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The effectiveness of complex therapy in patients with gout using carbon enterosorbent

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Abstract

Introduction. Gout is a serious medical, social and economic problem today. It becomes even more important due to its comorbidity. The relationship of pathogenetic mechanisms in the development and progression of gout and non-alcoholic fatty liver disease (NAFLD) has been proven. The presence of concomitant pathology enhances the inflammatory reaction in the body and significantly complicates the course of the underlying disease.

The aim of the study – to evaluate the indicators of systemic inflammatory response in patients with gout and gout with NAFLD when included in the complex therapy of the disease carbon enterosorbent carboline.

Materials and Methods. 123 patients with gout in the period of exacerbation were examined, who were divided into two groups. Group I included 65 patients with gout without liver damage, group II – 58 people with concomitant NAFLD. To determine the effectiveness of treatment, both groups were divided into subgroups: IA (27 people) and IIA (23 patients) who received conventional treatment. Subgroups IB (38 patients) and IIB (35 subjects) additionally received enterosorbent carboline. The control group consisted of 30 healthy individuals. A general clinical examination (collection of complaints, history, objective examination), determination of pain intensity on a visual-analog scale (VAS), biochemical (uric acid level (UA), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR)) and enzyme-linked immunosorbent assays (tumor necrosis factor-α) (TNF-α), interleukins 1 (IL-1β) and 10 (IL-10) were conducted.

Results. Patients in both groups had typical clinical signs of joint syndrome. In patients with gout an increase in UA, CRP, ESR, imbalance of cytokine regulation (IL-1β, TNF-α, IL-10) was revealed. These changes increased in the presence of concomitant NAFLD. Significant decrease in the concentration of UA, CRP, ESR, cytokine content after treatment was in all subgroups, but more in patients who received carbon enterosorbent with basic therapy.

Conclusions. The inclusion of the carbon enterosorbent carboline in the complex treatment of patients with gout and gout with NAFLD in the acute phase, promotes faster reverse dynamics of the clinical manifestations of the disease, accompanied by a more significant decrease of the level of UA, CRP, ESR and cytokines in blood serum.

Key words: gout; non-alcoholic fatty liver disease; treatment; enterosorbent.

Introduction

Gout is an urgent health problem, as well as a serious medical, social and economic problem given the high prevalence and predisposition to the development of acute recurrent arthritis, leading to poor quality of life, long-term disability, early disability [1-3].

The main factor in the pathogenesis of gout is a violation of purine metabolism, leading to increase in the concentration of uric acid (UA) and its metabolites in the serum and initiates the inflammatory process in the deposition of sodium monourate crystals [4].

An important role in the course of gout belongs to various comorbid conditions that complicate its timely diagnosis and treatment. A significant proportion of patients have obesity, disorders of lipid and carbohydrate metabolism, hypertension, which are part of the metabolic syndrome. Gout is often associated with liver disease, namely non-alcoholic fatty

liver disease (NAFLD), which is a significant problem in the world and affects 17–46 % of the adult population in Western countries [5-8].

The commonality of pathogenetic mechanisms in the development and progression of gout and NAFLD has been proved. The presence of liver pathology, as a comorbid condition, contributes to the inflammatory reaction in the body and significantly complicates the course of the underlying disease [9].

The aim of the study was to evaluate the indicators of systemic inflammatory response in patients with gout and gout with NAFLD when included in the complex therapy of the disease carbon enterosorbent carboline.

Materials and Methods. 123 patients with gout during the exacerbation were examined, including 118 (95.9 %) men and 5 (4.1 %) women. The mean age was (57.73±1.01) years. The diagnosis of gout was made on the basis of the ACR/EULAR criteria of 2015 and the order of the Ministry of Health of Ukraine No. 676 of October 12, 2006 "Clinical protocol for medical care for patients with gout". The diagnosis of NAFLD was established in accordance with the recommendations of EASL-EASD-EASO [10], the criteria of the Unified Clinical Protocol of Primary, Secondary (Specialized) Medical Care "Non-Alcoholic Steatohepatitis" (Order of the Ministry of Health of Ukraine of November 06, 2014 No. 826).

During the study, all patients were divided into two groups. Group I included 65 patients with gout without liver damage, group II – 58 patients with concomitant NAFLD. The control group consisted of 30 healthy individuals of representative age.

Depending on the treatment patients received, both groups were divided into subgroups: IA (27 patients) and IIA (23 patients), who received conventional treatment, which included diet, anti-inflammatory and analgesic drugs, hypouricemic therapy. Subgroups IB (38 patients) and IIB (35 patients) additionally took enterosorbent carboline (manufactured by the Institute of Experimental Pathology, Oncology and Radiobiology named after R.Ye. Kavetskyi, NAS of Ukraine) in the form of small granules 1 teaspoon 3 times a day for 10 days 2 hours before or after meals or medications.

