Journal of Ecohumanism
2024
Volume: 3, No: 8, pp. 12670 – 12684
ISSN: 2752-6798 (Print) | ISSN 2752-6801 (Online)
https://ecohumanism.co.uk/joe/ecohumanism
DOI: https://doi.org/10.62754/joe.v3i8.5995

Hyperuricemia and Gout: An Overview of Common Medical Condition

Raed Muawwadh Aifan Alfazi[1], Talal Nasser Almutairi[2], Ibrahim Saad Mohammed Al-Dosari[3], Rasmi Obaid Almutairi[4], Afnan Mohammed Aleid[5], Shatha Ali Ahmed Ammash[6], Muhanna Safar Musleh Almutari[7], Ghaniyah Mohammed Hussien Madkhaly[8]

Abstract

Hyperuricemia, defined as elevated serum uric acid levels (>6 mg/dL in women, >7 mg/dL in men), affects approximately 38 million Americans, with rising global prevalence due to Westernized diets and lifestyles. While often asymptomatic, hyperuricemia is associated with gout, nephrolithiasis, and systemic conditions like hypertension, metabolic syndrome, and cardiovascular disease. It results from increased uric acid production, decreased renal excretion, or a combination of both.This article provides a comprehensive overview of hyperuricemia, focusing on its etiology, pathophysiology, clinical manifestations, and management strategies, with an emphasis on gout and nephrolithiasis.The review synthesizes current literature on hyperuricemia, including its epidemiology, mechanisms, diagnostic evaluation, and treatment options. It also examines the role of dietary, genetic, and pharmacological factors in disease progression and management.Hyperuricemia is primarily managed through lifestyle modifications and pharmacological interventions. First-line treatment includes xanthine oxidase inhibitors like allopurinol, while uricosuric agents and recombinant uricase drugs are reserved for refractory cases. Dietary education, particularly a low-purine, low-fructose diet, is crucial for prevention and management. Complications such as gout, nephrolithiasis, and chronic kidney disease require tailored interventions, including urate-lowering therapy and urinary alkalinization.Hyperuricemia is a multifactorial condition with significant implications for gout, nephrolithiasis, and systemic health. Effective management requires a combination of lifestyle changes, pharmacological therapy, and patient education. While asymptomatic hyperuricemia often does not require treatment, symptomatic cases necessitate individualized care to prevent complications and improve quality of life.

Keywords: *Hyperuricemia, Gout, Nephrolithiasis, Allopurinol, Urate-Lowering Therapy, Xanthine Oxidase Inhibitors.*

Introduction

Hyperuricemia is characterized by elevated serum uric acid levels, typically exceeding 6 mg/dL in women and 7 mg/dL in men. This condition affects approximately 38 million Americans, with its prevalence rising globally as developing nations adopt Westernized diets and lifestyles [1]. While many individuals with hyperuricemia remain asymptomatic, the long-term implications for cardiovascular health, renal function, and overall morbidity remain unclear [1]. Hyperuricemia arises from either increased uric acid production, reduced excretion, or a combination of both mechanisms. Dietary purines contribute to roughly one-third of the body's daily uric acid production, with the remainder synthesized endogenously [1]. Elevated uric acid levels can also result from accelerated purine breakdown in conditions of high cell turnover, such as hemolysis, rhabdomyolysis, or tumor lysis, as well as impaired excretion due to genetic disorders, renal insufficiency, or metabolic syndrome [1]. Approximately two-thirds of uric acid is excreted via the kidneys, while the remaining one-third is eliminated through the gastrointestinal (GI) tract. However, these proportions may vary depending on medication use or dysfunction in renal or GI systems [1]. Although 85% to 90% of individuals with hyperuricemia are asymptomatic, elevated uric acid levels in the blood or urine can lead to clinical manifestations such as gout or nephrolithiasis [1]. Additionally, hyperuricemia and hyperuricosuria have been associated with a range of other disorders, including metabolic syndrome,

[1] Ksa, Ministry of Health, King Fahd General Hospital in Jeddah
[2] Ksa, Ministry of Health, Al-Muznib General Hospital
[3] Ksa, Ministry of Health, Wadi Al Dawasir General Hospital.
[4] Ksa, Ministry of Health, Prince Sultan Military Medical City
[5] Ksa, Ministry of Health, King Saud Medical City
[6] Ksa, Ministry of Health, Baisha General Hospital
[7] Ksa, Ministry of Health, Al-Quwayiyah General Hospital
[8] Ksa, Ministry of Health, Al Haqla Primary Health Care Center

Journal of Ecohumanism
2024
Volume: 3, No: 8, pp. 12670 – 12684
ISSN: 2752-6798 (Print) | ISSN 2752-6801 (Online)
https://ecohumanism.co.uk/joe/ecohumanism
DOI: https://doi.org/10.62754/joe.v3i8.5995

diabetes mellitus, cardiovascular disease, hypertension, atherosclerosis, obesity, and chronic renal disease [2][3][4][5][6]. These associations highlight the potential systemic impact of hyperuricemia beyond its direct clinical symptoms, underscoring the need for further research into its broader health implications.

Etiology

Hyperuricemia can result from either overproduction or decreased excretion of uric acid, often influenced by dietary, metabolic, and pharmacological factors.

Uric Acid Overproduction

A purine-rich diet, including alcohol (particularly beer), red meats (e.g., beef, lamb, veal), organ meats, and certain fish and shellfish (e.g., anchovies, tuna, shrimp), contributes to elevated uric acid levels [7][8]. Fructose, especially from high-fructose corn syrup and sugary sodas, exacerbates hyperuricemia by promoting uric acid production through hepatic metabolism via the aldolase reductase pathway. This is particularly concerning in children and adolescents, as it is linked to obesity [7][8]. Genetic disorders such as hypoxanthine-guanine phosphoribosyltransferase (HPRT) deficiency and phosphoribosylpyrophosphate (PRPP) synthetase overactivity also lead to uric acid overproduction. Additionally, conditions involving high cell turnover, such as lymphoproliferative or myeloproliferative diseases, tumor lysis, hemolysis, rhabdomyolysis, and extreme exercise, can increase uric acid levels [9].

Decreased Uric Acid Excretion

Reduced renal excretion of uric acid is another major cause of hyperuricemia. This can occur due to acute or chronic kidney disease, acidosis (e.g., lactic acidosis, ketoacidosis), hypovolemia, or the use of medications such as diuretics, niacin, pyrazinamide, and cyclosporine [9]. Other contributing factors include endocrine disorders (e.g., hyperparathyroidism, hypothyroidism), genetic conditions (e.g., Bartter syndrome, Down syndrome), and toxins like lead or beryllium [9].

Diuretic-Induced Hyperuricemia

Thiazide and loop diuretics are particularly associated with dose-dependent hyperuricemia and an increased risk of gout. These medications enhance renal uric acid reabsorption, either directly or through volume depletion, raising serum uric acid levels [10][11][12]. The relative risk of gout increases by nearly 80% with diuretic use [15]. For patients with gout flares, alternative antihypertensives such as angiotensin II receptor blockers (e.g., losartan) or angiotensin-converting enzyme inhibitors are recommended [16][17][18][19][20][21][22]. While xanthine oxidase inhibitors like allopurinol are commonly used to treat diuretic-induced gout, asymptomatic hyperuricemia typically does not require intervention [10][12][13][14]. In summary, hyperuricemia arises from a complex interplay of dietary, genetic, metabolic, and pharmacological factors. Understanding these underlying causes is essential for effective management and prevention of associated complications such as gout and metabolic disorders.

Epidemiology

Hyperuricemia is a common condition, affecting up to 21% of the general population and 25% of hospitalized patients, with many individuals remaining asymptomatic for years before clinical manifestations such as gout appear [23][24]. Elevated uric acid levels can persist for 10 to 15 years before symptoms develop, highlighting the condition's often silent progression [23][24]. Importantly, hyperuricemia is not inherently pathological, as it is highly prevalent in the general population and asymptomatic in 90% to 95% of cases [25]. The global incidence of hyperuricemia is rising, particularly in economically advantaged nations and developing countries adopting Westernized diets and lifestyles [23][26]. Certain populations, such as Pacific Islanders, exhibit particularly high rates of hyperuricemia [27]. Gender differences are also notable, with men experiencing higher rates of hyperuricemia than women. This disparity is attributed to the protective effects of estrogen, which reduces uric acid levels in premenopausal women. However, women become more susceptible to hyperuricemia after menopause, when estrogen levels decline [28][29].

Journal of Ecohumanism
2024
Volume: 3, No: 8, pp. 12670 – 12684
ISSN: 2752-6798 (Print) | ISSN 2752-6801 (Online)
https://ecohumanism.co.uk/joe/ecohumanism
DOI: https://doi.org/10.62754/joe.v3i8.5995

These epidemiological trends underscore the influence of dietary, lifestyle, and hormonal factors on the prevalence of hyperuricemia. As the condition continues to rise globally, understanding its distribution and risk factors is crucial for developing targeted prevention and management strategies.

