CHAPTER IX

MYOFASCIAL FIBROSIS

Myofascial fibrosis (MFF) is a multi-factorial syndrome of degenerative changes in tendomuscular, fascial and capsular formations, expressed by multiple tender points or nodules, predominantly at axial level, as a result of physical factors and neurovascular disturbances. Probably there are rheumatic, neurological, or traumatic changes which, more or less, earlier or later, are associated with characteristic manifestations of MFF, but in the majority of cases these symptoms are considered a consequence of other diseases. This way, the functional pathology of the tendons, together with capsules and muscles (Tendinitis, Tendocapsulitis, and Bursitis), are united under the generics of: Periarthritis, Bursitis, while Myofascial syndrome and Tender Points are appreciated as Peripheral Neurological Disturbances. This phenomenon has determined the appearance of terms like Fibrositis, Fibromyalgia, Tendomyositis, Myofasciitis, Polyalgic Syndrome, Diffuse Idiopatic Syndrome, Polyenthensitis and Trigger Points.

Studying the morphopathologic and physiopathologic particularities of these affections has showed evidence of common signs, demonstrating the etiological factors' unity development, with some particular clinical manifestations. MFF is frequently associated with vertebral column pathology, particularly with inter-vertebral osteochondrosis (IO). Studies done by rheumathologists over the last decade on myofascial fibrosis have underlined only some mechanisms of development of this process. It is well known that the majority of patients with intervertebral osteochondrosis will see a trauma physician, or will consult a neurologist when neurological disturbances will show up, but the myofascial manifestations would be appreciated in the late stage of the disease. The myofascial fibrosis, as a syndrome, is frequently manifested in many degenerative vertebral column diseases.

The exact incidence of MFF is unknown. According to some authors' data, the MFF incidence varies between 2.44% and 15% (R. Stanley, M.O. Pillemer, 1933 and A.B.Zbarovskii, 1997). The sickness is predominant among females - proximately 86% of cases (Gunos & all.,1981). The sickness debut is more frequent at 30-40 years of age, but is also seen in children and adolescents with skeletal anomalies, and in elders (60-70 years). The decrease among elders can be explained by the decrease in physical activity. Since in numerous degenerative changes the MFF does not show MFF signs in joints and vertebral column we concluded that the MFF incidence is higher among industrial factory workers.

Etiopathogeny

MFF etiopathogeny is unknown. Furthermore, the MFF etiology cannot be studied separately from the sickness responsible for these symptoms. The etiologic factors of the osteoarthrosis are responsible for starting the process in MFF. While osteoarthrosis

is the main cause of fibrous changes in periarticular formations (bursas, tendons, the supraarticular adipose tissue), the degenerative change anomalies and trauma of the veterbral column are the main causes of MFF in spinal, sacroiliac, superior and inferior extremity muscles.

Our studies, including a sample of over one thousand patients with vertebral column affections, have proven that in patients over 40 years, the inter-vertebral osteochondrosis is the main cause of MFF. In patients of 20 - 30 years old, MFF is caused by various trauma, either acute either chronic. For children and teenagers, the etiological factors are represented by axial skeleton anomalies. Fibromyalgia is very difficult to detect because the syndrome has a sub-clinical evolution and the first signs of sickness could be shown in worsening or acute periods of basic sickness, osteoarthrosis and inter-vertebral osteochondrosis as a rule. This way, the mechanical factor, physical over-demanding stereotype movements, chronic trauma, extended fluctuation and toxicity influence the osteoarthrosis and inter-vertebral osteochondrosis process activating the fibrous foci with intensive pain, frequently associated with movements, and contractions, muscular asthenia, functional limitations and morning stiffness.

Many hypotheses concerning MFF etiology exist:

- 1. Infectious hypothesis

Epstein-Baar, Herpes, Coxachie viruses, HIV, Parvoviruses, Borrelia Burgdorferi, all of them could probably could be the main etiological factor for this condition. The presence of these symptoms in post-viral syndrome, myalgia during viral infections, especially in the acute stage of viral infection with intoxication and immune disturbances development later sustain MFF viral etiology.

- 2. Immunological hypothesis

The immune hypothesis is suggested by CD_4 and CD_8 equilibrium disturbances, IL_2 excessive accumulation, NK cells activity inhibition, antinuclear antibodies and IgG deposits' presence. Simultaneously, this syndrome may be associated with some autoimmune diseases, e.g. Lupus Errythematosus, Dermathomyozitis.