Patients underwent general clinical examination (collection of complaints, history, objective examination), determination of pain intensity on a visual analog scale (VAS), biochemical (uric acid level (UA), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR)) and enzyme-linked immunosorbent assays (tumor necrosis factor-α) (TNF-α), interleukins 1 (IL-1β) and 10 (IL-10).

To assess the effectiveness of therapy, patients in both groups were monitored for complaints, assessment of joint syndrome, the dynamics of the level of UA, CRP, ESR and cytokines.

Mathematical and statistical processing of the obtained results was performed using the program Statistica 10.0 (“StatSoft”, USA) and the package of statistical functions Microsoft Office Excel 2016 (Microsoft Corp., USA). The arithmetic mean (M) and its error (m) were found. The results were presented as (M±m). Significance of differences between groups was assessed by Student's t-test for independent samples with normal distribution and Wilcoxon's U-test (Mann–Whitney) under non-parametric results. Differences were considered statistically significant at $p < 0.05$.

Results

Of the clinical symptoms, the main complaint in all patients was pain, as one of the manifestations of the joint syndrome, and restriction of movement in the joints. 53 (81.5 %) patients of group I and 54 (93.1 %) of group II had swelling of the affected joint with reddening of the skin in 45 (69.2 %) and 56 (97 %), respectively. The increase in local temperature was in 50 (77 %) and 54 (93.1 %) patients in both groups.

The intensity of pain according to VAS in patients of group II was 1.2 times higher than those examined in group I and was (56.34 ±1.00) and (69.21±1.04) mm, respectively ($p < 0.05$) .

Analysis of laboratory parameters in patients with gout before treatment revealed an increase in blood levels of UA, CRP, ESR, imbalance of cytokine regulation. It is known that in this pathology there is an inflammatory process, which is not limited to local changes in the joints, but also causes a corresponding reaction of the whole body.

Thus, in the examined group II there was an increase in the level of UA in the blood by 1.4 times compared with patients of group I, respectively (621.57±13.47) and (459.72±11.44) μmol/l ($p < 0.05$). The level of CRP was significantly 1.7 times more pronounced in patients with concomitant NAFLD than in group I. Increased ESR, as a criterion of activity and severity of the inflammatory process, occurred among all patients, but most in patients with concomitant liver disease – (29.12±1.04) mm/h, which is 1.5 times higher than in group I ($p < 0.05$).

There was a significant increase in the levels of IL-1β, TNF-α in both groups, and in patients with concomitant NAFLD, these values were higher ($p < 0.001$) than without liver damage.

The content of IL-1β compared with the control in group I increased 3.09 times, in group II – 6.70 times. The changes were statistically significant in all groups. The concentration of TNF-α had a similar dynamics, in patients of both groups 2.90 and 4.08 times higher than the control index. Indicators of IL-10 in patients of all groups were higher than control. The study of cytokine status revealed a statistically significant increase in the concentration of anti-inflammatory cytokine IL-10 in the blood plasma of patients of group I in 2.18 times, group II – 3.03 times.

Thus, gout is accompanied by pronounced changes in the cytokine system, which is manifested by an increase in both pro-inflammatory (IL-1β, TNF-α) and anti-inflammatory (IL-10) cytokines, which indicates the inclusion of the latter in the systemic response.

The effectiveness of treatment was assessed by changing the complaints of patients. In the dynamics of treatment in patients of both groups there was a decrease in clinical manifestations of the joint syndrome and improvement of their well-being, decreased local temperature over the affected joint. 39 (60.0 %) patients of group I and 46 (79.0 %) of group II after treatment still experienced mild pain in the affected joints. Swelling and redness of the skin over them occurred in 9 (17.0 %) and 5 (11.0 %) patients of group I, 13 (24.0 %) and 9 (16.0 %) – group II.

As can be seen in Fig. 1, in patients of subgroup IA after treatment the intensity of pain according to VAS decreased from (55.19 ±1.4) mm to (18.41±3.21) mm ($p < 0.001$), and in subgroup IB – from (57.16±1.4) mm to (11.66± 2.12) mm ($p < 0.001$). In subgroup IIA – from (69.04 ±1.67) mm to (30.48±4.68) mm ($p < 0.001$), and in subgroup II B (against the background of enterosorbent) – from (69.31±1.34) mm to (21.20±2.82) mm ($p < 0.001$).

The order of complex treatment and enterosorbent helped to decrease the level of UA, reduce the activity of the inflammatory process, pro- and anti-inflammatory cytokines in the blood serum (Table 1).

The dynamics of regression of UA level in blood serum after treatment in patients of group I was probably better compared with patients of group II. Against the background of BT, the level of UA decreased in subgroup IA by 1.14 times, and in subgroup IB, with additional intake of carboline – by 1.33 times. In subgroup IIA, the level of UA decreased by 1.24 times, $p < 0.001$, in subgroup IIB – 1.26 times. Treatment outcomes in subgroups IB and IIB were better than in subgroups IA and IIA ($p < 0.05–0.001$).