Pathophysiology

Clinical Manifestations

Hyperuricemia underlies several clinical conditions, most notably gout and uric acid nephrolithiasis. Gout, a metabolic disorder characterized by uric acid accumulation in blood and tissues, results in the precipitation of urate monohydrate crystals within joints. These crystals tend to form in acidic and cold environments, often affecting peripheral joints such as the big toe. Gout exhibits a male predominance, with a 4:1 male-to-female ratio [24]. Uric acid nephrolithiasis occurs when uric acid precipitates in the urine, primarily due to acidic urine, hypovolemia, and hyperuricosuria (defined as uric acid excretion exceeding 800 mg/day in men and 750 mg/day in women). Uric acid stones account for 5% to 10% of all urinary stones and may contain calcium components [30]. Hyperuricemia is also linked to hypertension, independent of comorbidities like obesity and diabetes. Studies suggest that even within normal uric acid ranges (≥5.3 mg/dL in men and ≥4.3 mg/dL in women), serum uric acid levels correlate with hypertension. Proposed mechanisms include renin-angiotensin system activation, oxidative stress, endothelial inflammation, endothelin-1 activation, and reduced nitrous oxide production [29][31][33]. Obesity and hyperuricemia are closely associated, with visceral adipose tissue promoting uric acid production and renal tubular dysfunction reducing uric acid excretion. While urate-lowering drugs have shown potential in reducing hypertension in adolescents, their adverse effects limit their use for this purpose [31]. Hyperuricemia is also associated with cardiac and renal diseases, though the causal relationship remains unclear due to overlapping risk factors. Notably, urate-lowering therapy has not been shown to prevent chronic kidney disease (CKD) and may worsen renal outcomes, making it unsuitable for primary prevention [34][35].

Mechanisms of Hyperuricemia

Uric acid, a byproduct of purine metabolism, circulates as urate at physiological pH. Purine metabolism primarily occurs in the liver, but tissues containing xanthine oxidase (e.g., cardiac, pulmonary) also contribute. Approximately two-thirds of uric acid is excreted by the kidneys, while the remainder is eliminated via the intestines. In the kidneys, urate is filtered, secreted, and largely reabsorbed in the proximal tubule. Unlike other mammals, humans lack functional uricase, an enzyme that converts urate to the more soluble allantoin, leading to higher uric acid levels [36]. Purine-rich diets, endogenous purine production, and conditions causing high cell turnover (e.g., rhabdomyolysis, hemolysis, tumor lysis) accelerate uric acid production. Beer, in particular, significantly increases uric acid levels due to its high purine content [37]. Genetic factors, such as phosphoribosylpyrophosphate (PRPP) synthetase overactivity and hypoxanthine-guanine phosphoribosyltransferase (HPRT) deficiency, also contribute to hyperuricemia [38][39].

Urate Transport in the Kidney

Impaired renal urate excretion is responsible for hyperuricemia in 90% of cases, involving decreased glomerular filtration, reduced tubular secretion, and enhanced reabsorption. The proximal tubule reabsorbs uric acid via the uric acid transporter 1 (URAT1), which can be stimulated by organic acids (e.g., lactate, acetoacetate), medications (e.g., niacin, pyrazinamide), and hypovolemia [2][41][42]. URAT1 inhibitors are effective uricosuric agents for treating hyperuricemia. Urate is then transported into the renal interstitium by the GLUT9 transporter [42]. In summary, hyperuricemia arises from complex interactions between dietary, genetic, and metabolic factors, with significant implications for gout, nephrolithiasis, hypertension, and cardiorenal diseases. Understanding these mechanisms is crucial for effective management and prevention of hyperuricemia-related complications.

Journal of Ecohumanism
2024
Volume: 3, No: 8, pp. 12670 – 12684
ISSN: 2752-6798 (Print) | ISSN 2752-6801 (Online)
https://ecohumanism.co.uk/joe/ecohumanism
DOI: https://doi.org/10.62754/joe.v3i8.5995

Histopathology

Hyperuricemia manifests histopathologically through the precipitation of monosodium urate crystals, which can be observed in various tissues. In joints, these crystals appear as classic "needle-shaped" structures when synovial fluid is aspirated and examined under polarized light microscopy. This finding is a hallmark of gouty arthritis, where urate crystals deposit in joint spaces, triggering inflammation and pain. In the urinary system, uric acid crystals form when urine pH is acidic (typically below 5.5). These crystals often exhibit a yellowish-brown color and can take on rhomboid shapes or cluster to form rosette-like patterns. The presence of such crystals in urine is indicative of hyperuricosuria and is a risk factor for the development of uric acid nephrolithiasis. These histopathological features provide critical diagnostic clues for hyperuricemia-related conditions, such as gout and uric acid kidney stones, and underscore the importance of microscopic examination in clinical evaluation.

History and Physical

History

Hyperuricemia itself is not a definitive indication for treatment, despite its associations with diabetes, hypertension, and cardiovascular disease. Most individuals with elevated uric acid levels remain asymptomatic and do not require long-term therapy. A detailed history should include dietary habits, particularly the consumption of purine-rich foods (e.g., red meat, seafood) and alcohol, as these are significant contributors to hyperuricemia. Additionally, a thorough review of the patient's medical history and current medications is essential to identify factors that may impair renal urate excretion or increase uric acid production. The two most common clinical manifestations of hyperuricemia are gout and uric acid nephrolithiasis. Patients with gout often report acute episodes of red, hot, and swollen joints, with the big toe (podagra) being the most frequently affected site [43]. In cases of uric acid nephrolithiasis, patients may present with renal colic, characterized by severe, acute flank, abdominal, or back pain that radiates to the groin. Other symptoms include hematuria, dysuria, nausea, vomiting, and urinary tract symptoms such as fever, cloudy urine, and frequent urination [44].

Physical Exam

There are no specific physical exam findings for hyperuricemia unless the patient presents with complications such as gout or nephrolithiasis. During an acute gout attack, the affected joint (commonly the big toe) appears erythematous, warm, and swollen. Gout typically involves a single joint at a time and is often described as causing "pain out of proportion to exam." In cases of uric acid nephrolithiasis, physical findings are generally nonspecific, though costovertebral angle tenderness may be present upon palpation. In summary, while hyperuricemia is often asymptomatic, a detailed history and physical exam are crucial for identifying associated conditions such as gout and nephrolithiasis. These findings guide further diagnostic evaluation and management.

Evaluation

Laboratory Studies

The evaluation of hyperuricemia begins with laboratory studies to confirm elevated uric acid levels of serum. Normal values are typically less than 6.8 mg/dL, with levels of 8 mg/dL or higher diagnostic of hyperuricemia. Gender-specific variations may apply. If nephrolithiasis is suspected, urinalysis may reveal microscopic hematuria, uric acid crystals, and a low urinary pH (<5.5). A 24-hour urine collection for uric acid excretion is recommended, with levels optimally below 600 mg/day on a low-purine diet. Excretion exceeding 800 mg/day indicates hyperuricosuria but does not distinguish between overproduction or underexcretion of uric acid. Additional laboratory tests, including a complete blood count (CBC) with differential, comprehensive metabolic panel (CMP), lipid profile, hemoglobin A1c (HgA1c), calcium, and phosphate levels, help identify underlying conditions such as malignancy, sickle cell disease, diabetes, and metabolic syndrome. These tests provide a broader context for hyperuricemia and guide further

Journal of Ecohumanism
2024
Volume: 3, No: 8, pp. 12670 – 12684
ISSN: 2752-6798 (Print) | ISSN 2752-6801 (Online)
https://ecohumanism.co.uk/joe/ecohumanism
DOI: https://doi.org/10.62754/joe.v3i8.5995

management. Imaging studies may also be warranted. Joint x-rays can evaluate unexplained swelling, though they are not required to diagnose gout. For suspected uric acid nephrolithiasis, renal ultrasound or non-contrast CT scans are preferred, as intravenous contrast can obscure the presence of stones.

Procedures

Joint aspiration is a key diagnostic procedure for gout. Synovial fluid analysis under polarized microscopy can identify needle-shaped, negatively birefringent uric acid crystals, confirming the diagnosis. This procedure is particularly useful in differentiating gout from other causes of joint inflammation. In summary, the evaluation of hyperuricemia involves a combination of laboratory tests, imaging studies, and, when necessary, joint aspiration. These tools help confirm the diagnosis, assess underlying causes, and guide appropriate management strategies.

Treatment / Management

Most patients with hyperuricemia are asymptomatic and do not require medical therapy, except for those undergoing cytolytic therapy for malignancy to prevent tumor lysis syndrome [45][46][47][48]. This recommendation is based on the cost and potential adverse effects of medications, which generally outweigh the benefits in asymptomatic individuals. However, treatment is indicated for patients with recurrent gout attacks, gouty bone erosion, structural joint injury, polyarticular disease, hyperuricosuric nephrolithiasis, or tophi. The American College of Rheumatology recommends treatment for patients experiencing two or more gout attacks annually, though a lower threshold may apply based on flare severity and patient preference [49].