- 3. Central nervous system hypothesis is based on the presence of functional neurological disturbances: diffuse pain, insomnia, fatigue, anxiety and depression. The antidepressive medication does not ameliorate the condition in patients with MFF, on the contrary, using the usual methods of MFF treatment which decrease MFF syndrome brings psychic improvements.

It is presumed that MFF and depression are the product of the same foci that are causing central misbalance with common psycho-physiological phenomena. These hypotheses only combined explain the MFF etiopathogenesis. Other authors are communicating about pain modulating disturbances with the decrease of the threshold of perception under neurochemical factors' action. These are attempts to suppress neuro-modulation disturbances caused by the β-endorphin, P-substance, which participate in formation of nociceptive sensation and vasodilator action. Some authors are explaining the MFF pathogenesis by decrease of serotonin, tryptophan and 5-hydroxyindolacetic acid. Serotonin level, which has supranodular control of sleep in MFF patients, is decreased. In this way, it is explained the positive result of Amitriptilin with serotoninergic action

or of fluoxetine chlorhydrate and 5-hydroxy-tryptophan with the same effects in treating MFF. Also glycolysis and energetic metabolism disturbances were found, related to decrease of triamine phosphate, which activates the pyruvate metabolism.

There are discussions about cerebral blood disturbances in thalamus and caudal nucleus, with changes in pain perception in the same CNS functional disturbances.

Thyroid gland disturbed functions also were found in patients with MFF, associated with muscular pain and sleep disorders. Somatomedine from serum is decreased as a result of changes in muscles' homeostasis. Prolactin hyper-production or decreases of calcitonin and changes in catecholaminergic system are suspected.

➢ 4. The peripheral conception has found many supporters. It is known that the histological changes (mucoids, fibroids and necrotic alterations) as a result of chronic local ischemia, the decrease of microcirculation and chronic trauma will decrease the ATP and phosphocreatine, in spite of lack of disturbances in energetic metabolism seen in spectroscopy or RMN. At the same time, patients with MFF have decreased concentration of LDH muscular iso-enzymes and slow lactates' production, and an increase in pyruvate concentration.

Our study has demonstrated that adolescents with vertebral column anomalies, the acute appearance of MFF take place after physical effort, sportive games, which are prone to intensify displacement and subluxation of vertebrae.

There are involved diverse mechanisms, sickness character, stage and phase of basic diseases etc., because the capsule is very rich in neural receptors, the degenerative process or trauma will cause local and distal pains (to regional muscles at about 10-15cm from place of injury).

Prolonged pain syndrome is frequently seen in persons doing physical work (workers, sportsmen), which leads to muscle spasm and continues with vascular spasm, with maintenance of hypoxic areas, these causing over-accumulation of lactic acid, and this will excessively increase the fibrous tissue. This vicious circle of spastic pains, spasm-pain-spasm persists until the pain syndrome is unbearable and functional changes will appear. The spasm zones and local ischemia are nothing else, but trigger points. First, these become perceptible being activated by local process at joint capsule level, later they can proceed on their own, being activated by other factors, like low temperature, intoxication and physical effort. The Trigger Points will lead to the appearance of areas with diffuse functional changes and consequently to insufficient function of myofascial formations, connected with decrease of microcirculation, tendomuscular tonus, which goes to the acceleration of degenerative process in joint. In other words, the degenerative process at the joint level, especially at vertebral column will start the myofascial changes. The last one does have an important role in joints' degenerative process acceleration. This mechanism of MFF development is more evident in cases when the starting factor is localized at the spinal column level as shown in table 2.9.1.

The attempts to explain MFF pathogeny as a local and isolated phenomenon at the muscular system level did had no succes in patients with osteoarthrosis: the pathological changes, like hypertrophy or atrophy of muscular fibers, were discovered in periarticular formation and regional muscles. The majority of authors are sustaining the neuro-sensitive changes' hypothesis in MFF mechanism. The exogenous factors could

work directly on sensitive receptors of neural endings and the endogenous sensitivities through central mechanism.

table 2.9.1

Localization of the trigger factors

Degenerative diseases of joints and vertebrae	Vertebral column (synovial joints, fibrous ring, paravertebral ligaments)	Trauma from physical overdemand, vertebral anomalies, vertebral subluxation
Internal organ pathologies, neuro-psychogenic disturbances	-----	Extension of fibrous ring ligaments Narrowing of intervertebral space
Reflexogenous pain area	Spine Marrow	Local henodynamic insufficiency. Neural formations irritation.

