The Use of Artrofoon in the Therapy of Disorders of the Paraarticular Apparatus

N. A. Khitrov

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In 30 patients with periarthritis of the shoulder joint, therapy with artrofoon relives pain and increases movement range; these effects were comparable with those produced by nonsteroidal antiinflammatory preparations. No changes in blood, urine, and ECG parameters were noted. No side effects requiring artrofoon withdrawal were recorded. In the control group, nonsteroidal antiinflammatory preparations were withdrawn in 3 patients, in whom symptoms of gastritis developed.

Key Words: *periarthritis; paraarticular apparatus; artrofoon; treatment with ultralow doses*

Periarthritis of the shoulder joint (PSJ) is the most prevalent pathology of paraarticular structures in humans; it is mediated by various mechanisms, is characterized by peculiar clinical picture, and is difficult for diagnosis, therapy, and prognosis. Great variety of PSJ forms can be explained by developed paraarticular apparatus of the shoulder joint responsible for various arm movements. PSJ is diagnosed in more then 10% patients visiting a rheumatologist. These are primarily individuals of working age (40-65 years) [1].

The causes of PSJ are not quite clear. Direct or indirect traumas, chronic microtraumas, physical overload, or inherited shoulder defects are possible risk factors. Degenerative and inflammatory processes play a role in the pathogenesis of PSJ. Disturbances in metabolic, neurotrophic, and still little studied immune mechanisms also underlie PSJ development [1,3].

For more precise evaluation of the nature of disturbances in PSJ, localization and character of pain, especially during motions, should be determined. Appearance of pain during movements can indicate involvement of subscapular, surpaspinal, infraspinal, and teres minor muscles. Dissociation between limited active and preserved passive movements is a typical sign. Capsulitis is also difficult for diagnosis, treatment, and prognosis. This condition (usually unilateral) develops after traumas, fractures, and algodystrophies. Pain is accompanied by restriction of both active and passive joint movements in all directions. Capsulitis (frozen shoulder) has a serious prognosis. Algodystrophy-related shoulder-hand syndrome characterized by acute causalgia and vasomotor and neurodegenerative changes in the hand (diffuse cold edema, cyanosis, muscular atrophy, and osteoporosis), also belongs to PSJ. The duration of PSJ depends on clinical variants: from few weeks to chronic long-term permanent or recurrent course with uncertain prognosis [1-3].

The choice of drugs for the treatment of PSJ (long-term treatment in many cases) is difficult because of poorly studied etiology of PSJ and complexity of pathomorphological, neurotrophic, immune, and inflammatory disorders.

The therapy of PSJ is based on the following principles:

1. Processes of immune inflammation predominate in PSJ, which is many times confirmed by the efficiency of nonsteroidal antiinflammatory drugs (NSAID) and local application of steroids.
2. The use of NSAID is indicated, but the duration of treatment with NSAID is not defined

Training and Research Medical Center, Presidential Property Management Department of the Russian Federation, Moscow

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because of abundance of nosological forms of PSJ; at the same time, long-term treatment with NSAID is fraught with various complications [9-11].

3. Local therapy with steroids is not always effective and is fraught with complications (osteoporosis, infection, *etc.*) [8].
4. It is desirable to use an antiinflammatory preparation containing ultralow doses of active matter for the therapy of PSJ, because it can be used for a long time and with minimum side effects.

For the treatment of PSJ we choose artrofoon (AF), an antiinflammatory preparation containing ultralow doses of antibodies to TNF-α. According to modern data, TNF-α is an essential component of the cytokine cascade underlying inflammation development [5]. Previous studies demonstrated high efficiency of AF in the treatment of osteoarthrosis and rheumatoid arthritis [4,7].

The aims of AF administration were pain relief, prevention of transformation of acute into chronic inflammation, long-term therapy with prophylactics of fibrosis, sclerosis, dystrophy, degeneration of paraarticular structures, reduction of concomitant therapy, and minimization of side effects. In some patients, AF was administered when other methods of PSJ treatment were ineffective.

We performed an open randomized study of clinical efficiency and tolerability of AF therapy *vs*. NSAID therapy in patients with PSJ.

MATERIALS AND METHODS

The main group (n=30) included 12 men and 18 women, mean age 59.4±8.9 years, history of the disease 6.5±3.8 years. The control group (n=30) comprised 11 men and 19 women, mean age 58.3±9.6 years, history of the disease 5.1±4.1 years. In many patients PSJ was presented by a combined pathology (Table 1). In the main group, AF was administered to 2 patients with gastrointestinal ulcer diseases and 1 patient after mastectomy for breast tumor (Table 2).

