buttock.

The psoas is a thick muscle composed of two parts: a) iliac: going from the iliac blade to the lesser trochanter; and b) psoas: going from the lateral side and lower edge of the lumbar vertebrae transverse processes to the lesser trochanter. Its main function is the hip flexion and help in its abduction and external rotation. If unilateral, its contracture causes lumbalgia of a longitudinal nature, the pain being radiated towards the anterior aspect of the thigh. If the lesion is bilateral, the pain is distributed horizontally in the lower lumbar part. Standing worsens the pain and getting up from low seating causes difficulty. There is no pain with cough or forced expiration. Pain does not disappear but improves with rest and with shrunk legs while in lateral decubitus. It may give a femoral, femorocutaneous, femorogenital and ilioinguinal nerve compression clinic. With the hyperextension of the lumbar spine and so pressing down the greater trochanter of the affected side, the patient may achieve a painless walking. On examination, patients should lie on their back.

The TPs must be searched between locations: a) It appears as a radiated pain towards the anteromedial side of the thigh and groin if pressing the lesser trochanter on the distal insertion of the muscle; b) Inside the iliac crest, while the patient tries to relax the abdominal muscles, pain appears in lumbar and sacroiliac regions; and c) indirect palpation of the psoas through the abdominal wall by pressing the psoas gradually, slowly and smoothly bellow the rectus abdominis against the lumbar spine. Pain may appear on the periumbilical area or below the lumbar spine.

The pyramidal muscle goes from the antero-internal aspect of the sacrum to the femur greater trochanter, although it usually presents large anatomical variations. Its main function is to be an external rotator and abductor of the femur. It also seems to help keeping the femoral head in the acetabulum. Its contracture causes pain in the buttock area, between the sacrum and the greater trochanter. The pain radiates towards the hip and to the back of the thigh. It increases when sitting or standing, getting worse with the activity but with no improvement while resting. Patients are continuously changing position while seated, looking for an antalgic posture (truck driver's disease) and having difficulty crossing the legs. It can compress neighboring nerve structures (as sciatic nerve) mimicking a sciatica.

On exploration, the gluteus maximus must be relaxed. The contraction of the pyramidal muscle is accompanied by a marked sensitivity along the line joining the greater trochanter with the medial aspect of the sacrum. TPs are located in the neighborhood of its insertion in the trochanter and in the inferior border of the sacrum below the postero-inferior iliac spine. A wide variety of therapy methods are today available for the management of myofascial syndrome, all with the same basic principle: restoring the normal length of muscle fibers at rest and eliminating palpable trigger points within the fibrous bands of the muscle. The treatment must be individualized and multidimensional. It is more successful starting treatment with conservative procedures and reserving the invasive techniques for when these fail [1,3,33].

Amongst the initial therapeutic measures to be taken in consideration, we will consider: a) eliminating triggering factors, especially those predisposing ones; b) rehabilitation and physical therapies, stretching techniques, heat or cold applications, massages, laser, acupuncture, ultrasounds and transcutaneous electrostimulation; these measures can help to release the muscle of the accumulated tension; and c) pharmacological treatment that

will be based on the use of NSAIDs, muscle relaxants, analgesics, antidepressants. Few studies are designed on the short- and long-term efficacy of this type of drugs for the improvement of the myofascial syndrome. The scientific evidence for the use of tricyclic antidepressants has been only proven in tension-type headache and in alterations of the temporomandibular joint. The degree of evidence of the benzodiazepines effectiveness in muscle spasm is moderate. Muscle relaxants are effective in the treatment of muscle spasms that affect the cervical region and in alterations of the temporomandibular joint, being of very limited value in other myofascial syndromes.