The impulses are modulated at the spinal cord level, nuclei of thalamus and cerebral cortex. Histamines, serotonin, badikinin, prostaglandin activate the skin receptors. They are intensifying neural fibers response to stimuli. The animal experiments have demonstrated that the pain receptors, as neural fibers are responsable for chemical or muscular activity changes and the C-fibers for serotonin, hystamine, bradikinin, and prostaglandin E_2. In this content, a very important attention is given to the sensitive nervous termination neuropeptide release, with intensified release of histamine. Irritation of efferent skeletal muscular fibers are causing pain, muscular contractions, the pain being felt not only in the muscles, but also in distant areas. Reflexogenic pain at the level of the posterior roots of spinal cord takes place. The modulation of the sensory impulses at the level of subarachnoid formations' pain is strongly controlled. This way, the MFF development mechanism is complicated, many aspects remaining unclear.

Morphologic assessment

The hystologic study of the specimen from damaged muscular areas has shown unspecific changes: appearance of fibrosis, dystrophic zones in areas with maximal TP activity, intensive distrophy, and interstitial disturbances were present, sometimes fibers' degeneration. In ganglia there were organized fibers with striates' disappearance, nuclear conglomerates, predominantly in perivascular areas.

In some cases, adipose and connective tissue have replaced the muscular fibers. In these ganglia also mucopolysaccharide infiltration was found, and necrotic foci with collagen accumulation.

Clinical picture

Because MFF syndrome presents mostly joint and periarticular degenerative changes, it is difficult to ascertain the symptomatology, especially if there are radicular manifestations frequently present in vertebral column disease. In these situations, first we have to addres the symptoms of the basic disease. Many times, after improvement of

basic disease, the worsening of MFF and especially the Tender Points as a result of increase of the subject activity, occur.

A very important role in clinical description in detail of each syndrome present in this disease is attributed to I. Trevelle and D. Simmons, 1989. Based on a large number of patients with this condition examined by these authors, they described the manifestation of each syndrome in diverse stages of sickness.

The Tender Point is a phenomenon characteristic to MFF as a site of high irritation of myofascial area. TP is located in area of skeletal muscular fibers within the limits of spasm area, the main feature being extreme pain on palpation, hypersensibility and vegetative disturbances. The vegetal-vascular changes: vascular spasm, skin coldness on palpation, abundant transpiration, pronounced dermography, excessive secretion in further areas, etc. are seen frequently in MFF. Tender Points represent the area of muscular hyper-excitation and ganglion presence and are activated by many factors, as physical over-activity and low temperatures. At the same time the Tender Point activation will cause the diffuse reflexogenic pain. TP, besides the myofascial formation, could be localized in tegument and periostal stratum.

MFF is predominant in young persons - (20-50) years. The area of muscle contraction especially the Tender Point traced by deep palpation can cause pain in different areas of the body with vegetative manifestations. The reflexogenic pains with TP usually are weak, chronic, and usually located in deep layers of tissues. Often they will appear at rest or with movements. At the same time, the reflexogenic pains could be started or intensified by pressing the Tender Point or by acupuncture. Those started by Tender Point excitation usually are monolateral, with segmental character and are not spread according to pain or neural zones, radiated from internal organs. The myofascial pains spread usually within the limits of same dermatom, myotom or sclerotom, but do not occupy the segment entirely. Patients usually explain the show-up of myofascial pain as related to previous acute trauma or sport. In the acute period of the MFF we can see local vascular spasm. Depending on the place of these fibrous formations and the activity of ganglia (TP), diverse manifestations will appear. The TP presence in cervical and occipital region will cause equilibrium disturbances, dizziness, and vertigo. In this case the motor neurons, which are in control of reflexogenic pain area, are overexcited. Concomitantly, the TP will show distal muscles' dysfunction. The activation of these foci endangers the CNS activity: nervousness, insomnia, etc. will appear, intensifying the pain and muscle rigidity under Trigger Point influence. The muscle stiffness usually shows up after rest, sleep or long break. The presence of myofascial Tender Point, active or passive in extension, will give or even intensify the pain. The pain syndrome during muscular extension will show EMG changes caused by muscular contraction. If the patient is not timely treated, the extension is blocked by muscle spasm, the movements will be limited and the pain will increase as well.