Acute Gout Management

Colchicine is commonly used to treat acute gout flares. It works by binding tubulin, preventing microtubule formation, and exerting anti-inflammatory and anti-fibrotic effects [50][51][52]. Patients initiating uric acid-lowering therapy should also receive prophylactic colchicine to reduce the risk of acute gout flares. Gradually introducing uric acid-lowering medications can further minimize flare risk [53].

Uric Acid-Lowering Medications

There are three classes of uric acid-lowering medications: uricosuric agents, xanthine oxidase inhibitors, and recombinant uricases. Five drugs are FDA-approved in the U.S.: allopurinol, febuxostat, probenecid, rasburicase, and pegloticase.

Uricosuric Agents: These medications increase renal and urinary excretion of uric acid by inhibiting the URAT1 transporter in renal proximal tubular cells, reducing reabsorption and lowering serum uric acid levels [54]. They are unsuitable for patients with hyperuricosuric nephrolithiasis and are most effective when urinary uric acid excretion is less than 800 mg/day.

- Probenecid: A second-line therapy for gout, probenecid inhibits URAT1 and other anion transporters, increasing uric acid excretion. It is less potent than xanthine oxidase inhibitors and is often used with colchicine for gout prophylaxis. However, it has numerous drug interactions and is relatively contraindicated in patients with advanced chronic kidney disease (CKD) [57][58][59].

- Benzbromarone: A potent URAT1 inhibitor used in some countries but not approved in the U.S. or Europe due to hepatotoxicity risks [60][61].

- Dotinurad: A highly selective URAT1 inhibitor available in Japan, showing efficacy comparable to benzbromarone and febuxostat. It is under evaluation for approval in the U.S. and Europe [63][64][65][66][67].

Journal of Ecohumanism
2024
Volume: 3, No: 8, pp. 12670 – 12684
ISSN: 2752-6798 (Print) | ISSN 2752-6801 (Online)
https://ecohumanism.co.uk/joe/ecohumanism
DOI: https://doi.org/10.62754/joe.v3i8.5995

- Lesinurad: Another URAT1 inhibitor that significantly increases urinary uric acid excretion. Production was discontinued in 2019 due to business considerations [68][69][70].

Adjunctive Agents: Losartan, atorvastatin, and fenofibrate have mild uricosuric effects and can be considered in patients with hypertension or hyperlipidemia [16][55][56]. Treatment for hyperuricemia is primarily indicated for symptomatic patients, particularly those with recurrent gout or complications. Uricosuric agents, xanthine oxidase inhibitors, and recombinant uricases are the mainstay of therapy, with colchicine often used for acute flares and prophylaxis. Careful consideration of patient-specific factors and potential adverse effects is essential for optimal management.

Xanthine Oxidase Inhibitors

Xanthine oxidase inhibitors block the hepatic conversion of xanthine to uric acid, reducing serum uric acid levels. Unlike uric acid, xanthine is non-toxic, does not cause gout, and is more soluble in urine, making it a safer metabolic byproduct [71]. These inhibitors are a cornerstone in the management of hyperuricemia and its complications.

Allopurinol

Allopurinol, a purine-based structural analog of hypoxanthine, is the preferred xanthine oxidase inhibitor for treating symptomatic hyperuricemia, gout, and hyperuricosuric nephrolithiasis [71][73]. It is also used prophylactically to prevent gouty arthritis and chemotherapy-induced hyperuricemia. Allopurinol is cost-effective and widely used, but treatment is typically lifelong. Compared to febuxostat, allopurinol offers superior renal protection, making it a safer option for patients with kidney disease [74]. For tumor lysis syndrome prophylaxis, allopurinol should be initiated 2-3 days before chemotherapy and continued for up to a week post-treatment [71]. Despite its efficacy, allopurinol use is often suboptimal, with many patients with gout either underdosed or not receiving long-term therapy [75]. Allopurinol can cause allergic reactions in up to 25% of patients, ranging from mild rashes and itching to severe hypersensitivity syndrome. The latter, though rare (1:1,000 patients), carries a mortality rate of 20%-25% and presents with Stevens-Johnson syndrome, toxic epidermal necrolysis, renal failure, hepatic injury, and eosinophilia [76][77][78]. Individuals of Han Chinese, Thai, Korean, and African American descent are at higher risk due to the HLA-B*58:01 allele, and genetic testing is recommended before initiating therapy in these populations [79]. Patients with renal failure are also at increased risk, which can be mitigated by starting at very low doses (<50 mg or <1.5 mg per mL/min of creatinine clearance) and titrating gradually [80].

Febuxostat

Febuxostat, a non-purine-based xanthine oxidase inhibitor, is an alternative for patients who cannot tolerate or fail allopurinol therapy. It is effective at standard dosages and can be used in patients with severe renal impairment (creatinine clearance as low as 15 mL/min) [81]. However, febuxostat has been associated with a 34% higher risk of cardiovascular mortality and a 22% higher overall mortality compared to allopurinol, leading to FDA restrictions on its use in 2019 [82].

Topiroxostat

Topiroxostat, another non-purine xanthine oxidase inhibitor, is currently approved only in Japan. Unlike allopurinol and febuxostat, it is unaffected by renal failure, making it suitable for patients with chronic kidney disease. Approved in 2013, post-marketing studies involving nearly 4,500 patients over five years have demonstrated its efficacy and safety, with no significant adverse drug reactions reported [84]. In summary, xanthine oxidase inhibitors like allopurinol, febuxostat, and topiroxostat are effective in managing hyperuricemia and its complications. Allopurinol remains the first-line therapy due to its cost-effectiveness and renal protective effects, though careful monitoring for hypersensitivity is essential. Febuxostat is a viable alternative but carries cardiovascular risks, while topiroxostat offers promise for patients with renal impairment, pending broader approval.

Journal of Ecohumanism
2024
Volume: 3, No: 8, pp. 12670 – 12684
ISSN: 2752-6798 (Print) | ISSN 2752-6801 (Online)
https://ecohumanism.co.uk/joe/ecohumanism
DOI: https://doi.org/10.62754/joe.v3i8.5995

Recombinant Uricase Drugs

Recombinant uricase drugs are reserved for patients with chronic gout refractory to standard therapies, such as xanthine oxidase inhibitors or uricosuric agents. Approximately 2% of gout patients fall into this category, characterized by intractable hyperuricemia, recurrent gout attacks despite therapy, or persistent subcutaneous tophi unresponsive to maximum dosages of conventional treatments [85][86].

Mechanism of Action

Uricase drugs enzymatically convert uric acid into allantoin, a water-soluble, non-toxic metabolite that is easily excreted by the kidneys. Unlike humans and higher primates, most mammals naturally produce uricase, which keeps their uric acid levels low. Recombinant uricase drugs do not alter uric acid production or excretion but are highly effective in reducing serum and urinary uric acid levels [87].

Rasburicase

Rasburicase, the first recombinant uricase, was FDA-approved in 2002 for managing hyperuricemia in cancer patients at risk of tumor lysis syndrome due to chemotherapy. It is particularly effective in patients with leukemia, lymphoma, or solid tumors, where rapid cell lysis can cause dangerously high uric acid levels. Rasburicase acts quickly (within 4 hours) and can prevent the need for hemodialysis. However, its use is limited by its short half-life (16-21 hours), high cost, and the rapid development of antidrug antibodies [88][89][90][91][92][93].

Pegloticase:

Pegloticase, a pegylated recombinant uricase, was FDA-approved in 2010 for refractory chronic gout. It was developed by attaching polyethylene glycol (PEG) to rasburicase, extending its half-life to 8.5 days and reducing immunogenicity. Despite this modification, pegloticase remains highly immunogenic, often requiring concomitant methotrexate to suppress immune reactions [85][96][97][98]. Pegloticase has demonstrated significant efficacy in clinical trials, reducing serum uric acid levels, resolving tophi, alleviating joint pain and swelling, and even lowering blood pressure in hyperuricemic patients without affecting kidney function [85][100]. However, its use is associated with infusion reactions and the development of antidrug antibodies, which can diminish its effectiveness. These issues can be mitigated by discontinuing the drug at the first sign of reduced efficacy or adverse reactions and by using immunosuppressive agents like methotrexate [85][101]. Combining pegloticase with methotrexate has shown improved response rates (71% vs. 38.5%) and reduced infusion reactions and antibody production compared to pegloticase alone [95][101][102]. However, gout flares are common (88%) during initial therapy, and the drug is costly. Anaphylaxis has also been reported, necessitating premedication with antihistamines and corticosteroids before each infusion [95].