There are no adequate studies in the literature that value with scientific evidence the effectiveness of opioids in this type of pain, although often used [34-39]. If the patient does not improve with these techniques in a period from 2 to 4 weeks procedures more aggressive should be considered, specifically the infiltrations of the TP. Infiltrations can be "dry", without administration of drugs or adding local anesthetics, botulinum toxin or steroids [40-43]. Infiltration with local anesthetic (LA) will cause a brief and reversible relaxation of the muscles by blocking the conduction in nerve endings; it will always cause a blockage of the nociceptors located in the thickness of the muscle what leads to a sensitive block which the infiltration with botulinum toxin (BT) laks. Local anesthetics inhibit the transport of sodium from outside to the inside of the membrane as they occupy a specific site in it (channel receptor), decreasing the number of potentials of action, the speed of depolarization and nerve conduction, prolonging the refractory period and inhibiting in a complete way the depolarization of the membrane.

The specific area to which local anesthetics bind seems to be the alpha subunit´s D4-S6 region of the sodium channels linked to voltage, a region that can only be reached from the intracellular side of the membrane [44,45]. BT is one of the most potent biological toxins known until now and is produced by the anaerobic bacteria Clostridium botulinum. It has a neurotoxic fraction consisting of a protein with a molecular weight of approximately 150,000 Daltons. There are 7 immunologically distinct serotypes of Clostridium botulinum (A, B, C1, D, E, F and G), all of them being acetylcholine release inhibitors, though considerably differing with respect to the characteristics of their effects and powers of action. The A serotype has been the most extensively studied and has proven to have good therapeutic applications; the B serotype has also been commercialized but has less lasting effects so the use of higher doses is required [46-50]. BT has a high affinity for the neuromuscular junction where the motor nerve endings contain the acetylcholine vesicles.

In normal circumstances acetylcholine is contained in the nerve endings vesicles. Nerve stimulation produces an increase of the calcium intraneuronal concentration causing a fusion of the vesicle membrane with the plasmalema of the nerve ending which, owing to a process of exocytosis, releases acetylcholine that crosses the synaptic cleft and causes muscle contraction by binding to muscle receptors. To facilitate this coupling between the cell membrane and the vesicles of acetylcholine there are some essential protein complexes for the fusion of the membranes known as SNARE (Soluble N-ethylmeleimide-sensitive factor Attacchment Protein Receptor), which include: a) vesicular proteins: VAMP (vesicle-associated membrane protein); b) Synaptic membrane proteins: SNAP-25 (synaptosome-associated protein of 25 kD); and c) syntaxin [50-51]. BT-A is injected into the muscular belly and acts on the motor plate and on the cholinergic fibers of the autonomyc nervous system. The neurotoxin is endocytosed by the presynaptic neuron of the euromuscular junction thus inhibiting the exocytosis of acetylcholine to the synaptic cleft.

This process is carried out in three steps: 1. Union: is the irreversible union of BT-A with the presynaptic cholinergic receptors. There are different protein receptors for different neurotoxins. 2. Internalization: It is the entry of BT-A into the presynaptic terminals through a process of endocytosis. 3. Neuromuscular block: it is the third and last step; once internalized, the toxin acts by means of peptidases dividing one or more of the SNARE proteins of each neurotoxin, inhibiting the coupling and fusion between vesicles and receptors.

BT-A exerts its action preferably on the presynaptic membrane protein SNAP-25, while the BT-B acts especially on the presynaptic vesicle´s membrane protein VAMP [49,50,52-55]. The inhibition of acetylcholine release paralyzes the muscle cell and causes a state of chemical denervation. As a reaction to chemical denervation, the axon of the alpha motorneurons emits new dendritic branches towards the muscle cell of which only one survives a few moths. The axons reaction to the chemical denervation explains the loss of effect of BT and results in a transient therapeutic effect which usually lasts between 3 and 4 months in clinical practice [49-53].

The use of BT-A as a treatment in neuromuscular disorders has been associated with an important analgesic effect. As an essential requirement for a rational use of this kind of therapy in pain control, the patient must suffer chronic pain secondary to a known or presumed diagnosis and who does not successfully respond to the different habitual analgesic treatments [56].

The analgesic effect of BT-A is due to a double action:

- Indirect: by modifying the excessive or dysfunctional muscle activity so decreasing muscle spasm. Dystonic muscle disorders improve with the toxin by inhibiting the cholinergic transmission of alpha motoneurons at the level of the motor plate and by inhibiting the function of the gamma motoneurons which decrease the fibers afferent input Ia on the reflex arc of traction [57,58].
- Direct: by modifying the activity of the proper nociceptive fibers.

