

Comparative Assessment of Adherence Parameters to Urate-Lowering Therapy in Patients With Gout

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Abstract: *The study aims to evaluate adherence to urate-lowering therapy (ULT) among patients with gout, to identify factors influencing adherence, and to compare the efficacy and tolerability of allopurinol and febuxostat. A total of 60 patients with a verified gout diagnosis were examined. Adherence was assessed using the Morisky–Green scale. The results demonstrated that more than half of the patients had low or moderate adherence, associated with insufficient awareness and irregular follow-up. Febuxostat showed higher treatment adherence and better achievement of target serum uric acid levels compared with allopurinol. Improving patient education and monitoring is essential for effective gout management.*

Key words: *gout, urate-lowering therapy, febuxostat, allopurinol.*

Introduction

Gout is a chronic systemic inflammatory disease belonging to the group of microcrystalline arthritis, characterized by the deposition of monosodium urate (MSU) crystals in various body tissues, predominantly in the joints, leading to the development of an inflammatory response [4]. The disease occurs in individuals with hyperuricemia, which is caused by environmental and/or genetic factors. According to the clinical guidelines of the Ministry of Health of the Russian Federation (2020), gout is defined as a chronic systemic tophaceous disease manifested by recurrent episodes of acute arthritis, the formation of tophi, and renal involvement, including nephrolithiasis and chronic urate nephropathy [1].

Epidemiological data indicate a steady increase in the incidence of gout over recent decades, which is associated with increased life expectancy, changes in dietary habits, and the growing prevalence of metabolic disorders such as obesity, arterial hypertension, and diabetes mellitus [7]. Population-based studies conducted in the United Kingdom and Germany have shown that gout is the most common cause of inflammatory arthritis in men over 30 years of age, accounting for 1.4% of the overall morbidity. In the Russian Federation, the prevalence of gout is approximately 0.3% among the adult population [2].

Modern approaches to gout therapy are based on clinical recommendations developed by the Association of Rheumatologists of Russia (2019), the European Alliance of Associations for Rheumatology (EULAR, 2016–2018), and the American College of Rheumatology (ACR, 2020). The most recent guidelines, published in Arthritis Care & Research in May 2020, outline the principles of acute gout management, indications for urate-lowering therapy (ULT), and recommendations on lifestyle modification and pharmacotherapy in patients with comorbidities [5].

The key therapeutic goal is to achieve and maintain serum uric acid levels within the target range — below 360 $\mu\text{mol/L}$, and below 300 $\mu\text{mol/L}$ in the presence of tophi. Achieving target uric acid levels helps prevent recurrent attacks and slow disease progression. This is accomplished through the use of urate-lowering agents [8]. According to ACR, EULAR, and ARR guidelines, effective management requires selecting an optimal urate-lowering agent (e.g., allopurinol or febuxostat), ensuring regular intake, appropriate dose titration, and laboratory monitoring [3].

The general principles of management state that every patient with gout should be well informed about the pathophysiology of the disease, the availability of effective treatment methods, and the importance of lifelong urate reduction to maintain serum uric acid below the target level (360 $\mu\text{mol/L}$). Each patient should receive lifestyle recommendations including weight reduction (if necessary), smoking cessation, abstinence from alcohol (especially beer and spirits) and sugar-sweetened beverages, avoidance of overeating and excessive intake of meat and seafood, and encouragement of low-fat dairy product consumption [6]. Regular physical activity should be recommended. Every patient should be systematically screened for comorbid conditions and cardiovascular risk factors, including chronic kidney disease (CKD), ischemic heart disease (IHD), heart failure, stroke, peripheral arterial atherosclerosis, obesity, hyperlipidemia, hypertension, and type 2 diabetes mellitus, with their prevention and management considered integral components of gout treatment [10].

However, the effectiveness of therapy largely depends on patient adherence to prescribed treatment. Adherence to gout therapy remains one of the key challenges in clinical practice, exerting a significant impact on therapeutic outcomes and disease prognosis [12]. Adherence is defined as the extent to which a patient's behavior corresponds to the healthcare provider's recommendations. In rheumatology, including gout, adherence rates vary widely, ranging from 30% to 60% according to different studies. Various tools and questionnaires are used to assess adherence, most commonly the Morisky–Green Adherence Scale (4- or 8-item version). Poor adherence may be attributed to insufficient patient awareness, fear of adverse effects, distrust in treatment, or lack of immediate therapeutic results. Additionally, regular follow-up, effective physician–patient communication, and patient perception of disease severity play a crucial role [9].

Comparative studies demonstrate that adherence is higher when using medications with a more pronounced and rapid therapeutic effect, fewer adverse reactions, and within the framework of educational programs. Studies conducted in Russia have shown a low level of adherence to urate-lowering therapy among gout patients [13]. In one study, only 39.1% of patients took urate-lowering drugs regularly, and 70.4% of them did not achieve target serum uric acid levels. Factors contributing to poor adherence include lack of patient education about the disease and the need for long-term therapy, irregular medical follow-up, drug side effects, and the complexity of dietary compliance [11].

Particularly relevant is the evaluation of adherence among patients receiving different urate-lowering agents, as tolerability, efficacy, and safety profiles may significantly influence compliance. Allopurinol has long been the drug of choice, but its use may be limited by adverse effects, especially in patients with comorbidities. Meanwhile, febuxostat, a newer-generation agent, has demonstrated high efficacy in reducing uric acid levels and a better tolerability profile, particularly in patients with renal impairment [15]. Studies have shown that febuxostat is associated with higher adherence compared to allopurinol — 63% versus 36%, respectively — likely due to its superior tolerability and fewer side effects. To improve adherence, patient education programs aimed at raising awareness of the disease and the importance of long-term treatment, as well as consistent follow-up and medical support, are essential [14].