Administration and Precautions

Before starting pegloticase, folic acid supplementation should begin at least four weeks prior, and other uric acid-lowering medications should be discontinued. Serum uric acid levels must be monitored before each infusion. Pegloticase is contraindicated in patients with glucose-6-phosphate dehydrogenase deficiency and is not recommended for asymptomatic hyperuricemia [95]. In summary, recombinant uricase drugs like rasburicase and pegloticase are highly effective for refractory hyperuricemia and chronic gout. While rasburicase is primarily used for tumor lysis syndrome, pegloticase offers a promising option for refractory gout, though its use requires careful monitoring and often adjunctive immunosuppressive therapy to manage immunogenicity and adverse effects.

Treatment Summary

The management of hyperuricemia and its associated conditions involves a stepwise approach tailored to the patient's specific clinical presentation and tolerance to medications.

Journal of Ecohumanism
2024
Volume: 3, No: 8, pp. 12670 – 12684
ISSN: 2752-6798 (Print) | ISSN 2752-6801 (Online)
https://ecohumanism.co.uk/joe/ecohumanism
DOI: https://doi.org/10.62754/joe.v3i8.5995

First-Line Therapy

- *Allopurinol* is the preferred initial treatment for hyperuricemia. It is effective, cost-efficient, and suitable for most patients, including those with gout or hyperuricosuric nephrolithiasis. Dosage adjustments are made to achieve optimal serum uric acid levels (<6 mg/dL) or 24-hour urinary uric acid excretion (<600 mg/day) [71][103][104].

Second-Line Therapy

- *Febuxostat* is recommended if allopurinol is ineffective, not tolerated, or contraindicated due to a genetic risk of allopurinol hypersensitivity syndrome (e.g., HLA-B*58:01 allele). It is particularly useful in patients with renal impairment but carries a higher risk of cardiovascular mortality compared to allopurinol [71][103][104].

Uric Acid Nephrolithiasis

- Treatment focuses on reducing urinary acidity (target pH >6.5) using potassium citrate or sodium bicarbonate, rather than solely addressing hyperuricosuria. Increasing urinary volume is also recommended to prevent stone formation [103][105].

Hyperuricosuric Calcium Nephrolithiasis

- Management involves optimizing urinary citrate levels (goal: 500-600 mg/day) with potassium citrate and reducing urinary uric acid excretion, typically with allopurinol [104][106].

Gout Prophylaxis

- *Probenecid*, often combined with colchicine, can be used for gout prophylaxis. However, it is not recommended for patients with uric acid nephrolithiasis or hyperuricosuria (>800 mg urinary uric acid/24 hours) due to the risk of exacerbating stone formation [103].

Refractory Hyperuricemia

- *Pegloticase* is reserved for patients with chronic, symptomatic hyperuricemia refractory to other treatments. It is highly effective but requires careful monitoring for infusion reactions and often adjunctive immunosuppressive therapy (e.g., methotrexate) to mitigate immunogenicity [95].

Tumor Lysis Syndrome

- *Rasburicase* is the treatment of choice for acute hyperuricemia due to tumor lysis syndrome. It rapidly lowers uric acid levels and prevents renal complications but is not indicated for gout management [36]. Treatment for hyperuricemia and its complications is individualized based on the underlying cause, patient tolerance, and clinical response. Allopurinol remains the cornerstone of therapy, with febuxostat, probenecid, pegloticase, and rasburicase serving as alternatives for specific scenarios. Adjunctive measures, such as urinary alkalinization and volume expansion, are critical for managing nephrolithiasis.

Differential Diagnosis

Hyperuricemia itself is asymptomatic, but its associated conditions, such as gout and nephrolithiasis, must be differentiated from other disorders with similar presentations. Key differential diagnoses include:

- Rheumatoid arthritis: Presents with joint inflammation but lacks urate crystals.

Journal of Ecohumanism
2024
Volume: 3, No: 8, pp. 12670 – 12684
ISSN: 2752-6798 (Print) | ISSN 2752-6801 (Online)
https://ecohumanism.co.uk/joe/ecohumanism
DOI: https://doi.org/10.62754/joe.v3i8.5995

- Pseudogout (calcium pyrophosphate deposition disease): Mimics gout but involves calcium pyrophosphate crystals.
- Other forms of arthritis: Includes septic or reactive arthritis.
- Hypothyroidism: Can cause joint pain and swelling.
- Alcoholic ketoacidosis: May present with metabolic disturbances resembling gout.
- Non-urate nephrolithiasis: Includes calcium oxalate or phosphate stones.
- Hemolytic anemia: Can cause elevated uric acid due to increased cell turnover.
- Hyperparathyroidism: Associated with hypercalcemia and nephrolithiasis.
- Malignancies: May lead to hyperuricemia due to tumor lysis or increased cell turnover.

Prognosis

Most individuals with hyperuricemia remain asymptomatic and do not require treatment. Symptomatic patients, such as those with gout or nephrolithiasis, can be effectively managed with medications. While hyperuricemia is associated with an increased risk of hypertension, metabolic syndrome, diabetes, cardiovascular disease, and renal disease, a definitive causal relationship has not been established. As a result, urate-lowering therapy is not routinely recommended for asymptomatic hyperuricemia.

Complications

Hyperuricemia is primarily associated with complications related to gout and nephrolithiasis, but it can also lead to other systemic issues. Potential complications include:

- Bone loss: Due to chronic inflammation and joint damage.
- Chronic kidney disease (CKD): Resulting from urate crystal deposition or nephrolithiasis.
- Gout: Characterized by recurrent, painful joint inflammation.
- Hypertension: Linked to hyperuricemia through mechanisms like oxidative stress and endothelial dysfunction.
- Joint damage and deformity: From chronic tophaceous gout.
- Tophi deposits: Subcutaneous urate crystal accumulations.
- Loss of mobility: Due to severe joint involvement.
- Nephrolithiasis: Including uric acid and calcium oxalate stones.
- Restricted range of motion: From joint inflammation and damage.
- Skin rashes: Often related to medication side effects.
- Allopurinol hypersensitivity syndrome: A severe, potentially life-threatening reaction to allopurinol, characterized by rash, organ failure, and systemic inflammation. Hyperuricemia must be differentiated from other conditions with similar symptoms, such as gout or nephrolithiasis. While

Journal of Ecohumanism
2024
Volume: 3, No: 8, pp. 12670 – 12684
ISSN: 2752-6798 (Print) | ISSN 2752-6801 (Online)
https://ecohumanism.co.uk/joe/ecohumanism
DOI: https://doi.org/10.62754/joe.v3i8.5995

most patients remain asymptomatic, those with symptoms can be effectively treated. However, hyperuricemia is associated with long-term risks of hypertension, metabolic disorders, and renal disease, though urate-lowering therapy is not standard for asymptomatic individuals. Complications primarily involve gout and nephrolithiasis but can extend to systemic issues like bone loss, joint damage, and severe drug reactions.

Deterrence and Patient Education

Patients with symptomatic hyperuricemia, such as those with gout, uric acid stones, or hyperuricosuric calcium nephrolithiasis, should receive prophylactic treatment, typically starting with allopurinol. For patients at risk of flares, especially those with renal failure, treatment should begin at a low dose and be gradually titrated upward to minimize adverse effects [80]. Dietary education is crucial, emphasizing a low-purine, low-salt, and low-fructose diet. Regular consultations with a dietitian can help patients adhere to these dietary modifications and improve outcomes.

Other Issues

Key considerations in managing hyperuricemia include:

- *Medication Optimization*: Many patients with gout are underdosed on uric acid-lowering medications. Doses higher than the standard 300 mg/day of allopurinol may be necessary to achieve target serum uric acid levels (<6 mg/dL) [75].

- *Allopurinol Hypersensitivity*: This rare but potentially fatal reaction is more common in African Americans and individuals of Chinese, Korean, and Thai descent due to the HLA-B*58:01 allele. Genetic testing is recommended before initiating allopurinol in these populations, and the drug should be avoided in those testing positive [59][79]. Patients with chronic kidney disease (CKD) are also at higher risk and should start with low doses, titrating upward every 2-4 weeks [78][80].

- *Pegloticase Use:* Pegloticase, used for refractory gout, should generally be administered with methotrexate to reduce immunogenicity. Patients should discontinue other uric acid-lowering drugs and begin folic acid supplementation at least four weeks prior. Premedication with steroids and antihistamines is required before each infusion [95].

- *Chronic Kidney Disease*: Xanthine oxidase inhibitors (e.g., allopurinol, febuxostat) are preferred in CKD patients, though starting doses may need adjustment. Among uricosuric agents, only benzbromarone (not available in the U.S. or Europe) is suitable for significant CKD [95].

- *Diuretic-Induced Hyperuricemia*: Patients with diuretic-induced hyperuricemia and gout can be treated with losartan or allopurinol but do not require therapy if asymptomatic [95].