Several studies have come to demonstrate that BT-A can reduce the release of neuropeptides such as the P substance and the peptide related to the calcitonin gene. It also suppresses the release of glutamate and other neurotransmitters and modulators of neural function such as adrenaline and noradrenaline. Due to these effects,

it can be considered that toxin A can block peripheral sensitization and indirectly reduce central sensitization [48,57-62].

Methods

The design of the study was prospective, controlled, longitudinal and randomized in which the evolution of 20 patients divided into two groups has been valued. The first group was given IncoBT-A type (T group). The second group was given IncoBT-A type plus an additional dose of 2% of lidocaine (TL group). Previously, both groups had responded positively to an infiltration test of the affected muscle with 2% of lidocaine. The main aim of the study was to test wether the addition of LA to the dose of BT would shorten the time of reduction of the VAS Scale. As a secondary objective we proposed the same possibility in the patient's quality of life by means of the Lattinen index and, finally, to assess the appearance of unpleasant side effects. Patients previous treatments included non-steroid anti-inflammatories, opioids, muscle relaxants and anticonvulsants. All patients had maintained a pharmacological treatment for at least three months without reducing the VAS below 5.

All patients undertook a detailed and detained exploration of the affected muscles until an accurate diagnosis was obtained. All the patients were duly informed, previously signing the corresponding consent of compassionate treatment. The exclusion criteria were the presence of neurological deficit in the affected area, previous treatment with Botulinum toxin and pregnancy. Infiltrations with contrast were performed in the operating room and under scopia control. A spinal needle with a tip Quinque 22 Gx3 ½ of 0.70x 88mm type was used for the infiltration procedure. For the localization of these muscles, the patient was placed in a prone position and, after disinfection of the skin, a needle guided by fluoroscopy was introduced at a 90-degree angle looking for the so-called tunnel vision of the needle which will only display the head of it.

We will have two reference points for each muscle, one on the surface and the other one deep inside the muscle, this latter being filled with contrast once reached and thus verifying the position. For the localization of the quadratus lumbarum, the surface reference was taken at a point two centimeters above the highest point of the iliac crest and, after rotating 90 degrees the Xr, the vertebral lamina was taken as the point of the inside (Figure 1).

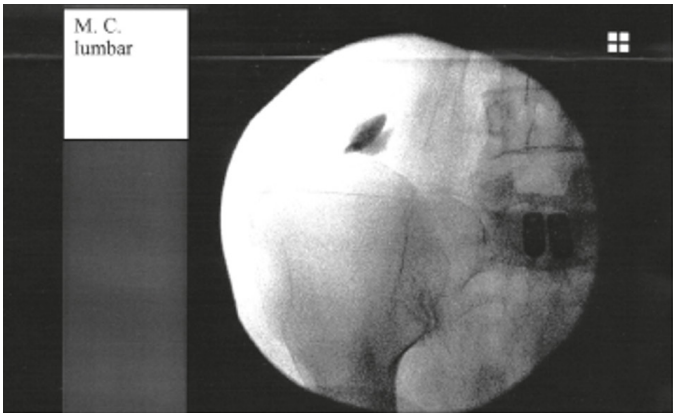

Figure 1: Quadratus lumbarum muscle localization with contrast.

For the localization of the iliopsoas we took as the surface reference the crossing point of the line joining the lumbar spinous processes with the intervertebral lines L3-L4 or L4-L5 and, after rotating 90 degrees the Xr, we moved along to the middle of the corresponding vertebral body, as the point of the inside reference (Figure 2). For the Pyramidal localization, we took the superior angle of the acetabular margin as the surface point of reference and the acetabulum own angle as the profundity point after removing 0,5 cm from the needle, because in this case it is not necessary to turn 90 degrees the Xr [3] (Figure 3).

