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REVIEW ARTICLE

Recovery of patients with gout

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What is not yet known on the issue addressed in the submitted manuscript

Complex recovery within the framework of dietary, pharmacological recommendations for patients with gout.

Research hypothesis

A literature review was conducted to generalize information about dietary and pharmacological recommendations for patients with gout.

The novelty added by manuscript to the already published scientific literature

For the first time, recommendations on dietary, drug treatment for patients with gout are summarized and systematized.

Abstract

Introduction. The incidence and prevalence of gout have increased worldwide in recent decades. Scientists at the Rochester Epidemiology Project (MN, USA) have seen a two-fold increase in the incidence of primary gout (patients without diuretic exposure) over a 20-year period, which ended in 1996. The increase of incidence may be related due to the difficulty and often unsatisfactory treatment options. The aim of the study was to systematize the recommendations on dietary treatment, and medication for patients with gout.

Materials and methods. An analytical, qualitative, and secondary study was performed in the form of a synthesis article. 115 sources were identified and analyzed; from this list, 44 sources were selected according to the impact score during the publication period and according to the level of recommendations.

Results. 44 articles were included. Most studies were small, retrospective analyses performed in single centers, with concerns for bias. Eleven studies (including five randomized controlled trials) reported improved patient outcomes following pharmacological interventions with known efficacy in gout, including allopurinol, prednisolone, NSAIDs and anakinra. Eight studies reported improved outcomes associated with non-pharmacological interventions: inpatient rheumatology consultation and a hospital gout management protocol. No studies to date have prospectively evaluated strategies designed to prevent re-admissions of patients hospitalized for gout flares.

Conclusions. Urate crystals is completely soluble when we can lower the serum level of uric acid to normal values, but this often requires long-term treatment. The early onset of rehabilitation of affected joints helps to reduce the articular inflammatory process, the pain syndrome and it delays the progression of the underlying pathology while improving the quality of life in patients with gout. Further research is needed to enable healthcare providers to individualize and optimize gout treatment strategies, ensuring that patients with gout receive effective, safe, and high-quality care.

Keywords: gout, recovery, management, prevention.

Introduction

Gout is a common metabolic disease manifested by recurrent inflammatory arthritis, which impairs patients' quality of life [1, 2]. In addition, gout and hyperuricemia increase the risk of associated cardiovascular complications and shorten patients' life expectancy [3-6].

Recent ACR guidelines have adopted a treatment strategy focused on sustained reduction of sodium urate crystals

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deposition in tissues [7-9] and long-term maintenance of low plasma urate levels (<6 mg/dL (<0.36 mmol/L)).

Patients with severe gout (presence of tophi, chronic arthropathy, and frequent relapses) are recommended to maintain even lower plasma sodium urate levels (<5 mg/dL (<0.30 mmol/L)). According to the 2012 EULAR guidelines, there is a consensus that urate-reducing drugs should be only used in patients with established gout [10-12].

The aim of the study

To evaluate the dietary and pharmacological recovery options in patients with gout.

Materials and methods

We searched for articles from 2012 to June 2022, using the terms „gout", „diet", „drugs", „topical treatment" and their synonyms in the following databases: PubMed, Cochrane Library, EMBASE, International Pharmaceutical Abstracts, American College of Rheumatology (ACR), European Alliance of Rheumatology Associations (EULAR).

The topics of the papers that we reviewed to write our article were related to the evaluation of the effectiveness of the treatment process (medication, diet therapy, physical therapy) for gout (in remission and exacerbation stages).

Results and discussions

After analysis of the search results, 44 publications were selected, which included randomized controlled trials, examinations and treatment protocols for patients with gout.

Treatment efficacy was determined against the background of registered drugs (allopurinol, febuxostat, glucocorticoids, NSAIDs, and biological therapy). The effectiveness of inpatient and outpatient treatment was evaluated, but unfortunately, to date, there is no data on the rehospitalization of these patients and the effectiveness of the outpatient treatment.

Currently, in addition to the „gold standard" in which monosodium urate crystals (MUC) in synovial fluid or tophus aspirate are identified, there are also methods of non-invasive examination. In 2015, the OMERACT working group proposed guidelines that describe all methods for the diagnosis of gout, which include invasive and non-invasive methods of examination. The main principles in evaluating gout treatment are recommended to consider the dynamics of urate deposition, joint inflammation, and bone erosion [42, 43].

Clinical parameters of monitoring during therapy can be Xray to determine the size of the tophi; ultrasonography, which demonstrates the presence of double contour sign and dual-energy computed tomography (DECT which determines the composition of various tissues as well as helps to detect crystal accumulations in the area of inflammation and allows visualization of the musculoskeletal system) can also be important indicator, which was confirmed by ACR/EULAR systematic literature review on gout imaging [2, 5, 8, 12-16, 27, 38, 42].

The main treatment for both acute and chronic forms of gout are well-known drugs [22-27].

Glucocorticoids. Oral glucocorticoids are often used in patients with a typical gout flare who can take oral medications but have contraindications for nonsteroidal anti-inflammatory drugs [23-25]. The dosing regimen of glucocorticoids is chosen individually for the patient depending on the severity of the flare (duration, dose, and routes of administration). Glucocorticoids in a short course of treatment show high effectiveness and have less risk of side effects compared to other drugs used to treat acute gout. Intra-articular injection of glucocorticoids may be recommended for those who cannot take oral medications. In addition, parenteral glucocorticoids may be indicated among those who cannot take medication orally and are not candidates for intra-articular therapy (e.g., for active inflamed joints >2). Intravenous methylprednisolone (20 mg) may be useful among those with polyarticular involvement, with intravenous access, and without contraindications to glucocorticoids. Intramuscular treatment with triamcinolone acetate (40-60 mg) may be an alternative treatment for patients with similar conditions [23-25].