Enhancing Healthcare Team Outcomes

Hyperuricemia is a multifactorial condition best managed by an interprofessional team, including internists, primary care providers, endocrinologists, urologists, rheumatologists, and oncologists. Most patients are asymptomatic and do not require treatment, as the cost and potential adverse effects of medications often outweigh the benefits. Uric acid-lowering therapy is primarily indicated for patients undergoing cytolytic therapy for malignancy to prevent tumor lysis syndrome [107][108]. The prognosis for benign hyperuricemia is generally good, though patients with malignancy may develop complications such as gout or renal impairment. Effective management relies on patient education, appropriate medication use, and regular monitoring to prevent complications and optimize outcomes. Collaborative care ensures that patients receive comprehensive, individualized treatment tailored to their specific needs.

Journal of Ecohumanism
2024
Volume: 3, No: 8, pp. 12670 – 12684
ISSN: 2752-6798 (Print) | ISSN 2752-6801 (Online)
https://ecohumanism.co.uk/joe/ecohumanism
DOI: https://doi.org/10.62754/joe.v3i8.5995

Conclusion

Hyperuricemia is a common metabolic condition with significant implications for joint, renal, and cardiovascular health. While many individuals remain asymptomatic, elevated uric acid levels can lead to debilitating conditions such as gout and nephrolithiasis, as well as contribute to systemic disorders like hypertension, metabolic syndrome, and chronic kidney disease. The pathophysiology of hyperuricemia involves a complex interplay of dietary, genetic, and pharmacological factors, with uric acid overproduction and impaired renal excretion being the primary mechanisms. Management of hyperuricemia is tailored to the patient's clinical presentation and underlying causes. First-line therapy typically involves xanthine oxidase inhibitors like allopurinol, which are effective, cost-efficient, and suitable for most patients. For those who cannot tolerate allopurinol or have refractory disease, alternatives such as febuxostat, uricosuric agents, and recombinant uricase drugs like pegloticase are available. However, these treatments require careful monitoring due to potential adverse effects, including hypersensitivity reactions and cardiovascular risks. Dietary and lifestyle modifications play a crucial role in managing hyperuricemia. Patients are advised to adopt a low-purine, low-fructose diet, reduce alcohol consumption, and maintain adequate hydration to prevent uric acid crystallization. Regular consultations with dietitians can help patients adhere to these recommendations and improve outcomes. Complications of hyperuricemia, such as gout and nephrolithiasis, require targeted interventions. Gout management often involves colchicine for acute flares and prophylactic urate-lowering therapy to prevent recurrence. For nephrolithiasis, treatment focuses on urinary alkalinization and volume expansion to reduce stone formation. Despite advances in treatment, challenges remain, particularly in managing asymptomatic hyperuricemia and addressing the long-term risks of cardiovascular and renal disease. While urate-lowering therapy is not routinely recommended for asymptomatic individuals, ongoing research is needed to clarify the role of hyperuricemia in systemic health and identify optimal management strategies. In conclusion, hyperuricemia is a multifaceted condition that demands a comprehensive, patient-centered approach. By combining pharmacological therapy, lifestyle modifications, and patient education, healthcare providers can effectively manage hyperuricemia, prevent complications, and improve the quality of life for affected individuals. Collaborative care involving internists, rheumatologists, dietitians, and other specialists is essential to achieving these goals.

References

Yip K, Cohen RE, Pillinger MH. Asymptomatic hyperuricemia: is it really asymptomatic? Curr Opin Rheumatol. 2020 Jan;32(1):71-79.

Barkas F, Elisaf M, Liberopoulos E, Kalaitzidis R, Liamis G. Uric acid and incident chronic kidney disease in dyslipidemic individuals. Curr Med Res Opin. 2018 Jul;34(7):1193-1199.

Song D, Zhao X, Wang F, Wang G. A brief review of urate transporter 1 (URAT1) inhibitors for the treatment of hyperuricemia and gout: Current therapeutic options and potential applications. Eur J Pharmacol. 2021 Sep 15;907:174291.

Bhole V, Choi JW, Kim SW, de Vera M, Choi H. Serum uric acid levels and the risk of type 2 diabetes: a prospective study. Am J Med. 2010 Oct;123(10):957-61

Borghi C, Rosei EA, Bardin T, Dawson J, Dominiczak A, Kielstein JT, Manolis AJ, Perez-Ruiz F, Mancia G. Serum uric acid and the risk of cardiovascular and renal disease. J Hypertens. 2015 Sep;33(9):1729-41; discussion 1741.

Borghi C. The role of uric acid in the development of cardiovascular disease. Curr Med Res Opin. 2015;31 Suppl 2:1-2.

Sanchez-Lozada LG, Andres-Hernando A, Garcia-Arroyo FE, Cicerchi C, Li N, Kuwabara M, Roncal-Jimenez CA, Johnson RJ, Lanaspa MA. Uric acid activates aldose reductase and the polyol pathway for endogenous fructose and fat production causing development of fatty liver in rats. J Biol Chem. 2019 Mar 15;294(11):4272-4281.

Russo E, Leoncini G, Esposito P, Garibotto G, Pontremoli R, Viazzi F. Fructose and Uric Acid: Major Mediators of Cardiovascular Disease Risk Starting at Pediatric Age. Int J Mol Sci. 2020 Jun 24;21(12)

Dong H, Xu Y, Zhang X, Tian S. Visceral adiposity index is strongly associated with hyperuricemia independently of metabolic health and obesity phenotypes. Sci Rep. 2017 Aug 18;7(1):8822.

Kahn AM. Effect of diuretics on the renal handling of urate. Semin Nephrol. 1988 Sep;8(3):305-

Carlsen JE, Køber L, Torp-Pedersen C, Johansen P. Relation between dose of bendrofluazide, antihypertensive effect, and adverse biochemical effects. BMJ. 1990 Apr 14;300(6730):975-8.

Hagos Y, Stein D, Ugele B, Burckhardt G, Bahn A. Human renal organic anion transporter 4 operates as an asymmetric urate transporter. J Am Soc Nephrol. 2007 Feb;18(2):430-9.

Weinman EJ, Eknoyan G, Suki WN. The influence of the extracellular fluid volume on the tubular reabsorption of uric acid. J Clin Invest. 1975 Feb;55(2):283-91.

Steele TH, Oppenheimer S. Factors affecting urate excretion following diuretic administration in man. Am J Med. 1969 Oct;47(4):564-74.

Journal of Ecohumanism
2024
Volume: 3, No: 8, pp. 12670 – 12684
ISSN: 2752-6798 (Print) | ISSN 2752-6801 (Online)
https://ecohumanism.co.uk/joe/ecohumanism
DOI: https://doi.org/10.62754/joe.v3i8.5995

Choi HK, Atkinson K, Karlson EW, Curhan G. Obesity, weight change, hypertension, diuretic use, and risk of gout in men: the health professionals follow-up study. Arch Intern Med. 2005 Apr 11;165(7):742-8.

Würzner G, Gerster JC, Chiolero A, Maillard M, Fallab-Stubi CL, Brunner HR, Burnier M. Comparative effects of losartan and irbesartan on serum uric acid in hypertensive patients with hyperuricaemia and gout. J Hypertens. 2001 Oct;19(10):1855-60.

Weinberger MH. Influence of an angiotensin converting-enzyme inhibitor on diuretic-induced metabolic effects in hypertension. Hypertension. 1983 Sep-Oct;5(5 Pt 2):III132-8.

Shahinfar S, Simpson RL, Carides AD, Thiyagarajan B, Nakagawa Y, Umans JG, Parks JH, Coe FL. Safety of losartan in hypertensive patients with thiazide-induced hyperuricemia. Kidney Int. 1999 Nov;56(5):1879-85.

Soffer BA, Wright JT, Pratt JH, Wiens B, Goldberg AI, Sweet CS. Effects of losartan on a background of hydrochlorothiazide in patients with hypertension. Hypertension. 1995 Jul;26(1):112-7.

Manolis AJ, Grossman E, Jelakovic B, Jacovides A, Bernhardi DC, Cabrera WJ, Watanabe LA, Barragan J, Matadamas N, Mendiola A, Woo KS, Zhu JR, Mejia AD, Bunt T, Dumortier T, Smith RD. Effects of losartan and candesartan monotherapy and losartan/hydrochlorothiazide combination therapy in patients with mild to moderate hypertension. Losartan Trial Investigators. Clin Ther. 2000 Oct;22(10):1186-203.

Tikkanen I, Omvik P, Jensen HA. Comparison of the angiotensin II antagonist losartan with the angiotensin converting enzyme inhibitor enalapril in patients with essential hypertension. J Hypertens. 1995 Nov;13(11):1343-51.

Buscemi S, Buscemi C, Borzì AM, Cosentino L, Rosafio G, Randazzo C, Colomba D, Di Raimondo D, Pluchinotta FR, Parrinello G. Metabolic and Cardiovascular Effects of Switching Thiazides to Amlodipine in Hypertensive Patients With and Without Type 2 Diabetes (the Diuretics and Diabetes Control Study). Metab Syndr Relat Disord. 2020 Mar;18(2):110-118.