In the main group, 12 patients received no previous therapy and 18 patients before AF treatment received NSAID, local injections of steroids with novocaine,

TABLE 1. PSJ Forms in Patients of the Main and Control Groups

Nosological form	Main group	Control group
Tenomyositis of the supraspinal muscle	17	19
Tenomyositis of the subscapular muscle	8	9
Subacromial bursitis	5	6
Shoulder-hand syndrome	4	2
Capsulitis	5	3
Arthrosis of the acromioclavicuar	12	11
Combined pathology	16	13

TABLE 2. Concomitant Diseases in Patients with PSJ

Concomitant pathology	Main group	Control group
Cardiovascular pathology	18	17
Atherosclerotic dyscirculatory encephalopathy	8	9
Pathology of hepatobiliary system	8	8
Chronic diseases of the kidneys, including urolithiasis	4	3
Diabetes mellitus	4	2
History of allergic reactions	9	6
Tumor diseases	1	0
Chronic gastritis	12	5
Gastrointestinal ulcer disease	2	0

application therapy, and physiotherapy, which were ineffective or led to insignificant positive dynamics. In the control group, 14 patients received no previous therapy and 16 patients before NSAID administration received application therapy, physiotherapy, and local injections of steroids with novocaine without clear-cut positive dynamics. No other therapy was prescribed during treatment with AF and NSAID except recommendations for regimen.

AF was given in a dose of 8 tablets per day for 3 months; after attaining improvement, the dose was lowered to 4 tablets per day. Some patients took 2 tablets 4 times a day (if the scheme with 8 separate doses was inconvenient). Patients of the control group received primarily diclofenac in a dose of 100 mg/day with lowering the dose after attaining improvement. Patients with risk factors for the development of NSAID-related side effects received selective cyclooxygenase-2 inhibitors in doses corresponding to the dose of diclofenac. Some patients of the control group received omez (omeprazole). AF and NSAID were not administered to pregnant and nursing women.

In patients of the main and control groups, general and local examinations were performed and HR, blood pressure, body weight and height were measured on day 1 of therapy and after 2 weeks and 1 and 3 months. Pain intensity at rest and during movements was evaluated by a 100-point visual analog scale (VAS), the amplitude of active shoulder joint movements was assessed in angular degrees. In parallel, the efficiency and tolerability of the administered drug were evaluated and patient's general state was assessed separately by the patient and physician.

Examination of the shoulder joint included X-ray and ultrasonic examination and magnetic resonance imaging (when indicated). Common and biochemical blood tests (glucose, total protein, transaminases, bilirubin, urea, creatinine), common urine test, and ECG were performed before the start and after completion of the treatment course.

RESULTS

Patient's well-being significantly improved against the background of both AF and NSAID treatment. This manifested in increased mood, reduced irritability, and sleep normalization primarily due to night pain relief.

In both groups, the pain in the shoulder joint gradually decreased (Fig. 1). In patients receiving AF, the decrease in joint pain during motion predominated and became significant by the 3rd month of therapy ($p<0.01$). Greater and significant ($p<0.01$) increase in movement range was also noted in these patients by this term (Fig. 2).

After completion of the treatment with AF, considerable improvement was noted in 15/14 patients (physician/patient assessment), improvement in 10/12 patients, and the absence of positive dynamics in 5/4 patients. In the group treated with NSAID, improvement was recorded in 18/16 patients, considerable improvement was noted in 9/12 patients, and the absence of positive dynamics in 3/2 patients. No negative dynamics was noted in both groups.

Therapeutic efficiency of AF was assessed as very good, good, satisfactory, and poor by 7, 9, 11, and 3 patients, respectively. Therapeutic efficiency of NSAID was assessed as very good, good, satisfactory, and poor by 8, 13, 6, and 3 patients, respectively. AF tolerability was estimated as very good, good, and satisfactory by 17, 10, and 3 patients, respectively. None patients estimated AF tolerability as bad and very bad. NSAID tolerability was rated as very good by 8 patients, good by 11 patients, satisfactory by 7 patients, and bad and very bad by 2 patients each.