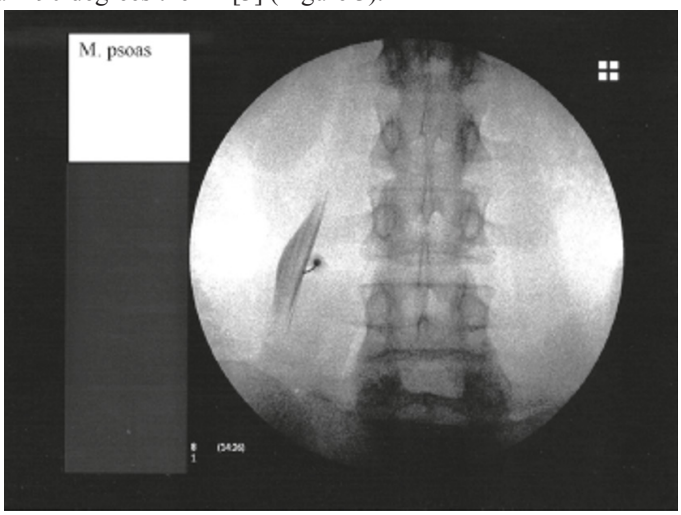

Figure 2: Psoas muscle localization with contrast.

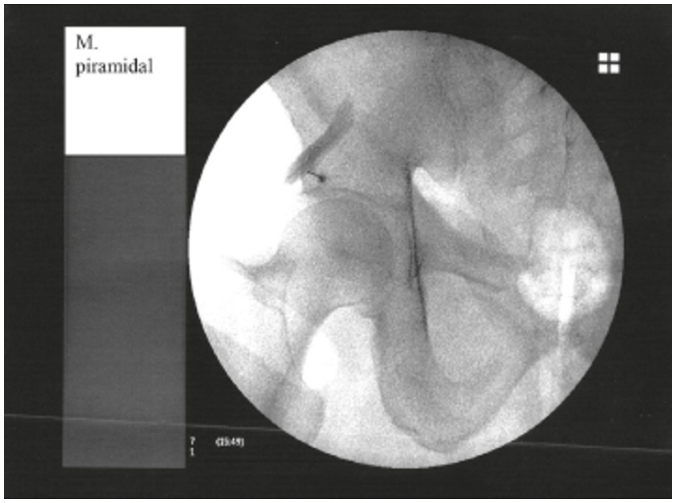

Figure 3: Pyramidal muscle localization with contrast.

One hundred Units of IncoBT- A type dissolved in 10 cc of physiological serum were infiltrated in the psoas and quadratus lumbarum and 50 Units dissolved in 8 cc in the pyramidal. The doses of lidocaine were of 60 mg for psoas and quadratus lumbarum muscles and 40 mg for pyramidal muscle, all of them undiluted. The patient follow-up was carried out by telephone at 3 and 7 days, and with a physical visit at 15 and 90 days. The pain intensity was assessed through the Visual Analog Scale (VAS), on a scale from 0 to 10) and the Lattinen index was used for the

quality of life control. It is an index that has also been used as pain control criteria or as an index of functional capacity.

This measuring tool is characterized by its brevity, picking up five items that gather at the same time five dimensions of the patient with chronic pain. These dimensions are: pain intensity, activity level, frequency of pain, use of analgesics and sleep at night. A total score can be obtained which is set up by the sum of the scores in each of the previous dimensions. The score of each item is carried out on a scale of four points, going from the lowest incidence to the greatest severity or distortion [63-67].

The professional who performed the assessment was unaware of the analgesic schedule used and was asking all the patients for the appearance of side effects. For the statistical analysis, it was used an analysis of the variance, ANOVA, supplemented by Mauchly's test for sphericity checking and by Greenhouse-Geisser test, with a confidence interval of 95%, considering p <0.05 to establish statistic differences.

Results

Twenty patients were included in the study. The demographic characteristics related to age and sex are shown in Table 1.

Variable		Data
Age, years	Range	34–66
	Mean	46.63 ± 7.361
Gender, n	Women / Men	12 / 8

Table 1: Demographic data.