Li L, Zhang Y, Zeng C. Update on the epidemiology, genetics, and therapeutic options of hyperuricemia. Am J Transl Res. 2020;12(7):3167-3181.

Williams LA. The History, Symptoms, Causes, Risk Factors, Types, Diagnosis, Treatments, and Prevention of Gout, Part 2. Int J Pharm Compd. 2019 Jan-Feb;23(1):14-21.

Campion EW, Glynn RJ, DeLabry LO. Asymptomatic hyperuricemia. Risks and consequences in the Normative Aging Study. Am J Med. 1987 Mar;82(3):421-6.

Singh G, Lingala B, Mithal A. Gout and hyperuricaemia in the USA: prevalence and trends. Rheumatology (Oxford). 2019 Dec 01;58(12):2177-2180.

Gosling AL, Matisoo-Smith E, Merriman TR. Hyperuricaemia in the Pacific: why the elevated serum urate levels? Rheumatol Int. 2014 Jun;34(6):743-57.

Wu X, You C. The biomarkers discovery of hyperuricemia and gout: proteomics and metabolomics. PeerJ. 2023;11:e14554.

Yokokawa H, Fukuda H, Suzuki A, Fujibayashi K, Naito T, Uehara Y, Nakayama A, Matsuo H, Sanada H, Jose PA, Miwa Y, Hisaoka T, Isonuma H. Association Between Serum Uric Acid Levels/Hyperuricemia and Hypertension Among 85,286 Japanese Workers. J Clin Hypertens (Greenwich). 2016 Jan;18(1):53-9.

Paquot N, Scheen AJ. [DPP-4 or SGLT2 inhibitor added to metformin alone in type 2 diabetes]. Rev Med Suisse. 2017 Aug 23;13(571):1410-1415.

Tian S, Liu Y, Xu Y, Feng A. Does obesity modify the epidemiological association between hyperuricemia and the prevalence of hypertension among Northern Chinese community-dwelling people? A Chinese population-based study. BMJ Open. 2019 Nov 21;9(11):e031803

Borghi C, Agabiti-Rosei E, Johnson RJ, Kielstein JT, Lurbe E, Mancia G, Redon J, Stack AG, Tsioufis KP. Hyperuricaemia and gout in cardiovascular, metabolic and kidney disease. Eur J Intern Med. 2020 Oct;80:1-11.

Ejaz AA, Johnson RJ, Shimada M, Mohandas R, Alquadan KF, Beaver TM, Lapsia V, Dass B. The Role of Uric Acid in Acute Kidney Injury. Nephron. 2019;142(4):275-283.

Hassan W, Shrestha P, Sumida K, Thomas F, Sweeney PL, Potukuchi PK, Rhee CM, Streja E, Kalantar-Zadeh K, Kovesdy CP. Association of Uric Acid-Lowering Therapy With Incident Chronic Kidney Disease. JAMA Netw Open. 2022 Jun 01;5(6):e2215878.

Rincon-Choles H, Jolly SE, Arrigain S, Konig V, Schold JD, Nakhoul G, Navaneethan SD, Nally JV, Rothberg MB. Impact of Uric Acid Levels on Kidney Disease Progression. Am J Nephrol. 2017;46(4):315-322.

Yakupova SP. Gout. New opportunities of diagnosis and treatment. Ter Arkh. 2018 May 11;90(5):88

Shiraishi H, Une H. The effect of the interaction between obesity and drinking on hyperuricemia in Japanese male office workers. J Epidemiol. 2009;19(1):12-6.

de Brouwer APM, Christodoulou J. Phosphoribosylpyrophosphate Synthetase Superactivity. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Amemiya A, editors. GeneReviews® [Internet]. University of Washington, Seattle; Seattle (WA): Sep 23, 2008.

Dewulf JP, Marie S, Nassogne MC. Disorders of purine biosynthesis metabolism. Mol Genet Metab. 2022 Jul;136(3):190-198.

Dalbeth N, Gosling AL, Gaffo A, Abhishek A. Gout. Lancet. 2021 May 15;397(10287):1843-1855.

Zhao Z, Liu J, Yuan L, Yang Z, Kuang P, Liao H, Luo J, Feng H, Zheng F, Chen Y, Wu T, Guo J, Cao Y, Yang Y, Lin C, Zhang Q, Chen J, Pang J. Discovery of novel benzbromarone analogs with improved pharmacokinetics and benign toxicity profiles as antihyperuricemic agents. Eur J Med Chem. 2022 Nov 15;242:114682.

Bobulescu IA, Moe OW. Renal transport of uric acid: evolving concepts and uncertainties. Adv Chronic Kidney Dis. 2012 Nov;19(6):358-71.

Shi, C., Zhou, Z., Chi, X., Xiu, S., Yi, C., Jiang, Z., ... & Liu, Z. (2023). Recent advances in gout drugs. European Journal of Medicinal Chemistry, 245, 114890.

Ordon, M., Bota, S. E., Kang, Y., & Welk, B. (2023). The Incidence and Risk Factors for Emergency Department Imaging in Acute Renal Colic. Journal of Endourology, 37(7), 834-842.

Journal of Ecohumanism
2024
Volume: 3, No: 8, pp. 12670 – 12684
ISSN: 2752-6798 (Print) | ISSN 2752-6801 (Online)
https://ecohumanism.co.uk/joe/ecohumanism
DOI: https://doi.org/10.62754/joe.v3i8.5995

Yang N, Yu Y, Zhang A, Estill J, Wang X, Zheng M, Zhou Q, Zhang J, Luo X, Qian C, Mao Y, Wang Q, Yang Y, Chen Y. Reporting, presentation and wording of recommendations in clinical practice guideline for gout: a systematic analysis. BMJ Open. 2019 Jan 29;9(1):e024315.

Alqarni NA, Hassan AH. Knowledge and practice in the management of asymptomatic hyperuricemia among primary health care physicians in Jeddah, Western Region of Saudi Arabia. Saudi Med J. 2018 Dec;39(12):1218-1225.

Engel B, Schacher S, Weckbecker K, Stausberg A, Gräff I. [Acute Gout in Emergency Admissions - Patient Characteristics and Adherence of Care Processes to Current Guidelines]. Z Orthop Unfall. 2018 Dec;156(6):653-661.

Buzas R, Tautu OF, Dorobantu M, Ivan V, Lighezan D. Serum uric acid and arterial hypertension-Data from Sephar III survey. PLoS One. 2018;13(7):e0199865.

FitzGerald JD, Dalbeth N, Mikuls T, Brignardello-Petersen R, Guyatt G, Abeles AM, Gelber AC, Harrold LR, Khanna D, King C, Levy G, Libbey C, Mount D, Pillinger MH, Rosenthal A, Singh JA, Sims JE, Smith BJ, Wenger NS, Bae SS, Danve A, Khanna PP, Kim SC, Lenert A, Poon S, Qasim A, Sehra ST, Sharma TSK, Toprover M, Turgunbaev M, Zeng L, Zhang MA, Turner AS, Neogi T. 2020 American College of Rheumatology Guideline for the Management of Gout. Arthritis Rheumatol. 2020 Jun;72(6):879-895.

Sadiq NM, Robinson KJ, Terrell JM. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): May 29, 2023. Colchicine.

Terkeltaub RA. Clinical practice. Gout. N Engl J Med. 2003 Oct 23;349(17):1647-55.

Leung YY, Yao Hui LL, Kraus VB. Colchicine--Update on mechanisms of action and therapeutic uses. Semin Arthritis Rheum. 2015 Dec;45(3):341-50.

Doherty M, Jenkins W, Richardson H, Sarmanova A, Abhishek A, Ashton D, Barclay C, Doherty S, Duley L, Hatton R, Rees F, Stevenson M, Zhang W. Efficacy and cost-effectiveness of nurse-led care involving education and engagement of patients and a treat-to-target urate-lowering strategy versus usual care for gout: a randomised controlled trial. Lancet. 2018 Oct 20;392(10156):1403-1412.

Enomoto A, Kimura H, Chairoungdua A, Shigeta Y, Jutabha P, Cha SH, Hosoyamada M, Takeda M, Sekine T, Igarashi T, Matsuo H, Kikuchi Y, Oda T, Ichida K, Hosoya T, Shimokata K, Niwa T, Kanai Y, Endou H. Molecular identification of a renal urate anion exchanger that regulates blood urate levels. Nature. 2002 May 23;417(6887):447-52.

Milionis HJ, Kakafika AI, Tsouli SG, Athyros VG, Bairaktari ET, Seferiadis KI, Elisaf MS. Effects of statin treatment on uric acid homeostasis in patients with primary hyperlipidemia. Am Heart J. 2004 Oct;148(4):635-40.

