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MODERN METHODS OF TREATING GOUT

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Abstract: Gout is a systemic tophi disease from the group of microcrystalline arthritis, which is characterized by the deposition of monosodium urate crystals in various tissues and the inflammation that develops in connection with this in individuals with hyperuricemia caused by environmental and/or genetic factors. Over the past decades, it has been considered one of the most studied and treatable rheumatic diseases, however, the frequency of errors made when prescribing therapy for patients with gout remains extremely high.

Keywords: padagra, allopurinol, dose, research, therapy.

According to T. R. Mikuls et al., allopurinol is inadequately prescribed in only three parameters studied (dose adjustment in the presence of renal failure, combined use of allopurinol and azathioprine, treatment of asymptomatic hyperuricemia) in 25–57% of cases. Another large study demonstrated that the majority of patients with gout do not undergo the necessary laboratory monitoring when prescribed allopurinol and colchicine [22]. Some mistakes in the treatment of gout by doctors are made more often than by patients when self-medicating. For example, refusal of any therapy even during an acute attack of arthritis or the use of only analgesics to relieve it, failure to prescribe urate-lowering drugs in medical practice are 2 times more common than when patients with gout self-medicate [20].

The main clinical manifestation of gout is an acute attack of arthritis, which occurs suddenly, mainly between two o'clock in the morning and seven o'clock in the morning, and is characterized by severe pain, quickly increasing to severe pain (within several hours the signs of arthritis reach maximum intensity), severe hyperemia and hyperthermia. In half of the cases, arthritis is accompanied by fever. Most often, one joint is affected (up to 90% of cases); sometimes the attack occurs in the form of oligoarthritis. The duration of the first attacks of arthritis ranges from several days to 1-2 weeks, after which there is an asymptomatic interval called the inter-attack period. The duration of interictal periods can vary from several days to several years. Most often, at the onset of the disease, the first metatarsophalangeal joint is affected (about 2/3 of cases), less often the metatarsal joints, knee and ankle joints. The

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development of bursitis and tenosynovitis is possible. In women, small joints of the hands are often affected, especially the interphalangeal joints. Provoking factors for the development of an attack of arthritis are injuries, hypothermia, alcohol intake, heavy consumption of meat and fatty foods, surgical interventions, fasting; Often the onset of gout is associated with taking diuretics and low doses of acetylsalicylic acid. The frequency and duration of gout attacks in the absence of adequate treatment gradually increase, and the inter-attack periods progressively shorten, new joints are involved, and the effectiveness of anti-inflammatory drugs decreases. As a result, the course of arthritis becomes chronic, tophi are formed (deposits of monosodium urate crystals), which are revealed upon examination in the form of subcutaneous formations, usually in the area of the ears and joints; stones form in the kidneys. In women with reduced renal function, subcutaneous tophi can form already in the first years of the disease.

In the vast majority of cases (according to international studies, their share reaches 90%), nonsteroidal anti-inflammatory drugs (NSAIDs) are used to relieve attacks of gouty arthritis. They are recommended as first-line drugs by experts of the European League Against Rheumatism on the diagnosis and treatment of gout [28] and in the absence of contraindications (severe renal failure, heart failure, exacerbation of peptic ulcer disease, anticoagulant therapy, hypersensitivity) are the drugs of choice. The advantages of NSAIDs are the ability to significantly reduce the duration of acute attacks of gouty arthritis and relative safety with short-term use. There are few comparative studies of the effectiveness of various anti-inflammatory drugs in patients with gout. Most of them did not show any significant advantages of drugs that are non-selective with respect to cyclooxygenase-2 (COX-2) inhibition over selective ones [23]. Studies conducted at the Institute of Rheumatology of the Russian Academy of Medical Sciences showed that the selective COX-2 inhibitor nimesulide, when used in patients with gout, was more effective than diclofenac sodium, including in patients with chronic tophi gout, and the granular form of nimesulide was superior to the tablet form [3]. The use of selective COX-2 inhibitors may be preferable given their greater safety. When prescribing NSAIDs to elderly patients, in the presence of a history of ulcers and other risk factors for gastrointestinal complications, parallel use of gastroprotectors is mandatory [27]. To reduce the risk of side effects of NSAIDs when a clinical effect occurs, a gradual reduction in their dose is recommended, but NSAIDs should be completely discontinued no earlier than 2 days after the symptoms of arthritis disappear. It is also possible to use NSAIDs to prevent joint attacks in patients with chronic gouty arthritis, especially with parallel therapy with allopurinol [27].