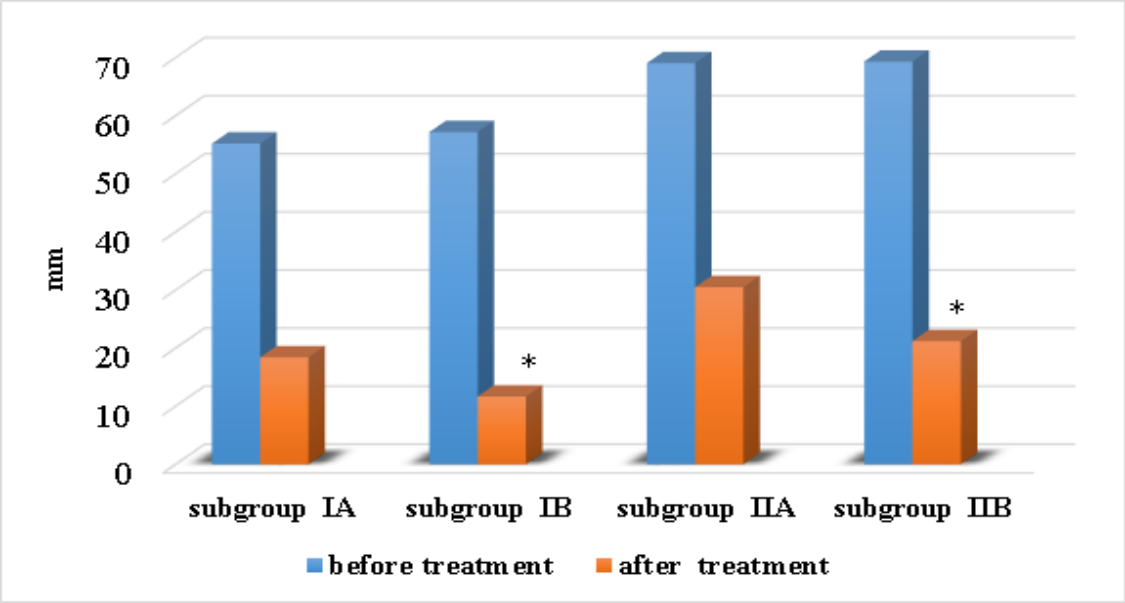

Fig.1. The intensity of pain according to VAS in patients with gout and gout with NAFLD before and after treatment

Note: * – probability of difference between subgroups IA and IB, IIA and IIB before and after treatment (p <0.001).

Table 1

Dynamics of laboratory parameters in patients with gout and gout with NAFLD before and after treatment (M ± m)

Factor	Control group n=30	Subgroup IA n=27		Subgroup IB n=38		Subgroup IIA n=23		Subgroup IIB n=35		P
		before treatment	after treatment	before treatment	after treatment	before treatment	after treatment	before treatment	after treatment	
UA, μmol/l	309.13 ±14.16	444.01 ±18.5*	389.03 ±14.55*	470.87 ±14.38*	353.01 ±7.96*#	657.03 ±11.64*	529.27 ±12.32*	598.29 ±20.14*	473.95 ±7.75*#	p<0.001
CRP, mg/l	3.39 ±0.17	10.36 ±0.95*	6.36 ±0.50*	12.06 ±1.01*	3.51 ±0.37#	19.05 ±2.91*	8.04 ±0.63*	19.94 ±1.92*	7.79 ±0.36*	p<0.001
ESR, mm/h	6.47 ±0.65	20.59 ±1.45*	11.37 ±0.77*	18.47 ±1.14*	7.95 ±0.59#	27.00 ±1.51*	14.43 ±0.86*	30.51 ±1.37*	11.94 ±0.42*#	p<0.001
IL 1-β, pg/ml	1.80 ±0.14	5.45 ±0.21*	4.07 ±0.18*	5.65 ±0.19*	3.38 ±0.15*#	11.96 ±0.67*	7.44 ±0.22*	12.13 ±0.60*	6.83 ±0.26*	p<0.001
TNF-α, pg/ml	4.30 ±0.20	13.17 ±0.41*	10.79 ±0.33*	11.97 ±0.36*	8.98 ±0.21*#	17.89 ±0.38*	12.80 ±0.44*	17.33 ±0.37*	8.91 ±0.16*#	p<0.001
IL 10, pg/ml	5.20 ±0.19	11.36 ±0.52*	9.79 ±0.39*	11.33 ±0.42*	7.89 ±0.25*#	16.56 ±0.71*	13.01 ±0.57*	15.18 ±0.61*	10.51 ±0.31*#	p<0.001

Notes: * – probability of difference of factors in relation to the control group (p <0.001); p – probability of difference in subgroups IA and IB, IIA and IIB before and after treatment; # – the probability of difference between subgroups IA and IB after treatment, IIA and IIB after treatment (p <0.05–0.001).

