Chronic gout: a review of approaches to treatment

UM Sibanda,[1] A Zhou,[2] O Omoteso,[1] S Melamane,[1] N Sibiya,[1] B Ndzamba[1]

[1] Faculty of Pharmacy, Rhodes University, South Africa

[2] Department of Pharmacy, School of Health Sciences, University of KwaZulu-Natal, South Africa

Corresponding author, email: u.sibanda@ru.ac.za

Abstract

Gout is an inflammatory disorder characterised by joint immobility due to monosodium urate crystals deposits. The prevalence of gout is increasing owing to several factors, including dietary patterns, cardiometabolic disorders, and certain medications, amongst others. Central to gout pathophysiology is the accumulation of uric acid, which subsequently forms monosodium urate crystals, which can deposit in joints, forming tophi and instigating the inflammatory process and pain. The diagnosis and monitoring of gout include synovial aspiration, imaging tools, and plasma uric acid measurement. Nevertheless, some of the detection tools present several drawbacks, therefore necessitating innovative developments towards detection and monitoring approaches. From a therapeutic standpoint, the goal is to relieve pain and inflammation and maintain desired plasma uric acid levels. Therefore, the pharmacological interventions include a variety of modalities such as NSAIDs, corticosteroids, xanthine oxidase inhibitors, and drugs aiming to promote renal excretion of uric acid. Despite the availability of these treatment approaches, however, gout management remains a challenge, necessitating strategic innovative approaches. A heightened understanding of uric acid metabolism presents opportunities for visualisation and development of efficacious treatment approaches for gout. Furthermore, use of technological advancements in drug formulation strategies, such as nanoparticles, can offer additional avenues to improve gout management. The incorporation of pharmacogenetics is envisaged to also improve the prognosis of gout, through strides aiming to personalise gout management. Lastly, improved patient education on gout management can yield positive outcomes.

Keywords: chronic gout, hyperuricaemia, monosodium urate, urate-lowering therapies, novel therapies

https://doi.org/10.36303/SAPJ.3381

Introduction

Chronic gout is a progressive disease caused by the deposition of monosodium urate crystals and hyperuricaemia; it is the most common inflammatory arthritis.[1] Chronic gout is characterised by persistent inflammation of the joints, formation of tophi, bony erosions, and progressive cartilage damage.[2] Chronic gout is highly prevalent in the elderly and occurs more commonly in men over the age of 40, who are reported to be approximately twice as likely to develop the condition compared to women. Results from a global disease burden study estimated that 55.8 million people were diagnosed with gout.[1,3]

The prevalence of gout is attributed to various risk factors such as ageing, use of certain prescription medicines, dietary and lifestyle changes, and rising burden of comorbid conditions.[1] Recurrent attacks of gout are associated with the consumption of alcoholic beverages such as beer and wine. Medications that are associated with increased risk of gout include angiotensin-converting enzyme inhibitors, diuretics, cyclosporine, and β-blockers. Gout is associated with several comorbid conditions such as diabetes, renal disease, hypertension, and hyperlipidaemia.[4] Chronic gout treatment is aimed at preventing gout flares, reversal of tophus formation and reducing urate deposition. The mainstay treatment is the use of uric acid-lowering agents, first-line treatment consists of xanthine oxidase inhibitors with second-line treatment including uricosuric agents. Advances in chronic gout treatment have been focused on improved newer uric acid-reducing agents such as febuxostat and pegloticase and novel anti-inflammatory agents such as canakinumab.[5]