Feher MD, Hepburn AL, Hogarth MB, Ball SG, Kaye SA. Fenofibrate enhances urate reduction in men treated with allopurinol for hyperuricaemia and gout. Rheumatology (Oxford). 2003 Feb;42(2):321-5.

Granados JC, Bhatnagar V, Nigam SK. Blockade of Organic Anion Transport in Humans After Treatment With the Drug Probenecid Leads to Major Metabolic Alterations in Plasma and Urine. Clin Pharmacol Ther. 2022 Sep;112(3):653-664.

LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. National Institute of Diabetes and Digestive and Kidney Diseases; Bethesda (MD): Jul 10, 2020. Probenecid.

Khanna D, Fitzgerald JD, Khanna PP, Bae S, Singh MK, Neogi T, Pillinger MH, Merill J, Lee S, Prakash S, Kaldas M, Gogia M, Perez-Ruiz F, Taylor W, Lioté F, Choi H, Singh JA, Dalbeth N, Kaplan S, Niyyar V, Jones D, Yarows SA, Roessler B, Kerr G, King C, Levy G, Furst DE, Edwards NL, Mandell B, Schumacher HR, Robbins M, Wenger N, Terkeltaub R., American College of Rheumatology. 2012 American College of Rheumatology guidelines for management of gout. Part 1: systematic nonpharmacologic and pharmacologic therapeutic approaches to hyperuricemia. Arthritis Care Res (Hoboken). 2012 Oct;64(10):1431-46.

LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. National Institute of Diabetes and Digestive and Kidney Diseases; Bethesda (MD): Sep 5, 2017. Benzbromarone.

Lee MH, Graham GG, Williams KM, Day RO. A benefit-risk assessment of benzbromarone in the treatment of gout. Was its withdrawal from the market in the best interest of patients? Drug Saf. 2008;31(8):643-65.

Reinders MK, van Roon EN, Jansen TL, Delsing J, Griep EN, Hoekstra M, van de Laar MA, Brouwers JR. Efficacy and tolerability of urate-lowering drugs in gout: a randomised controlled trial of benzbromarone versus probenecid after failure of allopurinol. Ann Rheum Dis. 2009 Jan;68(1):51-6.

Hosoya T, Furuno K, Kanda S. A non-inferiority study of the novel selective urate reabsorption inhibitor dotinurad versus febuxostat in hyperuricemic patients with or without gout. Clin Exp Nephrol. 2020 Mar;24(Suppl 1):71-79.

Hosoya T, Sano T, Sasaki T, Fushimi M, Ohashi T. Dotinurad versus benzbromarone in Japanese hyperuricemic patient with or without gout: a randomized, double-blind, parallel-group, phase 3 study. Clin Exp Nephrol. 2020 Mar;24(Suppl 1):62-70.

Iqbal A, Iqbal K, Farid E, Ishaque A, Hasanain M, Bin Arif T, Arshad Ali S, Rathore SS, Malik M. Efficacy and Safety of Dotinurad in Hyperuricemic Patients With or Without Gout: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Cureus. 2021 Apr 12;13(4):e14428.

Omura K, Miyata K, Kobashi S, Ito A, Fushimi M, Uda J, Sasaki T, Iwanaga T, Ohashi T. Ideal pharmacokinetic profile of dotinurad as a selective urate reabsorption inhibitor. Drug Metab Pharmacokinet. 2020 Jun;35(3):313-320.

Kuriyama S. Dotinurad: a novel selective urate reabsorption inhibitor as a future therapeutic option for hyperuricemia. Clin Exp Nephrol. 2020 Mar;24(Suppl 1):1-5.

Wu JY, Chang YT, Lin YC, Lee CH, Loh EW, Wu MY, Chang YS, Tam KW. Efficacy and Safety of Lesinurad in Patients with Hyperuricemia Associated with Gout: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Pharmacotherapy. 2018 Nov;38(11):1106-1119.

Cicero AFG, Fogacci F, Kuwabara M, Borghi C. Therapeutic Strategies for the Treatment of Chronic Hyperuricemia: An Evidence-Based Update. Medicina (Kaunas). 2021 Jan 10;57(1)

Journal of Ecohumanism
2024
Volume: 3, No: 8, pp. 12670 – 12684
ISSN: 2752-6798 (Print) | ISSN 2752-6801 (Online)
https://ecohumanism.co.uk/joe/ecohumanism
DOI: https://doi.org/10.62754/joe.v3i8.5995
Fam AG. Difficult gout and new approaches for control of hyperuricemia in the allopurinol-allergic patient. Curr Rheumatol Rep. 2001 Feb;3(1):29-35.
Qurie A, Preuss CV, Musa R. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Jun 26, 2023. Allopurinol.
Aziz N, Jamil RT. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Jul 25, 2023. Biochemistry, Xanthine Oxidase.
Rundles RW. The development of allopurinol. Arch Intern Med. 1985 Aug;145(8):1492-503.
Park S, Lee JP, Kim DK, Kim YS, Lim CS. Superior effect of allopurinol compared to febuxostat on the retardation of chronic kidney disease progression. PLoS One. 2022;17(2):e0264627.
Sarawate CA, Patel PA, Schumacher HR, Yang W, Brewer KK, Bakst AW. Serum urate levels and gout flares: analysis from managed care data. J Clin Rheumatol. 2006 Apr;12(2):61-5.
Singer JZ, Wallace SL. The allopurinol hypersensitivity syndrome. Unnecessary morbidity and mortality. Arthritis Rheum. 1986 Jan;29(1):82-7.
Hande KR, Noone RM, Stone WJ. Severe allopurinol toxicity. Description and guidelines for prevention in patients with renal insufficiency. Am J Med. 1984 Jan;76(1):47-56.
Yaseen W, Auguste B, Zipursky J. Allopurinol hypersensitivity syndrome. CMAJ. 2023 Apr 03;195(13):E483.
Quach C, Galen BT. HLA-B*5801 Testing to Prevent Allopurinol Hypersensitivity Syndrome: A Teachable Moment. JAMA Intern Med. 2018 Sep 01;178(9):1260-1261.
Stamp LK, Taylor WJ, Jones PB, Dockerty JL, Drake J, Frampton C, Dalbeth N. Starting dose is a risk factor for allopurinol hypersensitivity syndrome: a proposed safe starting dose of allopurinol. Arthritis Rheum. 2012 Aug;64(8):2529-36.
Becker MA, Schumacher HR, Wortmann RL, MacDonald PA, Eustace D, Palo WA, Streit J, Joseph-Ridge N. Febuxostat compared with allopurinol in patients with hyperuricemia and gout. N Engl J Med. 2005 Dec 08;353(23):2450-61.
White WB, Saag KG, Becker MA, Borer JS, Gorelick PB, Whelton A, Hunt B, Castillo M, Gunawardhana L., CARES Investigators. Cardiovascular Safety of Febuxostat or Allopurinol in Patients with Gout. N Engl J Med. 2018 Mar 29;378(13):1200-1210.
Xie, H., Hu, N., Pan, T., Wu, J. C., Yu, M., & Wang, D. C. (2023). Effectiveness and safety of different doses of febuxostat compared with allopurinol in the treatment of hyperuricemia: a meta-analysis of randomized controlled trials. BMC Pharmacology and Toxicology, 24(1), 79.
Ishikawa T, Maeda T, Hashimoto T, Nakagawa T, Ichikawa K, Sato Y, Kanno Y. Long-Term Safety and Effectiveness of the Xanthine Oxidoreductase Inhibitor, Topiroxostat in Japanese Hyperuricemic Patients with or Without Gout: A 54-week Open-label, Multicenter, Post-marketing Observational Study. Clin Drug Investig. 2020 Sep;40(9):847-859.
Schlesinger N, Lipsky PE. Pegloticase treatment of chronic refractory gout: Update on efficacy and safety. Semin Arthritis Rheum. 2020 Jun;50(3S):S31-S38.
Richette P, Doherty M, Pascual E, Barskova V, Becce F, Castañeda-Sanabria J, Coyfish M, Guillo S, Jansen TL, Janssens H, Lioté F, Mallen C, Nuki G, Perez-Ruiz F, Pimentao J, Punzi L, Pywell T, So A, Tausche AK, Uhlig T, Zavada J, Zhang W, Tubach F, Bardin T. 2016 updated EULAR evidence-based recommendations for the management of gout. Ann Rheum Dis. 2017 Jan;76(1):29-42.
Schlesinger N, Yasothan U, Kirkpatrick P. Pegloticase. Nat Rev Drug Discov. 2011 Jan;10(1):17-8.
Cammalleri L, Malaguarnera M. Rasburicase represents a new tool for hyperuricemia in tumor lysis syndrome and in gout. Int J Med Sci. 2007 Mar 02;4(2):83-93.
Ueng S. Rasburicase (Elitek): a novel agent for tumor lysis syndrome. Proc (Bayl Univ Med Cent). 2005 Jul;18(3):275-9.
Davidson MB, Thakkar S, Hix JK, Bhandarkar ND, Wong A, Schreiber MJ. Pathophysiology, clinical consequences, and treatment of tumor lysis syndrome. Am J Med. 2004 Apr 15;116(8):546-54.
Pui CH, Mahmoud HH, Wiley JM, Woods GM, Leverger G, Camitta B, Hastings C, Blaney SM, Relling MV, Reaman GH. Recombinant urate oxidase for the prophylaxis or treatment of hyperuricemia in patients With leukemia or lymphoma. J Clin Oncol. 2001 Feb 01;19(3):697-704.
Majumdar S, Sharma N, Sengar M, Thorat J, Nayak L, Bonda A, Bagal B, Rajendra A, Sethi A, Jain H. A phase II study to evaluate the efficacy of low-dose rasburicase (1.5mg) in adolescent and adult acute leukemia and high-grade lymphomas with tumor lysis syndrome. Leuk Lymphoma. 2023 Mar;64(3):628-638.
Shaikh SA, Marini BL, Hough SM, Perissinotti AJ. Rational use of rasburicase for the treatment and management of tumor lysis syndrome. J Oncol Pharm Pract. 2018 Apr;24(3):176-184.
Rivera-Gamma, S., & Davis, M. E. (2023). CE: Tumor Lysis Syndrome: An Oncologic Emergency. AJN The American Journal of Nursing, 123(3), 30-35.
Singh, S., & Owens, S. A Systematic Review of the Efficacy of Pegloticase as a Treatment for Chronic Gout. Podiatric Medical Review, 15.
Sherman MR, Saifer MG, Perez-Ruiz F. PEG-uricase in the management of treatment-resistant gout and hyperuricemia. Adv Drug Deliv Rev. 2008 Jan 03;60(1):59-68.
Sundy JS, Ganson NJ, Kelly SJ, Scarlett EL, Rehrig CD, Huang W, Hershfield MS. Pharmacokinetics and pharmacodynamics of intravenous PEGylated recombinant mammalian urate oxidase in patients with refractory gout. Arthritis Rheum. 2007 Mar;56(3):1021-8
Hershfield MS, Ganson NJ, Kelly SJ, Scarlett EL, Jaggers DA, Sundy JS. Induced and pre-existing anti-polyethylene glycol antibody in a trial of every 3-week dosing of pegloticase for refractory gout, including in organ transplant recipients. Arthritis Res Ther. 2014 Mar 07;16(2):R63.
Sundy JS, Baraf HS, Yood RA, Edwards NL, Gutierrez-Urena SR, Treadwell EL, Vázquez-Mellado J, White WB, Lipsky PE, Horowitz Z, Huang W, Maroli AN, Waltrip RW, Hamburger SA, Becker MA. Efficacy and tolerability of