Under external factors, causing muscle contraction, the pain will aggravate. In myofascial fibers the affected muscle force is diminished not because of hypertrophy or pain. It was recognized that the reflexogenic pain can cause sensitive disturbances and in some cases, in this area, the vasomotor activity will increase: lacrimation, vasomotor

rhinitis, perspiration, etc. In this case the motor neurons of muscles from reflexogenic zone are activated. As a rule, in the TP area, there is evidence of muscle tension on palpation. In the majority of cases, the contraction and the muscle spasm will disappear with one treatment course. Tender Points are very painful on palpation, yet the pain decreases increasing the distance from TP. The deep palpation by pressure of fibrous formations will initially generate a convulsive reaction of superficial muscles, then a latent one in the muscles with TP. In accordance with more authors, the pain is worse in sternocleidomastoidians, great pectorals, scapulars, paravertebral extensors, gluteal and femoris medialis muscles. Tender Points do not provoke pains at rest, but when they are activated, the pain will appear in reflexogenic zones. In reflexogene areas the pain will show up also after acupuncture.

The EMG examination will show insignificant changes in myofasciitis when muscles are at rest and in Tender Points will activate the electromyography, if they are located over a painful reflexogene area. Sometimes we will see a defense response, allowing TP contracture removal by muscles in the same EMG unit. Lately, very much attention was given to the presence of Tender Points in this disease. According to the American College of Rheumatology, there are characteristic Tender Points for this disease. The painful TP are caused and intensified by external factors: colds, humidity, chronic trauma, emotional disturbances, intoxication, and vibrations.

Patients are frequently seen by a neurologist or psychiatrist for hypochondria, hysteria, neurasthenia and asthenoneurotic syndrome. Many are under a cardiologist treatment for tachycardia, arrhythmia, and insignificant ECG changes. Less often is arterial hypertension and hypotonia.

Location of Tender Points According to ACR (1990)

1. Occiput - at the occipital muscles insertion
2. Low cervical - anterior aspects of the intertransverse spaces at C5-C7
3. Trapezius - at the midpoint of the upper border
4. Supraspinatus - at origins, above the scapula near the medial border
5. Second rib - upper lateral to the second costochondral junction
6. Lateral epicondyle - 2 cm distal to the lateral epicondyles
7. Gluteal - in upper outer quadrants of buttocks in anterior fold of muscle
8. Greater trochanter - posterior to the trochanteric prominence
9. Knee - at the medial fat pad proximal to the joint line

In some areas there were present symptoms of peripheral vessels pathology: Raynaud syndrome and acrocyanosis. Among digestive disturbances there are gastralgia, billiary tract and intestinal dyskinesia. In females urogenital disorders are met: dysmenorrhea and menopause. The majority of MFF patients will present diverse changes at the joints' level (coxofemoral, knee, elbow, and spine and lumbosacral area). Often the MFF is associated with scapulohumeral and coxofemoral periarthritis.

Biologic Examination

The examination of a large number of patients did not show inflammatory changes of erythrocyte sedimentation rate; the CBC was unchanged and also there were no immune changes. Some authors mentioned possible changes of dehydrogenate lactate. The

damaged muscular tissue will show increase of IL_2 and decrease of IL_{4-5}. In some cases there were changes of creatinine phosphokinase level.

The positive diagnosis is based on patient history and physical examination findings of myofascial system examination.

MFF diagnostic criteria proposed by N. Gunnus (1981)

A. Obligatory criteria

☑ Diffuse, generalized or reduced pain (not less then 3 months)

☑ Absence of other possible causes for MFF: endocrine, rheumatic, oncology disturbances proved by lab test.

B. Major criteria

☑ The presence of at least five Tender Points

C. Minor criteria

☑ Pain increase with physical efforts
☑ Paint sensibility at weather changes
☑ Activation of the process by emotion and stress
☑ Chronic fatigue
☑ Generalized asthenia
☑ Migraine
☑ Irritable bowel syndrome
☑ Mild edema of the extremities
☑ Limbs' numbness, inferior & superior.