Nonsteroidal anti-inflammatory drugs (NSAIDs) are very good alternatives to oral glucocorticoids in the treatment of acute gout [24-26]. They are particularly appropriate in the younger patients who do not have a renal, cardiovascular, or active gastrointestinal disease. Naproxen (500 mg twice daily) or indomethacin (50 mg three times daily) are usually used. However, other NSAIDs such as ibuprofen (800 mg three times a day), diclofenac (50 mg twice three times a day), celecoxib (100 mg twice a day), and meloxicam (15 mg a day) are just as effective. The effectiveness of NSAIDs is best seen within the first 48 h of a flare of gout and can be discontinued two to three days after clinical symptoms disappear. However, there are contraindications to the use of NSAIDs: chronic kidney disease (with creatinine clearance <60 ml/min), active gastrointestinal ulcers, cardiovascular disease (especially heart failure), or concomitant treatment with anticoagulants. Side effects from short-term use of NSAIDs are rare but include gastrointestinal distress and impaired renal function [26]. Triamcinolone acetonide (up to 40 mg for large joints and 20 mg for medium joints) or methylprednisolone acetate is commonly used. Although the evidence for its use in the treatment of gout flares is limited, it can be a relatively safe and effective treatment choice.

The prescription of *colchicine* is most often associated with the ineffective use of NSAIDs. Colchicine in doses of 0.5 - 1.0 mg (maximum dose of 2 tablets), with long-term use, has no side effects (including cardiovascular complications) in 90% of patients, which has been proven in numerous randomized trials [27, 28, 32, 33, 40].

Interleukin-1 (IL-1) inhibitors. Although IL-1 inhibitors may be beneficial for some patients with acute gout attacks, they are usually reserved for those for whom other available treatments have failed or for those with contraindications [29]. Anakinra (100 mg daily) is the preferred IL-1 inhibitor for the treatment of acute gout because of its short half-life and relatively modest cost compared with other IL inhibitors. It is administered subcutaneously daily until gout exacerbation symptoms subside and may be useful among patients with an active infection [30].

Allopurinol according to the international guideline is the drug of choice at the beginning of gout treatment [34]. Its dose varies from 100 mg to 800 mg per day. Most often,

patients take a maintenance dose of 100 mg and a treatment dose of 300 mg per day. If gout is resistant, the dosage can increase, but so does the frequency of side effects, which include skin lesions (rash), kidney impairment (acute kidney injury), intestinal problems (diarrhea) and vascular system disorders (eosinophilia, thrombocytopenia) [20, 34, 35].

Febuxostat, like allopurinol, is a xanthine oxidase inhibitor and according to the latest recommendations is prescribed to patients with hyperuricemia and gout who cannot tolerate allopurinol [21, 36]. The daily dosage of febuxostat varies from 40 to 120 mg per day, preferably prescribed in the evening after meals. To prevent flares of gout during the first weeks of treatment, this drug is prescribed in combination with colchicine or NSAIDs. Side effects develop are less frequent compared allopurinol and efficacy is much higher. However, the following side effects have been described: increased transaminases and allergic manifestations [36-38].

Probenecid is the drug of choice in patients with gout who have impaired excretion of uric acid through kidney. Probenecid improves excretion, but in renal impairment, this drug is limited because it can worsen the renal function [39].

In addition to drug therapy, there are now dietary and lifestyle recommendations by the American College of Rheumatology and EULAR aimed at preventing metabolic disorders and reducing serum urate levels. The guidelines recommend a balanced diet rich in vegetables with adequate amounts of plant and animal foods and lifestyle modifications for patients with gout. The American College of Rheumatology has created multiple nonpharmacological dietary recommendations. These recommendations include general advices regarding diet and lifestyle modifications [13, 18, 41].

The 2021 EULAR guideline for lifestyle improvement in people with gout described nutritional supplements that can be included in patients' diets. New methods of dietary modification in gout patients are constantly being sought, particularly the use of supplements and vitamin C, but this has not proven to improve the quality of life of gout patients. The evidence for dietary impact on gout has been rated as low or very low [15-17, 19].

Lifestyle changes that include losing weight, stopping excessive alcohol consumption, and stopping purine-rich foods, reduce urate levels in patients with gout. Nevertheless, sometimes this is not enough, and patients are recommended to initiate pharmacological therapy. In gout, clear indications have been developed for the initiation of pharmacological therapy to reduce urate: frequent (2 yearly) flares of gout; the presence of a chronic form and the presence of a tophaceous form of gout [31, 41].

Conclusions

(1) Crystal urate deposition is fully reversible in cases where we can lower the serum level of uric acid to normal values, often requiring long-term treatment.

(2) The early rehabilitation of affected joints helps to reduce more effectively the articular inflammatory process, the pain syndrome, and it delays the progression of the underlying pathology and improves the quality of life of patients with gout.

(3) Further research is needed to enable healthcare providers to individualize and optimize gout treatment strategies, ensuring that patients with gout receive effective, safe and high-quality care.

Declaration of conflicting interests

Nothing to declare.

Authors' contribution

All authors contributed equally to the research, data analysis, and writing of the manuscript. All authors read and approved the final article.

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