Journal of Ecohumanism
2024
Volume: 3, No: 8, pp. 12670 – 12684
ISSN: 2752-6798 (Print) | ISSN 2752-6801 (Online)
https://ecohumanism.co.uk/joe/ecohumanism
DOI: https://doi.org/10.62754/joe.v3i8.5995

pegloticase for the treatment of chronic gout in patients refractory to conventional treatment: two randomized controlled trials. JAMA. 2011 Aug 17;306(7):711-20.

Sundy JS, Becker MA, Baraf HS, Barkhuizen A, Moreland LW, Huang W, Waltrip RW, Maroli AN, Horowitz Z., Pegloticase Phase 2 Study Investigators. Reduction of plasma urate levels following treatment with multiple doses of pegloticase (polyethylene glycol-conjugated uricase) in patients with treatment-failure gout: results of a phase II randomized study. Arthritis Rheum. 2008 Sep;58(9):2882-91.

Botson JK, Saag K, Peterson J, Parikh N, Ong S, La D, LoCicero K, Obermeyer K, Xin Y, Chamberlain J, LaMoreaux B, Verma S, Sainati S, Grewal S, Majjhoo A, Tesser JRP, Weinblatt ME. A Randomized, Placebo-Controlled Study of Methotrexate to Increase Response Rates in Patients with Uncontrolled Gout Receiving Pegloticase: Primary Efficacy and Safety Findings. Arthritis Rheumatol. 2023 Feb;75(2):293-304.

Botson JK, Obermeyer K, LaMoreaux B, Zhao L, Weinblatt ME, Peterson J. Improved joint and patient-reported health assessments with pegloticase plus methotrexate co-therapy in patients with uncontrolled gout: 12-month exploratory outcomes of the MIRROR open-label trial. Arthritis Res Ther. 2022 Dec 27;24(1):281.

KC M, Leslie SW. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Oct 15, 2023. Uric Acid Nephrolithiasis.

Leslie, S. W., Sajjad, H., & Bashir, K. (2023). 24-Hour Urine Testing for Nephrolithiasis: Interpretation and Treatment Guidelines. StatPearls [Internet].

Kaur P, Bhatt H. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): May 15, 2023. Hyperuricosuria.

Yu TF. Urolithiasis in hyperuricemia and gout. J Urol. 1981 Oct;126(4):424-30.

Yu KH, Chen DY, Chen JH, Chen SY, Chen SM, Cheng TT, Hsieh SC, Hsieh TY, Hsu PF, Kuo CF, Kuo MC, Lam HC, Lee IT, Liang TH, Lin HY, Lin SC, Tsai WP, Tsay GJ, Wei JC, Yang CH, Tsai WC. Management of gout and hyperuricemia: Multidisciplinary consensus in Taiwan. Int J Rheum Dis. 2018 Apr;21(4):772-787.

Janssen CA, Jansen TLTA, Oude Voshaar MAH, Vonkeman HE, van de Laar MAFJ. Quality of care in gout: a clinical audit on treating to the target with urate lowering therapy in real-world gout patients. Rheumatol Int. 2017 Sep;37(9):1435-1440.

فرط حمض اليوريك والنقرس: نظرة عامة على حالة طبية شائعة

الملخص:

الخلفية :فرط حمض اليوريك، الذي يُعرف بارتفاع مستويات حمض اليوريك في الدم (>6 ملغ/ديسيلتر لدى النساء، >7 ملغ/ديسيلتر لدى الرجال)، يؤثر على حوالي 38 مليون أمريكي، مع زيادة انتشاره عالميًا بسبب الأنماط الغذائية ونمط الحياة الغربية. ورغم أنه غالبًا ما يكون بدون أعراض، يرتبط فرط حمض اليوريك بالنقرس، وتكون حصوات الكلى، وأمراض جهازية مثل ارتفاع ضغط الدم، ومتلازمة التمثيل الغذائي، وأمراض القلب والأوعية الدموية. ينتج عن زيادة إنتاج حمض اليوريك، انخفاض إفرازه الكلوي، أو كلاهما معًا.

الهدف :تقديم نظرة شاملة عن فرط حمض اليوريك مع التركيز على أسبابه، وفيزيولوجيته المرضية، ومظاهره السريرية، واستراتيجيات إدارته، مع التركيز على النقرس وحصوات الكلى.

الطرق :تستعرض هذه المراجعة الأدبيات الحالية حول فرط حمض اليوريك، بما في ذلك علم الأوبئة، والآليات، والتقييم التشخيصي، وخيارات العلاج. كما تناقش دور العوامل الغذائية، الوراثية، والدوائية في تطور المرض وإدارته.

النتائج :يُدار فرط حمض اليوريك بشكل رئيسي من خلال تعديلات نمط الحياة والتدخلات الدوائية. يشمل العلاج الأولي مثبطات إنزيم الزانثين أوكسيداز مثل الألوبورينول، بينما تُستخدم العوامل المطرحة لليورات وأدوية اليوريكاز المؤتلفة في الحالات المقاومة. يُعد التثقيف الغذائي، وخصوصًا الحمية منخفضة البيورين والفركتوز، أمرًا أساسيًا للوقاية والإدارة. تتطلب المضاعفات مثل النقرس، وحصوات الكلى، وأمراض الكلى المزمنة تدخلات مخصصة، بما في ذلك العلاج المخفض لليورات وقلوية البول.

الخاتمة :فرط حمض اليوريك حالة متعددة العوامل لها تأثيرات كبيرة على النقرس، وتكون حصوات الكلى، وصحة الجسم بشكل عام. تتطلب الإدارة الفعالة مزيجًا من تغييرات نمط الحياة، العلاج الدوائي، وتثقيف المرضى. بينما لا يتطلب فرط حمض اليوريك بدون أعراض علاجًا في العادة، فإن الحالات المصحوبة بأعراض تستلزم رعاية فردية لمنع المضاعفات وتحسين جودة الحياة.

الكلمات المفتاحية: فرط حمض اليوريك، النقرس، حصوات الكلى، ألوبورينول، العلاج المخفض لليورات، مثبطات إنزيم الزانثين أوكسيداز.