The diagnosis can be ruled if A + B criteria and 3 items from point C are present, or presence of an A criteria plus 3-4 tender points of B and 5 points of C are present.

Differential Diagnosis

Because periarthritis and myositis do have many common aspects with MFF, it is difficult to make a differential diagnosis. In periarthritis, the characteristic location of the process is corespondent to anatomical topography with earlier or later inclusion of tendomuscular system. In the affected areas there is an excessive growth of fibrous tissue. If the periarthritis is caused by vertebral column pathology, many times it can be associated with MFF of regional muscles. The inter-vertebral osteochondrosis is the main cause of the development and this is a reason why it is very difficult to make a differential diagnosis in early, incipient stage of the disease. In osteochondrosis, pain will show up under the influence of same factors, with little differences: the pains are of segmental character, and this will ease the finding of the affected vertebra. Also the thickening of regional muscles is missing and the disk subluxation and herniation are present.

In localizing the process in the lumbar region, it is needed to exclude the lypomatous ganglions in subcutaneous fascia. These ganglions at Th_{XII}-L_{II} level will give abdominal and lumbar pains.

The difficulties of MFF differential diagnosis originate also from association of other sicknesses: oncological, infectious, retrocecal appendicitis, and aortic aneurysm with dissection, nephrolithiasis, urogenital chronic process, lymphoganulomatosis and osteitis.

The EMG for patients with intervertebral osteochondrosis is showing neurogenous and neurovascular changes, depending on the level of spinal lesions. The spine X-ray in patients with intervertebral osteochondrosis will show characteristic degenerative changes. In the late stage of inter-vertebral osteochondrosis, fibrous foci will be seen in different areas.

Treatment

The treatment efficiency depends on the gravity and spread of the pathologic process.

table 2.9.2

Treatment steps in MFF

I Step	Acute access relief
	1. Rest 2. Analgethics 3. Anti-inflammatory drugs 4. Miorelaxant remedia – maximal doses 5. Angioprotective agents 6. Ionoplasmic therapy – low doses 7. Analgesics, costicosteroids, intramuscularly în TP 8. Diet - excluding acide products, spices, and alcohol.
II Step	Complete pain, inflammation and spasm liquidation
	1. Limited physical activity. 2. Non-steroidal anti-inflammatory drugs – low doses 3. Angioprotective agents – medium doses 4 Miorelaxant remedia – medium doses 5. Physical therapy: a. ionoplasmic therapy; b. UVW; c. magnitotherapy; d. electrophoresis with various analgesic and anti-inflammatory agents 6. Kinetotherapy a. massage; b. gymnastics
III Step	Recovery. Complete recovery of the muscular functional condition. Normalisation of the nervous, endocrine and vascular systems' activity)
	1. Balneotherapy: a. sulfur baths; b. radon baths; c. mud baths; d. other mineral baths 2. Aquatic procedures – swimming 3. Exercise

In the early, incipient stage of the disease, the positive response to antiinflammatory non-steroidal medication (diclofenac, indomethacine, phenylbutazone), will help to confirm the diagnosis. These indications in association with muscle relaxants (Midocalm 0.08 x 3 times/day, Myolastan 50 mg BiD, Baclofen 5 ml TiD, Sirdalud 2 ml TiD) will reduce the muscle stiffness and pain. Some authors have seen favorable results with local steroids (Hydrocortisone, Kenalog), which can also be used in combination with local anesthetics (novocaine). The antidepresants have a basic place in the MFF treatment: Amitriptyline, Melipramin, all possessing stimulating action. Good results were

obtained also from physiotherapy: magnetotherapy, novocaine electrophoresis, ultrasound, laser beam and finally, but not the last Ionoplasmotherapy. The treatment at health resorts is also (sulfuric, sadon, saline and hydrosaline baths, etc,) benefic for MFF patients. For microcirculation improvement paraffin and mud baths should be applied.

Ionoplasmic therapy

Good results were obtained with ionoplasmotherapy using the ROTOR apparatus. Under action of strong electrical wave, the negative O_2 ions are transformed into positive ones. And they, with a high speed, will penetrate the affected areas, similar to acupuncture, at the receptors' level, improving the local microcirculation, reducing concomitantly the lactic acid in the affected areas, with pain suppression, and also causing disappearance of muscle spasm and stiffness.