Among the indicators of the inflammatory process activity (ESR, CRP) there was a decrease in ESR ($p < 0.001$) and the concentration of CRP ($p < 0.001$) in the dynamics of treatment in both groups. The order of BT in subgroup IA caused a decrease in the content of CRP and ESR in 1.63 times and 1.81 times, respectively. It should be noted that in patients of subgroup IB after the use of enterosorbent decreased the concentration of CRP in 3.44 times ($p < 0.001$), and ESR – 2.32 times ($p < 0.001$), compared with the control group, these indicators were normalized ($p > 0.05$). In patients with concomitant NAFLD with the use of BT, the content of CRP decreased by 2.37 times, and ESR – by 1.87 times. In subgroup IIB in combination with enterosorbent there was a decrease in CRP by 2.56 times ($p < 0.001$), ESR – by 2.55 times ($p < 0.001$).

When using BT, the level of IL-1β in subgroup IA decreased in 1.34 times, TNF-α – 1.22 times ($p < 0.001$), and IL-10 – 1.16 times ($p < 0.05$). In subgroup IB, with additional intake of enterosorbent, the level of IL-1β in the serum decreased by 1.67 times, TNF-α – by 1.33 times, IL-10 – by 1.44 times ($p < 0.001$).

In patients of subgroup II A, the content of IL-1β in the serum after the course of BT decreased 1.6 times, TNF-α - 1.40 times, IL-10 - 1.27 times ($p < 0.001$). Joining the treatment of enterosorbent carboline allowed increasing the effectiveness of treatment. Thus, the level of IL-1β in the serum decreased by 1.78 times, TNF-α – by 1.95 times, IL-10 – by 1.44 times ($p < 0.001$).

Evaluating the above results, we can assume that the comprehensive treatment of gout and gout with NAFLD in combination with carbon enterosorbent, reduces the clinical manifestations of the disease, reduces the activity of the inflammatory process in the body, the content of both pro- (IL-1β, TNF-α) and anti-inflammatory cytokines (IL-10).

Discussion

Gout is a chronic genetically caused inflammatory disease with increased serum concentration of UA (hyperuricemia) and its subsequent deposition in the form of sodium monourate crystals in the joint tissue and periarticular areas, in the walls of blood vessels, skin, internal organs [11]. Hyperuricemia is not only a “concomitant risk factor” for gout, but a major pathophysiological factor that causes arthritis attacks, tophi formation and joint damage, so eliminating hyperuricemia is a key principle in the fight against the disease [4]. A feature of gout is its chronic course, due to persistent inflammation and can be combined with chronic degenerative diseases of the joints. Numerous studies prove that in the attack-free interval there is a persistent low-intensity inflammation in the tissues of the joints. The same

cytokines responsible for acute outbreaks can be detected in lower concentrations between attacks [12, 13].

Gout becomes even more important due to its comorbidity. The combination of gout and NAFLD is an urgent issue today, as both diseases are multisystem with a high level of comorbidity, with metabolic and cardiovascular disorders, leading to reduced treatment effectiveness and progression of complications [14, 15].

When they are combined, there is an increase in the inflammatory response, increased CRP, ESR, cytokine imbalance, which persists after treatment and requires continued anti-inflammatory, detoxification therapy.

Enterosorption is an effective adjunct to comprehensive treatment, as it suppresses the systemic inflammatory response, helps to compensate for the immune system, provides non-drug stimulation of natural defense systems and improves the function of internal organs [16, 17].

Conclusions

The results of the study showed that patients had typical clinical signs of gout: pain and restriction of movement in the joints, their swelling, redness, fever. When gout was combined with NAFLD, the clinical symptoms were more pronounced.

Gout is accompanied by an active inflammatory process, significant changes in the cytokine system, manifested by an increase in serum levels of CRP, ESR, pro-, and anti-inflammatory cytokines, and these indicators increase in case of concomitant NAFLD.

The use of complex therapy in patients with gout led to improved clinical manifestations of the disease, reduced concentrations of UA, CRP, ESR, the content of both pro-inflammatory (IL-1β, TNF-α) and anti-inflammatory (IL-10) cytokines. The same was observed when combining BT with carboline ($p < 0.001$). In patients with gout in combination with NAFLD, despite greater changes in these indicators before treatment, this complex therapy also led to a decrease in their values. However, normalization of the studied parameters did not occur. In general, the positive dynamics of these indicators was better in the subgroups that received carboline ($p < 0.001$).

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Conflict of Interests

The authors declare no conflict of interest.

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