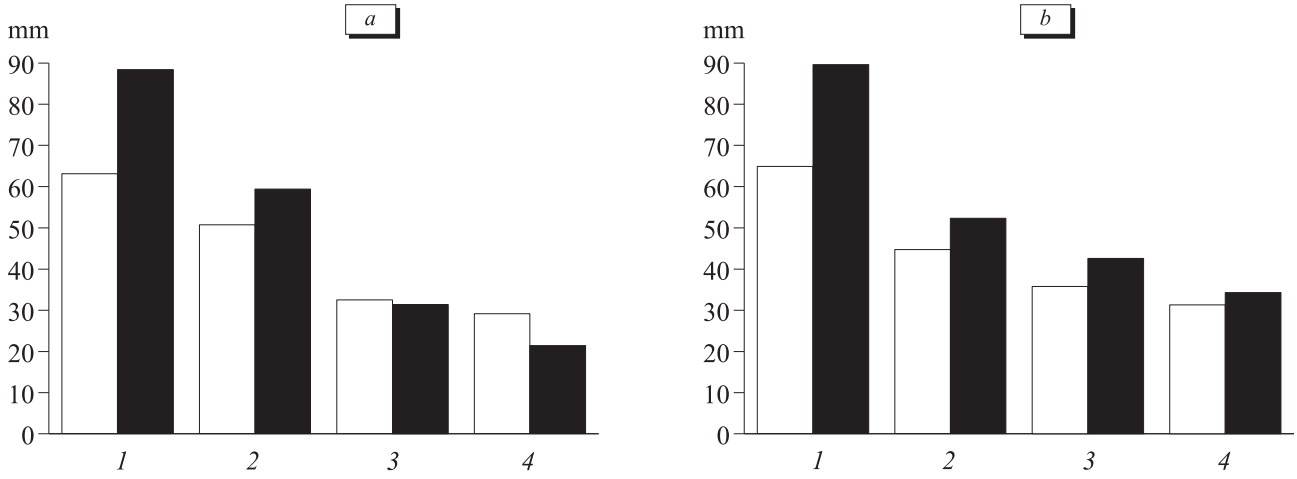

Fig. 1. Intensity of shoulder joint pain in PSJ patients of the main (*a*) and control (*b*) groups. *1*) before treatment; *2*) after 2 weeks; *3*) after 1 month; *4*) after 3 months. Light bars: pain at rest; dark bars: pain during movement.

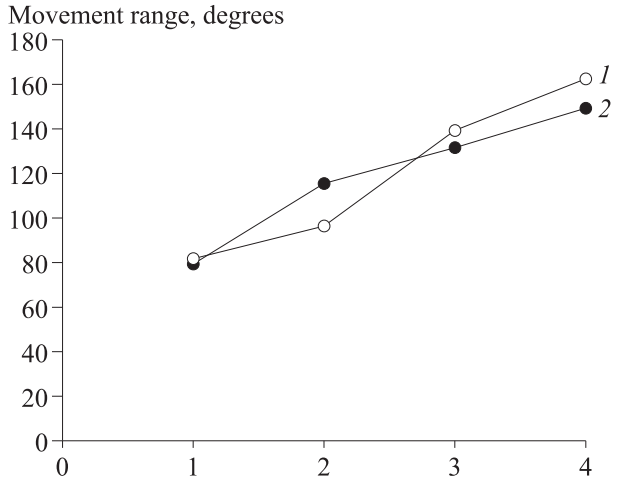

Fig. 2. Movement range in the shoulder joint (angular degrees) against the background of AF (*1*) and NSAID (*2*) therapy. *1*) before treatment; *2*) after 2 weeks; *3*) after 1 month; *4*) after 3 months.

One patient reported aggravation of shoulder joint pain during the first 2 weeks of AF treatment. One patient of the AF group with arterial hypertension reported blood pressure elevation, which required no additional therapy and was not associated (by patient's opinion) with AF treatment. In one female patient, symptoms of dyspepsia were noted during the first week of AF treatment; they disappeared without correction and was not related (by patient's opinion) with AF treatment. No other complications and disease aggravations were noted against the background of AF therapy. During NSAID therapy, blood pressure elevation requiring additional drug correction was observed in 4 patients with arterial hypertension, symptoms of dyspepsia persisting from 1 week to 3 months were noted in 5 patients, of them 3 patients had symptoms of gastritis and NSAID were withdrawn in these patients.

Blood parameters remained unchanged throughout the treatment period. No changes in urine parameters were noted. ECG did not change in both groups.

Thus, the following conclusions can be made:

1. AF is effective in patients with PSJ: it relieves pain, increases range of movements, and normalizes psychic and somatic status.
2. No side effects and complications requiring AF withdrawal were noted in the main group; while in the control group, NSAID were withdrawn in patients (10%) with developed clinical picture of gastritis.
3. AF is a preparation of choice in cases when NSAID are contraindicated or other methods of treatment are ineffective.

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