Ionoplasmic treatment for fibromyalgia was used for the first time in our clinic on 87 patients, out of which there were 65 females and 22 males patients of 21 to 65 years old, average age was 43. The majority of the patients were doing physical labor with prolonged physical effort - 43 patients, history of long colds periods was found in 35 patients, skeletal anomalies were present in 18 patients: scoliosis, hyperlordosis, kiphosis, coxa valgus, coxa varus, genu varum, genu valgum etc. Fibromialgia was associated with other diseases in 31 patients: intervertebral osteochondrosis, osteoarthrosis, spastic colon, ischemia, local pains, predominantly in buttocks, lumbar, femoral, trapezium muscles etc. were present in all patients. At the same time, patients were complaining of more pain in Tender Points, also muscle spasm, fibrous nodules of different sizes and functional limitations.

EMG examination has revealed decrease of voltage in gluteal and spinal muscle (waves height decrease and their asynchrony, deformity and decrease of number). Many patients became disabled from pains while working. The disease is more frequent in females of 40-45 years of age. The sickness is worse in spring and fall.

Our study was performed on two groups of patients: Group I - 42 patients with fibromyalgia treated only with ionoplasmic procedure and group II - 27 patients treated with ionoplasmic and nonsteroidal anti-inflammatory medication and a Group III of 18 patients on placebo. From above data we concluded that ionoplasmic treatment is of high efficiency in treatment of fibromyalgia. It was very good in 36 % and good -satisfactory in 63% of patients, compared to placebo of 5-16 % of patients of pain amelioration.

The second group (group II) of ionoplasmic plus nonsteroid anti-inflammatory medication treatment over 15-25 days period, have shown better outcome then ionoplasmic alone (See table 1). Local pains, Tender Points and muscular asthenia has not vanished in 4-8 % patients under ionoplasmic treatment and only in 3-5 % of combination (Ionoplasmic plus anti-inflammatory medication) treatment. Functional limitation (muscular spasm, etc,) was same in 11-13 % of group I, while all vanished in group II. Adding anti-inflammatory non-steroidal medication improved efficiency of ionoplasmic treatment especially in patients with symptoms of inflammation, or fibromyalgia associated with osteoarthrosis, osteochondrosis or other inflammatory disease.

Our conclusion was that that fibromyalgia can be treated with ionoplasmic method,

but also there are other methods of treatment, especially when the disease is associated concomitantly with other diseases: of internal organs, neurological or orthopedic origin. There is a need for a detailed evaluation and selection of best and appropriate treatment for each patient.

Fibromyalgia is more complicated then its symptoms may reveal, and involving many systems: tendo-muscular, neuralgic, vascular and metabolic. All these should be taken in consideration and the treatment should be directed to all of the involved systems.

Case report

Patient D., 58 years. Diagnosis: Myofascial syndrome.

Complaints: pains in lumbar-sacral area intensified at moves, walking, physical strain and prolonged rest. The pains are characterized as diffuse, yet more pronounced in the glutei muscles, with disease duration of 2 years. The condition onset was gradual, occurring after a cold.

Physical examination: the patient is active, normal walking, overweighed, with normally developed muscular system. In the lumbar-sacral region, by digital palpation, pains are provoked, there are observed painful nodules of 0.7-1.0 cm and 4.0 cm in diameter, not mobile. The muscles are contracted.

Spine X-ray did not show any changes.

Global EMG showed decreased wave amplitude, high frequency, with some modified oscillations and waves' non-synchronization.

The biochemical blood assessments showed no abnormalities.

The treatment was realized by means of ionoplasmic therapy, lasting daily 10-12 minutes. Entirely, 12 sessions were performed.

Treatment results were assessed as good. The pains and muscular spasm were gone, and the spine function came back to normal.

The myofascial syndrome, a frequent condition in general population has pain as primary symptom. Since in this condition, the microcirculation is decreased and the growth of the fibrous tissue occurs, the chronic local hypoxia appears, leading to severe disturbances in local metabolism, and aggravating even more the pathologic process. Oxygen ions' flow was directed towards the nervous structures causing consequent microcirculation improvement, as well as of the oxidation and antioxidation system, normalization of the hemato-tissular barrier.

More pronounced effect was seen in combination of the ionoplasmic therapy with analgesic and anti-inflammatory agents (indomethacin and diclofenac).