In Table 2 we gather the muscles affected and infiltrated by patient in each group. With regard to pain, the group T basal VAS score was of 6.8 ± 0.789, while in the TL group it was 7.3 ± 0.949. In both groups there was an important and statistically significant reduction of the VAS score (p <0.001) at 90 days. In the three-days assessment, the VAS score in the group T was 6.5 ± 0.527, while in the TL group it was 3.7 ± 0.823, showing a statistically significant difference (p <0.001). In the evaluation at 7 and 15 days, the VAS score of the TL group was lower than the VAS score of the toxin group alone but without significant statistical difference. At 90 days, the VAS score of the T group was superior to that of the TL group but neither was a significant statistical difference appreciated (Table 3).

		Toxin group	Toxin/lidocaine group
Psoas, C. lumbar and pyramidal		2	3
Psoas, C. lumbar		3	
Psoas and pyramidal		1	2
C. lumbar and pyramidal	Psoas	1	2
	C. lumbar	1	1
	Pyramidal	2	2

Table 2: Relationship of patients and affected and treated muscles in both groups.

VAS	Botulinum toxin	Toxin B. Lidocaine
Baseline	6.8 ± 0.789	7.3 ± 0.949
3 days	6.5 ± 0.527	3.7 ± 0.823
7 days	4.5 ± 1.179	3.4 ± 0.699
15 days	3.2 ± 0.632	2.9 ± 0.605
90 days	3.6 ± 0.966	3.9 ± 0.738

Table 3: Average values of the VAS in both groups.

In Figure 4 we can see the evolution of the VAS score curve along the time in both groups. In relation to the Lattinen index, the T group basal assessment was 13 ± 1.524 and 13.3 ± 1.635 in the TL group. The value of the index at 90 days was reduced in a statistically significant way (p<0.001) in both groups, 7.9 ± 0,738 in T group and 7,4 ± 0,699 in TL group. In the assessment made three days later a significant statistical difference comparing both groups was also appreciated. In T group the value was 13.00 ± 1.491 and in the TL group the value was 8.4 ± 1.897 (p <0.001). Although the values of the TL group are inferior to those of T group in the controls at 7, 15 and 90 days, there is no statistical difference found in these cases (Table 4).

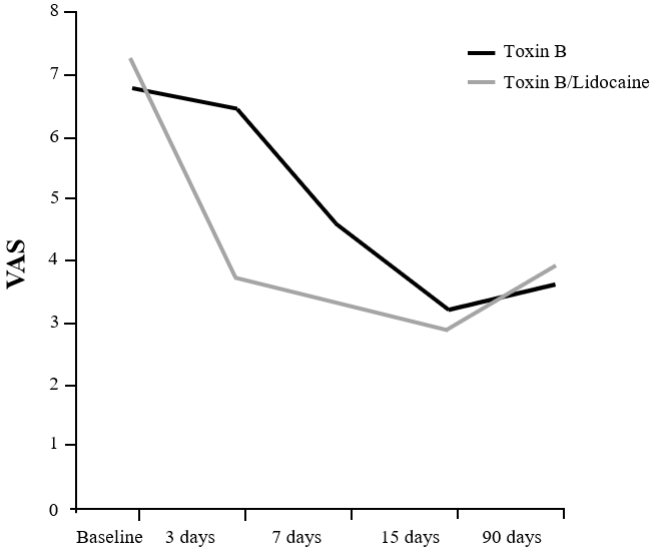

Figure 4: VAS evolution curves in both groups.

Lattinen Index	Botulinum toxin	Toxin B. Lidocaine
Baseline	13.9 ± 1.524	13.3 ± 1.635
3 days	13.0 ± 1.491	8.4 ± 1.897
7 days	8.6 ± 1.350	7.9 ± 0.994
15 days	7.8 ± 0.789	7.6 ± 0.699
90 days	7.9 ± 0.738	7.4 ± 0.699

Table 4: Average values of the Lattinen Index in both groups.

In figure 5 the evolution of the Lattinen index curve over time in both groups can be observed. There was no description of any relevant side effect, except in three patients. One presented a transient functional impotence in the lower right limb that spontaneously ceased after three days of the infiltration, and two patients with mild flu-like symptoms accompanied by mild

myalgias.