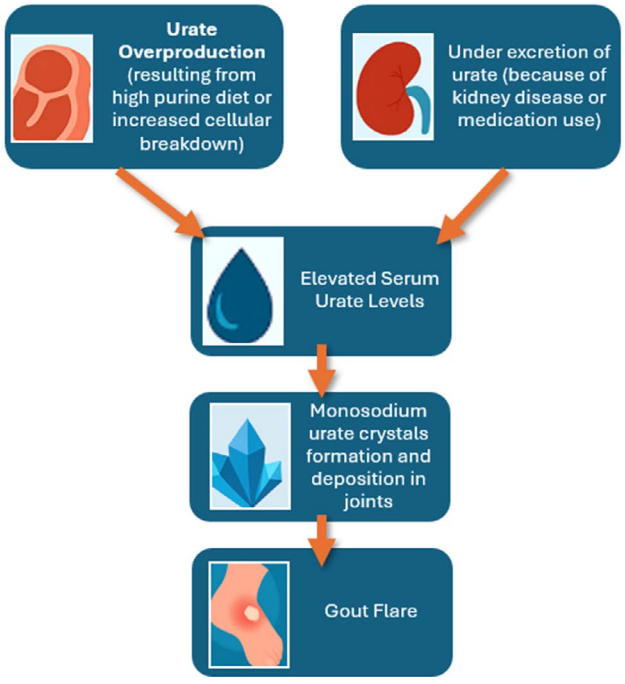

Figure 1: Schematic presentation of the pathophysiology of gout[6,8]

Pathophysiology of gout and progression to chronic disease

Pathophysiology progression of gout begins with hyperuricaemia, the primary risk factor for gout. Hyperuricaemia arises from an imbalance in uric acid production and excretion.[6] Under normal

conditions, purines from diet or from catabolism of nucleic acids are converted to hypoxanthine. Hypoxanthine is metabolised by the enzyme xanthine oxidase to uric acid.[7] This is ultimately excreted in urine.

Hyperuricaemia results from decreased excretion or increased production of uric acid. Decreased excretion of uric acid occurs due to chronic kidney disease, acute kidney injury, hyperparathyroidism, dehydration, or use of medications like diuretics, aspirin, and ciclosporin.[6] On the other hand, overproduction of uric acid results from high purine diet (e.g. red meat, seafood and fructose-rich beverages) and increased cellular turnover and breakdown (as seen in conditions such as tumour lysis syndrome and psoriasis).[6] Often, hyperuricaemia stems from mixed causes including obesity, metabolic syndrome, genetic predisposition, and hormonal factors.[6,8]

At a physiological pH of approximately 7.4, uric acid loses a proton, forming urate ions, which bind to abundant extracellular sodium to form monosodium urate.[9] This compound has limited solubility in body fluids, and when serum uric acid levels exceed the solubility threshold (~6.8–7.0 mg/dL), crystals can precipitate. Factors such as low temperatures, local pH changes, and cartilage composition promote crystal formation, which often occurs in peripheral joints like the first metatarsophalangeal joint (podagra).[9] Initially, even with crystal deposition, an individual can be without symptoms due to protective protein layers shielding the crystals from immune detection. Most people at this stage never develop gout.[6]

Clinical presentation and diagnosis

Gout typically progresses from acute gout attacks to chronic gout. In the acute phase, patients often develop sudden, severe pain with noticeable swelling and redness of the affected joint, tendon or bursa. Chronic gout, which results from recurrent gout attacks, is associated with chronic mono- or poly-articular inflammation, tophus formation, deposition of monosodium urate crystals, cartilage damage, which ultimately cause bone erosion and destruction of the joint. Chronic gout involving multiple joints can cause significant debilitation.[10,11] Tophaceous gout, a severe form of gout, may develop in patients after several years of recurrent gout attacks and in patients with untreated chronic gout.[4,12] Tophi formation usually occurs within or around the joints and may also involve subcutaneous deposition. Tophi commonly form large masses in locations such as fingers, knees, elbows, helices of the ear and the first metatarsophalangeal joints.[11] A study by Bieber et al. highlighted two single clinical cases studies of patients who presented with chronic tophaceous gout without previous gouty attacks which reflected that in rare cases chronic gout manifests initially as tophi.[11] Joint aspiration is considered the gold standard diagnosis, as it is more reliable in confirming gout through microscopic analysis of synovial fluid for the presence of monosodium urate crystals. However, joint aspiration is not always feasible and easily accessible; it is therefore less commonly used in clinical practice.[4] Hyperuricaemia on its own is not sufficient for a confirmative gout diagnosis. The diagnosis of gout can be supported by clinical features such as elevated serum uric acid levels, erythrocyte sedimentation rate or C-reactive protein, podagra and specialised imaging modalities.[4,13] X-rays are easily accessible and more beneficial in chronic gout than in the early stages of gout. In the early stages of gout, radiographic findings show soft-tissue inflammation and offer very little diagnostic value. Despite its low sensitivity, radiography is useful in the diagnosis of gout that has progressed. Radiographic findings that can be seen in chronic gout include, marginal or juxta-articular erosions with overhanging edges and the presence of dense tophaceous nodules within soft tissues.[4] Ultrasound (US) is a valuable tool in chronic gout, as it can reveal tophi that may not be seen on a physical exam and detect the "double contour" sign of urate deposits on the cartilage.[4,14] US can also detect joint effusions, inflammation of the synovium, small crystal deposits, and bone erosions, often before these changes are visible on X-rays.[4]