The use of the meadow saffron plant (Colchicum autumnale), the use of which for medicinal purposes has a long history, has not lost its relevance. Thus, the first-line treatment for acute attacks of gout includes colchicine, an extract of meadow saffron bulb, which is comparable in effectiveness to NSAIDs. The most common regimen for prescribing colchicine, used in clinical practice for more than 40 years: a single dose of the drug at a dose of 1 mg followed by 0.5 mg every 1–3 hours (no more than 6 mg in 12 hours) until the onset of a clinical effect [14]. However, when using this regimen, even before clinical improvement is achieved, side effects (diarrhea, nausea, vomiting) often occur, which may require discontinuation of the drug. In addition, the use of colchicine is associated with a risk of developing agranilocytosis and liver damage. In case of renal failure, the dose of colchicine should be reduced, and if the glomerular filtration rate is less than 10 ml/min, its use is contraindicated. Recent studies have shown that taking significantly lower doses of colchicine (0.5 mg 2–3 times a day), which is

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characterized by significantly better tolerability, including in patients with reduced renal function, can be no less successful [19]. Like NSAIDs, colchicine can be used long-term to prevent exacerbations in patients with chronic gout [27]. However, it should be remembered that with prolonged use of even low doses of colchicine, the development of neuromyopathy is possible, especially in patients with reduced renal function. There have been no randomized studies comparing the effectiveness of NSAIDs and colchicine in patients with gout.

If there are contraindications to the use of NSAIDs and colchicine, glucocorticoids (GC) can be used to relieve an acute attack of gout. The initial dose of prednisolone, prescribed orally and taken for 1–3 days, averages 30 mg/day, then it is gradually reduced until the drug is completely discontinued over 1–2 weeks. If a large number of joints are involved, the initial dose can reach 50 mg/day, and the duration of administration increases [13]. J. A. Allovay et al. showed that the use of intramuscular injections of triamcinolone acetonide at a dose of 60 mg/day led to relief of arthritis slightly faster compared to indomethacin, although these differences were not statistically significant [5]. Recently published data from a double-blind study of the use of the NSAID naproxen at a dose of 500 mg twice a day and prednisolone at a dose of 35 mg/day for 5 days in 120 patients with gouty arthritis showed completely comparable efficacy of the drugs. According to the authors, a short course of GC therapy can serve as an alternative to the use of NSAIDs in relieving attacks of gouty arthritis. Attention should be paid to the high incidence of side effects when taking both naproxen (37% of patients) and prednisolone (34% of patients) [17]. The main disadvantage of systemic GC therapy, in addition to the large number and frequency of side effects, is the frequent development of exacerbation of arthritis, especially with a rapid reduction in the dose of GCs and their withdrawal.

Along with the systemic use of GC, a good clinical effect, especially during attacks of arthritis involving 1-2 joints, can be achieved using intra-articular injections of GC. A recent study using intra-articular injections of low doses of triamcinolone (10 mg in the knee joint and 8 mg in other smaller joints) showed that a single dose of the drug was sufficient to relieve arthritis in 95% of patients within 48 hours after injection [12].

Local application of cryotherapy can also help reduce the duration of taking NSAIDs and colchicine and reduce the duration of arthritis attacks [27].

Despite the ease of stopping attacks of arthritis, especially at the onset of the disease, timely administration of antihyperuricemic drugs is fundamentally important. Thus, the main goal of gout therapy, in addition to relieving acute attacks of arthritis, is to persistently reduce the serum level of uric acid (UA) to a state in which the likelihood of developing attacks of arthritis and the formation of tophi is minimal.