The present study aimed to perform a comparative assessment of adherence parameters to urate-lowering therapy in patients with gout receiving allopurinol and febuxostat, taking into account clinical and demographic characteristics and factors influencing treatment compliance.

Materials and methods. The study included 60 patients with a verified diagnosis of gout who sought specialized care at the Arthrology Department of the multidisciplinary clinic of the Tashkent Medical Academy for therapy adjustment.

The diagnosis of gout was established according to the ACR/EULAR classification criteria (2015). Hyperuricemia was diagnosed when serum uric acid (UA) exceeded $360 \mu\text{mol/L}$, in accordance with EULAR (2006) recommendations.

All patients received urate-lowering therapy, primarily allopurinol, which was initiated at a dose of 100 mg/day with subsequent dose escalation by 100 mg every 2–3 weeks until the target uric acid level was achieved. In cases of insufficient therapeutic response at the maximally tolerated allopurinol dose and/or the occurrence of adverse effects, patients were switched to febuxostat at an initial dose of 80 mg/day, which could be increased to 120 mg/day if necessary.

To prevent gout flares during urate-lowering therapy initiation, nonsteroidal anti-inflammatory drugs (NSAIDs) at minimally effective doses or colchicine 0.5 mg/day were prescribed. In cases of contraindications or intolerance to these agents, glucocorticoids (GCs) were administered at a dose of 7.5 mg/day (prednisone equivalent).

After six months of therapy, adherence was assessed using the Morisky–Green Medication Adherence Scale, consisting of four dichotomous (yes/no) questions. Responses were scored as 0 or 1 points, respectively, with total scores interpreted as follows:

- 4 points — high adherence;
- 3 points — moderate adherence;
- ≤ 2 points — low adherence.

All participants underwent a comprehensive clinical and laboratory evaluation, including anthropometric measurements, general and biochemical blood tests (glucose, lipid profile, creatinine, urea, C-reactive protein [CRP], and uric acid), as well as instrumental examinations such as electrocardiography (ECG), echocardiography, renal and joint ultrasound, and joint radiography.

Additionally, adherence to non-pharmacological measures and lifestyle modification was evaluated.

Results. Among the 60 patients enrolled in the study, men predominated (71%), while women accounted for 29%. The mean age was 54.3 ± 8.3 years, with the majority aged 42–60 years. The mean disease duration was 4.57 ± 1.35 years. The frequency of gout flares ranged from 1 to 4 episodes per year (mean = 2.23 ± 0.32). The first metatarsophalangeal joint was most commonly affected (91%), followed by the ankle joints (62%). The knee, small hand joints, and elbow joints were less frequently involved — 34%, 22%, and 6%, respectively.

The serum uric acid (SUA) level ranged from 392 to $775 \mu\text{mol/L}$, averaging $504.8 \pm 83.7 \mu\text{mol/L}$. Comorbidities were detected in 86% of patients, with arterial hypertension (76%) being the most prevalent.

Adverse reactions to allopurinol were observed in 9 patients (15%), including pruritus ($n = 4$), urticaria ($n = 2$), and elevated transaminase levels ($n = 3$). Dietary assessment revealed that 82% of patients did not adhere to dietary recommendations or violated them systematically. Irregular medical follow-up and absence of prior urate-lowering therapy were identified in 64% of participants.

Regarding concomitant therapy, ACE inhibitors were used by 60% of patients, calcium channel blockers by 32%, and β -blockers by 18%. Thiazide diuretics were taken by 48%, and acetylsalicylic acid by 70%.

After six months of treatment, 68% of patients continued urate-lowering therapy, and target SUA levels were achieved in 60% of them. The effectiveness was higher in the febuxostat group (76%) compared to the allopurinol group (48%) (after three months — 57% and 48%, respectively).

The analysis of adherence according to the Morisky–Green scale demonstrated that among patients receiving allopurinol, high adherence was observed in 25%, moderate in 40%, and low in 35% of cases. In contrast, in the febuxostat group, high adherence was recorded in over 50% of patients, and no treatment discontinuations were reported.

Regarding lifestyle modification, adherence was high in 30%, moderate in 40%, and low in 30% of patients. Readiness for therapy adjustment was high in 38%, moderate in 45%, and low in 17% of participants. The obtained results demonstrate significant differences in patient adherence to urate-lowering therapy depending on the medication used. The higher adherence in the febuxostat group may be explained by its better tolerability, lower incidence of side effects, and higher clinical efficacy in achieving target uric acid levels. Patient awareness and compliance with dietary and non-pharmacological recommendations remain insufficient despite their importance for disease control. The high prevalence of comorbidities, particularly hypertension, and the frequent use of medications that increase uric acid levels necessitate a comprehensive and individualized therapeutic approach.

Overall, the findings of this study are consistent with previously published national and international data, emphasizing the crucial role of adherence in achieving effective urate-lowering therapy and preventing gout flares.

Conclusion. The results of this study demonstrate that patient adherence to urate-lowering therapy remains suboptimal, despite the proven efficacy of pharmacological treatment in preventing gout progression. Low and moderate adherence rates were observed in more than half of the patients, which was associated with insufficient awareness, irregular follow-up, and neglect of dietary recommendations.

Among urate-lowering drugs, febuxostat showed higher treatment adherence and efficacy compared to allopurinol, which may be due to its better tolerability and more predictable urate-lowering effect.

Given the chronic nature of gout, the presence of multiple comorbidities, and the long-term character of therapy, comprehensive measures are required to improve adherence. These include structured patient education, individualized therapy selection, and regular monitoring of treatment effectiveness.

Improving adherence to urate-lowering therapy should be viewed as a key component of gout management, directly influencing the achievement of target serum uric acid levels and long-term disease control.

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