Computed tomography (CT) and dual energy computed tomography (DECT) are useful in chronic gout for detecting tophi and bone erosions, particularly in deeper joints. DECT can specifically identify urate deposits, quantify tophi, and detect subclinical disease, making it helpful when joint aspiration is not feasible. Conventional CT can show hyperdense nodules but cannot reliably distinguish urate from other crystals without DECT.[4]

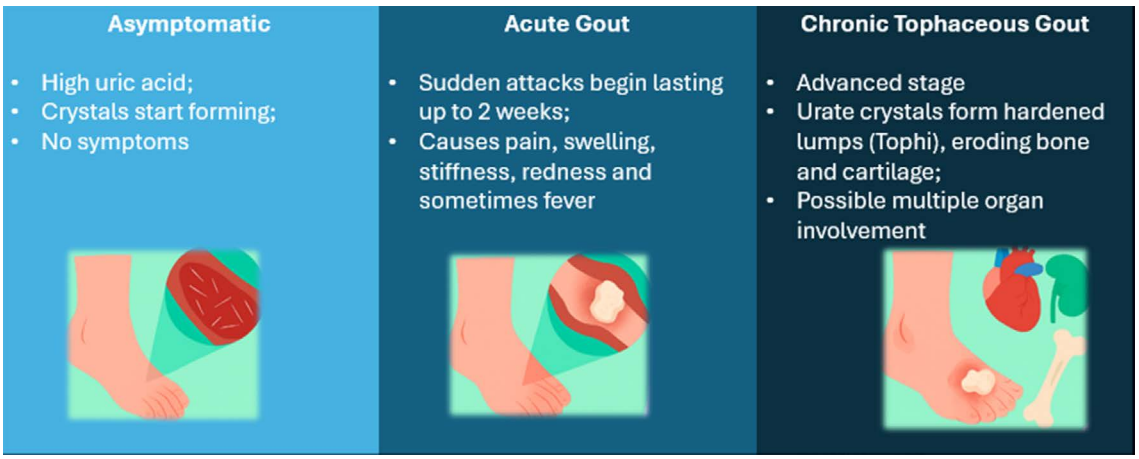

Figure 2: Overview of intermittent and tophaceous gout pathology and clinical presentation[6,7,9,10]

Treatment

Nonpharmacological treatment of gout

Nonpharmacological treatments for gout primarily emphasise dietary modifications, weight management, and complementary acute interventions.[15–17] Numerous studies have demonstrated that weight loss, achieved through diet, exercise, or bariatric surgery, can lead to a decrease in serum uric acid levels and a reduction in the frequency of gout flares.[15–17] In fact, some studies observed changes in serum uric acid ranging from -168 to +30 micromol/L, with 75% reporting a decrease in flare occurrences.[15] Other strategies, such as the application of topical ice, have been shown to provide significant pain relief, demonstrated by a mean difference of 3.33 cm on pain scales.[16] Conversely, the consumption of enriched skim milk powder and tea did not yield improvements in serum uric acid levels or flare frequency.[16] Furthermore, dietary patterns inspired by the Mediterranean, low-purine, or dietary approaches to stop hypertension (DASH diets) have been associated with lower serum uric acid levels and, in certain cases, a reduced incidence of gout flares.[17]