In most cases, it is advisable to prescribe antihyperuricemic drugs after the first attack of arthritis, but with low serum levels of uric acid in a small proportion of patients, it is sufficient to use non-drug treatment methods. For several centuries, a low-purine diet has been successfully used in the treatment of gout, which is based on limiting the diet of animal products rich in purines (primarily meat, fish and seafood). The basic principles of the diet, which have remained relevant in our time, were described by the English physician and philosopher J. Locke back in the 17th century. It has been shown that strict adherence to a low-purine diet leads to a decrease in serum UA levels by 60–120 μmol/L [9]. A good urate-lowering effect was also established for a low-calorie diet (1600 kcal/day). A decrease in serum uric acid levels occurred already in the first days of therapy, and after 16 weeks of dieting, normouricemia was achieved in 58% of

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patients [7]. This result can be explained by the effect of diet on metabolic disorders that contribute to the development of hyperuricemia and gout, primarily by reducing the levels of insulin, triglycerides and body mass index. Avoiding alcohol is of great importance.

The most commonly used pharmacological agent for the correction of hyperuricemia is allopurinol, a xanthine oxidase inhibitor. Its role in the treatment of gout is so high that in 1988, J. Hitchings and G. Elion were awarded the Nobel Prize in Medicine for the discovery of a number of drugs, including allopurinol. The drug is prescribed in a low dose, as a single dose, no more than 50–100 mg/day and no earlier than 2–4 weeks after the relief of an attack of arthritis. Subsequently, the dose of allopurinol is gradually increased every 3–4 weeks until the target serum sUA level is achieved. Less commonly, in no more than 10% of patients, uricosuric drugs are prescribed, which include probenecid, sulfinpyrazone and benzbromarone. Unlike allopurinol, the dose of which can be easily adjusted in the presence of renal failure depending on the decrease in glomerular filtration rate and serum creatinine level, the use of uricosuric drugs can be dangerous even with a slight decrease in renal function. Currently, these funds are not registered in our country.

In the first weeks of therapy with allopurinol and uricosuric drugs, low doses of NSAIDs or colchicine may be prescribed to prevent exacerbations of arthritis. If an attack of arthritis develops while taking allopurinol, its dose does not change during the exacerbation.

The uricosuric effect is also characteristic of some drugs belonging to other groups. A pronounced decrease in UA levels, exceeding 20% of the initial level, can be achieved with the use of fenofibrate, prescribed for hypertriglyceridemia not corrected by diet, including in patients with type 2 diabetes mellitus (DM2) [6, 11]. A significant decrease in serum UA levels, amounting to 19%, was also demonstrated when this drug was taken together with allopurinol [10]. Losartan, an angiotensin II receptor antagonist, has a uricosuric effect, which allows it to be successfully used in patients with gout with arterial hypertension [25]. It should be remembered that uricosuric activity is not a group effect of fibrates and angiotensin II receptor antagonists. The uricosuric effect of high doses of vitamin C (4–8 g/day) has been proven, but even with the use of vitamin C in a daily dose of 500 mg for 2 months, the decrease in serum UA levels reached 30 μmol/L [15]. The advantage of these drugs over the actual uricosuric drugs is the possibility of using them in patients with nephrolithiasis.

In patients with gout and in cases of chronic hyperuricemia, the use of urine-alkalinizing drugs that promote the dissolution and prevention of the formation of uric acid and mixed stones is justified, given the presence of urate nephrolithiasis in most patients with gout, the frequency of which in this disease is hundreds of times higher than the population [26]. One such remedy is Blemaren, used to dissolve urate and urate-oxalate stones in the urinary tract and prevent their formation. The drug changes the pH of urine from acidic to neutral, thereby providing optimal conditions for the dissolution of stones and preventing the crystallization process. If the urine pH is constantly maintained at 6.2–7.0, this leads to the gradual dissolution of uric acid stones and prevents their formation. In addition, taking citrate mixtures prevents the formation of uric acid and calcium oxalate stones and improves the solubility of calcium oxalate in urine [21].