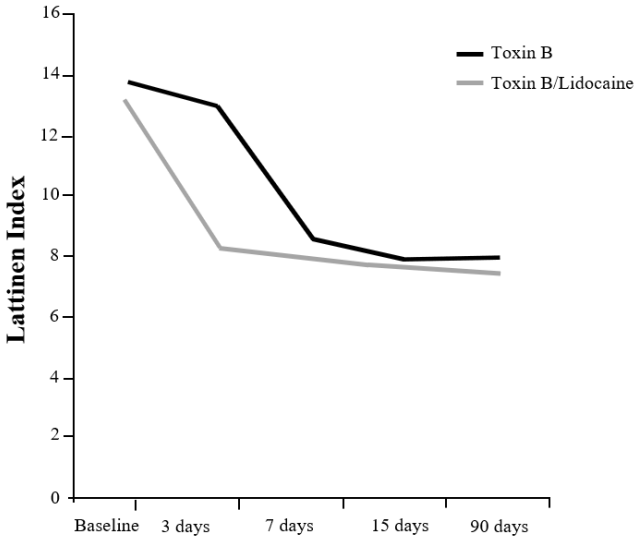

Figure 5: Lattinen Index evolution curves in both groups.

Discussion

Myofascial pain is one of the main causes of pain in the general population, usually evolving towards chronicity despite empirically used treatments [24,68]. In spite of its high prevalence it remains underdiagnosed and undertreated. Characterized by the presence of acute or chronic pain triggered by the presence of one or several muscular points with hypersensitivity, Travel and Simon, in their integrated hypothesis, attributed the motor plate dysfunction as the trigger points possible etiology, existing an underlying muscle injury due to overload as a predisposing component [7].

There is no a consensus doctrine to establishing a gradual cascade for the treatment of this syndrome. The main difficulty in establishing a pre-determined therapeutic pattern lies in the proper etiological and pathophysiological heterogeneity of the myofascial syndrome. However, it is accepted that treatment must be individualized, multidisciplinary and multimodal, taking into account pharmacological therapy, interventional techniques, stretching physical therapy of the affected muscles, massage over the painful nodules, relaxation practices and biological feedback and acupuncture, being pain relieve and functional loss restoration the fundamental objective of the treatment [24,50,69,70]. While there are several studies confirming the goodness of BT-A in the treatment of myofascial syndrome because of the ability to control muscle spasm and direct analgesic action [21,42,71], in a systematic review of 23 randomized clinical trials with infiltration of trigger points, published in 2001, it was concluded that the nature of the injected substance does not make any difference in the results and that the infiltration of any substance does not obtain therapeutic benefits compared to a dry puncture, which is supported by high-quality clinical trials [43]. Neither does Pereda find benefit in his review [72].

Nevertheless there are common positions in the admission that the use of BT-A in the treatment of myofascial syndrome pain should be reserved for refractory cases, in those that conservative treatments have failed [21,73-75]. Other works show a benefit of BT-A versus saline solution or dry needle or versus triamcinolone or methylprednisolone. In the latter case, it is interesting to know that the difference in BT-A efficacy is greater than when the control is saline [40-42,76-78]. Precisely, in the study of Kamanli [40] there is no demonstration of superiority of botulinum toxin against lidocaine. In a compilation where the results of all the studies on the effectiveness of BT are collected, it has been observed a pain improvement in 76% of the 278 patients included in the different studies [79].

On the contrary, in Wheeler's work no significant differences were found between botulinum toxin and the saline, both in the pain scale and in quality of life [80]. Lang, on the other hand, argues that the myofascial syndrome pain improves when placing needles in the trigger points without injecting any drug or infiltrating physiological saline [81], however, the post-infiltration pain generated by dry infiltration is more intense and durable than the experienced by patients treated with lidocaine [1].