The use of citrate drugs in patients with gout, which promote alkalinization of urine and resorption of stones, may be important, especially at the beginning of treatment with allopurinol.

The possibility of using biologically active additives in patients with gout that promote alkalinization of urine and have a uricosuric effect is being considered. Administration of the

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biologically active supplement urisan, the main components of which include various types of ginger, led to a 1.5-fold increase in UA excretion by the kidneys and a significant decrease in the level of uricemia [2].

It is assumed that some glucose-lowering drugs that increase tissue sensitivity to the action of insulin can also contribute to a decrease in serum UA levels. Prescribing metformin (biguanide group) in a daily dose of 1500 mg to patients with gout with type 2 diabetes or pre-diabetes disorders of carbohydrate metabolism led to a decrease in serum sUA levels by more than 20%, and with long-term use - to a decrease in adherence to NSAID therapy and a reduction in the frequency of arthritis attacks [8]. A decrease in serum UA levels has been reported for troglitazone (a group of thiazolidinediones) [24]. A study of the possibility of using another thiazolidinedione, rosiglitazone, in patients with gout in combination with type 2 diabetes is nearing completion. In addition to the beneficial effect on carbohydrate metabolism, preliminary data indicate a significant decrease in serum UA levels after 6 weeks of therapy [1]. Interestingly, there was no effect on renal excretion of UA biguanides and thiazolidinediones. It is assumed that the urate-lowering effect of drugs is based on the ability to reduce the synthesis of UA due to a decrease in the formation of free fatty acids in the liver, the overproduction of which under conditions of insulin resistance leads to hyperuricemia [16].

The optimal selection of therapy for patients with gout, therefore, should be carried out strictly individually, always taking into account the possibility of combining medications, the presence of comorbid conditions, with the maximum use of modern methods of treatment and prevention.

Literature:

1. Елисеев М. С., Барскова В. Г. Влияние росиглитазона на показатели углеводного и уратного обмена у больных подагрой: Тез. докл. IV Всероссийского диабетологического конгресса. — М., 2008. — С. 102.

2. Ильина А. Е., Барскова В. Г. Применение урисана при подагре // Современная ревматология. — 2008. — № 1. — С. 81–83.

3. Кудаева Ф. М., Елисеев М. С., Барскова В. Г. и др. Сравнение скорости наступления анальгетического и противовоспалительного эффектов различных форм нимесулида и диклофенака натрия при подагрическом артрите // Тер. архив. — 2007. — № 5. — С. 35–40.

4. Насонова В. А., Барскова В. Г. Ранние диагностика и лечение подагры — научно обоснованное требование улучшения трудового и жизненного прогноза больных // Научно-практическая ревматология. — 2004. — № 1. — С. 5–7.

5. Allovay J. A., Moriarty M. J., Hoogland Y. T. et al. Comparison of triamcinolone acetonide with indomethacin in the treatment of acute gouty arthritis // J. Rheumatol., 1993; 20: 111–113.

6. De La Serna G., Cadarso C. Fenofibrate decreases plasma fibrinogen, improves lipid profile and reduces uricaemia // Clin. Pharmacol. Ther., 1999; 66: 166–172.

7. Dessein P., Shipton E., Stanwix A. et al. Beneficial effects of weight loss associated with moderate calorie/carbohydrate restriction, and increased proportional intake of protein and unsaturated fat on serum urate and lipoprotein levels in gout: a pilot study // Ann. Rheum. Dis., 2000; 59: 539–543.

8. Eliseev M. S., Barskova V. G., Volkov A. V. et al. The efficacy and safety of metformin treatment in gouty patients with insulin resistence syndrome (pilot case control 6-months study) // Ann. Rheum. Dis., 2005; 64 (suppl. 3): 500.

9. Emmerson B. T. The management of gout // N. Engl. J. Med., 1996; 334: 445–451.

ISSN: 2582-4686 SJIF 2021-3.261,SJIF 2022-2.889
ResearchBib Impact Factor: 8.848 / 2023

10. Feher M. D., Hepburn A. L., Hogarth M. B. et al. Fenofibrate enhances urate reduction in men treated with allopurinol for hyperuricaemia and gout // Rheumatology, 2003; 42: 321–325.

11. Feher M. D., Caslake M., Foxton J. et al. Atherogenic lipoprotein phenotype in 2 diabetes: reversal with fenofibrate // Diabetes Metab. Res. Rev., 1999; 15: 395–399.

12. Fernandez C., Noguera R., Gonzalez J. A. et al. Treatment of acute attacks of gout with small doses of intraarticular triamcinolone acetonide // J. Rheumatol., 1999; 26: 2285–2286.

13. Groff G. D., Franck W. A., Raddatz D. A. Systemic steroid therapy for acute gout: a clinical trial and review of the literature // Seminars Arthritis Rheum., 1990; 19: 329–336.

14. Hollander J. L. Arthritis and Allied Conditions: A Textbook of Rheumatology. 6th ed. Philadelphia: Lea & Febiger, 1960.

15. Huang H. Y., Appel L. J., Choi M. J. et al. The effects of vitamin C supplementation on serum concentrations of uric acid: results of a ra ndomized, controlled trial // Arthritis Rheum., 2005; 52: 1843–1847.

16. Iwatani M., Wasada T., Katsumori K. Troglitazone decreases serum uric acid concentrations in type II diabetic patients and nondiabetic // Diabetologia, 2000; 43: 814–815.

17. Janssens H. J., Janssen M., van de Lisdonk E. H. et al. Use of oral prednisolone or naproxen for the treatment of gout arthritis: a double-blind, randomised equivalence trial // Lancet, 2008; 371: 1854–1860.

18. Mikuls T. R., Farrar J. T., Bilker W. B. et al. Suboptimal physician adherence to quality indicators for the management of gout and asymptomatic hyperuricaemia: results from the UK General Practice Research Database (GPRD) // Rheumatology (Oxford), 2005; 44: 1038–1042.

19. Morris I., Varughese G., Mattingly P. Colchicine in acute gout // BMJ, 2003; 327: 1275–1276.

20. Neogi T., Hunter D. J., Chasson C. E. et al. Frequency of inappropriate management of acute gout attacks // Arthritis & Rheumatism, 2004; 50 (suppl. 9): S339.

21. Pak C. Y., Peterson R. Successful treatment of hyperuricosuric calcium oxalate nephrolithiasis with potassium citrate // Arch. Intern. Med., 1986; 146 (5): 863–867.

22. Singh J. A., Hodges J. S., Toscano J. P. et al. Quality of care for gout in the US needs improvement // Arthritis Rheum., 2007; 57: 822–829.

23. Slesinger N. Management of acute and chronic gouty arthritis // Drugs, 2004; 64 (21): 2399–2416.

24. Tsunoda S., Kamide K., Minami J. et al. Decreases in serum uric acid by amelioration of insulin resistance in overweight hypertensive patients: Effects of a low-energy diet and an insulin-sensitizing agent // Am. J. Hypertens, 2002; 15: 697–701.

25. Wurzner G., Gerster J. C., Chiolero A. et al. Comparative effects of losartan and irbesartan on serum uric acid in hypertensive patients with hyperuricemia and gout // J. Hypertens, 2001; 19: 1855–1860.

26. Wyngaarden J. B., Kelley W. N. (eds). Gout and Hyperuricemia. London: Grune & Stratton, 1976: 233–52.

27. Zhang W., Doherty M., Bardin T. et al. Clinical Studies Including Therapeutics (ESCISIT) EULAR Standing Committee For International Part II: Management. Report of a task force of the EULAR evidence based recommendations for gout // Ann. Rheum. Dis., 2006; 65: 1312–1324.

28. Zhang W., Doherty M., Pascual-Gymez E. et al. EULAR evidence based recommendation for the diagnosis and management of gout // Ann. Rheum. Dis., 2005; 64 (suppl. 3): 501.