Despite the fact that Pereda in his review points out that there is no enough evidence to confirm the effectiveness of BT-A, it is not less true that this is due more to the poor quality of the studies and to an insufficient sample than to the lack of a demonstrated intrinsic efficacy of the toxin; in fact, in the same review, it is suggested its non-recommendation but neither is its use discouraged, insisting that prospective studies with a greater number of patients and with a more appropriate design are necessary [72]. In any case, the use of BT-A for the treatment of myofascial syndrome of different location is very widespread in daily clinic. This wide use is seen reflected in numerous publications describing the different techniques and dosage of application of the toxin. The results obtained in these studies suggest an important beneficial effect of the toxin with a clear improvement of patients both in the evolution of the VAS and in the quality of life indexes [2,24,42,43,50,70,73-76].

Another debatable issue is on the dose of BT-A and the dilution that should be used for its administration. The amount injected must be the minimum necessary to achieve the desired clinical objectives [70-82] while, at the same time, it is recommended the use of a minimum injection volume and a little amount of physiological saline dilution in order to reduce to the maximum the drug diffusion to other unwanted nearby muscle groups and to avoid the appearance of side effects [83]. However, it is important to mention that in other studies in which larger volumes were used, no major complications were reported what tells us about the important safety profile of the drug [21-50]. There are different guidelines for the use of BT-A in the myofascial syndrome. The most common are two, one is that which proposes the infiltration inside the trigger point or its surroundings, guided by EMG findings or by palpation, and the second one that which is directed to the muscle to be treated in order to infiltrate it widely.

The doses and dilutions used vary considerably depending on each of these perspectives and explain the great variety among

the different dose recommendations and dilutions proposed by the authors. In general, the ones focused on the trigger points propose lower doses and dilutions and those directed to the muscle use higher doses and dilutions [68-84]. In our case, when focusing the infiltration towards the muscle, we use dilutions of 10 cc for psoas and quadratus lumbarum muscles and 8 cc for the pyramidal muscle, with a dose of 100 U for the former muscles and 50 U for the latter one, without having appreciated any diffusion to neighboring muscular groups or unpleasant adverse effects. BT-A has a prolonged analgesic effect that even exceeds the motor effect, whose interval is 2-6 months, being also known the existence of a short latency period of 7-10 days until an effective onset of its action [42,74,85].

The fact that prior to treatment with IncoBT-A all the patients of the two groups had been administered an infiltration with lidocaine, being positive in all cases, was what encouraged us to shorten the latency period of IncoBT-A with additional doses of lidocaine, this time undiluted to avoid an excessive volume administration in the affected muscle. Local anesthetics produce a predictable, brief and reversible relaxation of the musculature caused by the blockage of nerve conduction at the nerve endings, while BT acts on the neuron terminations of the motor plate, preventing the release of the acetylcholine. Their action is exercised in different places and with different characteristics. As stated above, the action of local anesthetics is almost instantaneous and short, while that of BT is deferred and lasting over time, so that they can be complementary and agonistic in their final effect.

The statistically significant fact that the VAS score and Lattinen index are lower at three days evaluation in the TL group versus the T group confirms clinically our assesments. The absence of adverse effects in both groups confirms the goodness of the technique and the low risk taken when adding small amounts of lidocaine to the dose of IncoBT-A for pain relief as well as the quality during the first days of the administration of treatment [86-88].

Conclusion

The myofascial syndrome of the pelvic girdle presents a high prevalence, it encompasses very varied pictures, arriving to the conclusion that it represents up to 80% of the chronic lumbar pain that reaches the pain units. Treatment must be individualized, multidisciplinary and multimodal. IncoBT-A is an alternative to the treatment of this picture when conservative therapy has failed. Although in the latest systematic reviews it does not show evidence enough to confirm its effectiveness, this is due more to the poor quality of the studies carried out, so the urgent need to perform methodologically rigorous studies in order to confirm the real effectiveness of BT-A in this syndrome.

Lidocaine is a widely used local anesthetic in myofascial syndrome therapy due to its lower myotoxic effect. It has sometimes been used as a test prior to BT administration and on other occasions as a proper treatment of the syndrome. Its addition to IncoBT-A treatment allows a latency time shortening in pain improvement and in quality of life without the appearance of noteworthy adverse effects. Advances in understanding the BT structure and its function will allow to modify the molecule in order to produce new structures capable of inhibiting afferent nociceptive function without having effect on other the neurons, including the motor neuron.

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