Pharmacological therapy

Gout attacks usually spontaneously resolve in approximately seven days without any treatment but the most important first intervention is the rapid removal of pain and inflammation.[18] The second level of intervention is the management of chronic gout arthritis by lowering serum uric acid levels.[19] Acute gout flares must be immediately treated using one or more anti-inflammatory drugs, viz., nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids and/or colchicine as the first-line options.[20] This treatment should ideally start within 12–48 hours of onset of a gout flare.[9] All the listed anti-inflammatory drugs are effective, and selection should be guided by patient safety, taking into account existing comorbidities and potential contraindications.[21]

Analgesics and anti-inflammatory agents

Nonsteroidal anti-inflammatory drugs

NSAIDs act by inhibiting the enzyme cyclooxygenase (COX), thereby alleviating pain and inflammation.[22] Based on this mechanism, NSAIDs are classified into two main categories: non-selective COX inhibitors and selective COX-2 inhibitors.[22] The most frequently prescribed non-selective NSAIDs include ibuprofen, administered orally at 400 mg three times daily; indomethacin, administered orally at 50 mg three to four times daily; piroxicam, administered orally at 40 mg once daily for 4–6 days; and naproxen, given orally at an initial dose of 750 mg followed by 250 mg three times daily.[23,24] Etoricoxib is the only COX-2 selective inhibitor indicated for the management of gout attacks, administered orally at a dose of 90–120 mg once daily (for acute symptomatic treatment, maximum of eight days).[24] Van Durme et al. reported a 50% reduction in pain after 24 hours of treatment with NSAIDs. All NSAIDs are equally effective in treating acute flares; therefore, selection should be based on the patient's response and the severity of the side-effects.[23,25] COX-2 selective NSAIDs can alter renal haemodynamics, leading to salt and water retention, which may worsen hypertension and increase the risk of acute heart failure.[15] The use of NSAIDs should be limited to a maximum of 10 days or should be discontinued once both inflammation and pain have resolved.[26]

Alkaloids (Colchicine)

Colchicine essentially functions by disrupting the molecular pathology involved in the inflammatory response to urate crystal deposition in joint tissue.[18] Oral colchicine is prescribed at an initial dose of 0.5–1 mg followed by 0.5 mg every six hours, with a maximum daily dose of 2.5 mg.[23,24] In patients with moderate renal impairment (GFR 10–50 ml/min), the colchicine dose should be reduced by half. [24,27] In cases of severe renal impairment (GFR < 10 ml/min), colchicine should be avoided entirely.[27] Conjunctive use of colchicine with non-selective NSAIDs may increase the risk of gastrointestinal side-effects such as ulceration and haemorrhage.[22,24]

Corticosteroids

Corticosteroids are only administered orally if NSAIDs are poorly tolerated or contraindicated, such as in patients with peptic ulcer disease, those receiving warfarin therapy, or individuals with renal impairment, hypertension, or heart failure.[28] Oral prednisone or prednisolone is normally prescribed at 40 mg daily for five days.[24,28] Selecting the most viable treatment for an acute attack depends on the tolerance and comorbidities of the patient to avoid harsh side-effects and contraindications, respectively.

Serum uric acid-lowering agents

According to the American College of Rheumatology (ACR) guidelines, uric acid-lowering therapy must be initiated for all patients with one or more subcutaneous tophi or who have experienced one or two acute gout attacks in one year.[29] The aim of this therapy is to achieve and maintain serum uric acid levels below 6 mg/dL to prevent deposits, with monitoring every six months to guide treatment maintenance or adjustment as needed. In cases of severe gout, the European League Against Rheumatism recommends that uric acid levels should be lower than 5 mg/dL for patients with severe gout. Low serum levels of uric acid will ensure that urate crystals do not form, and joint inflammation is prevented.[25] Once the tophi and gout flares are resolved, uric acid-lowering therapy should continue indefinitely as a lifelong therapy.

During the initial weeks of therapy, patients may experience more frequent gout flares as tissue uric acid deposits are mobilised in response to the sudden reduction in serum levels.[30] Hence, uric acid-lowering therapy should be initiated at a low dose and gradually increased, accompanied by low-dose colchicine or an NSAID for the first six months to prevent gout flares. Furthermore, uric acid-lowering drugs should not be initiated during an acute gout attack, however, if the patient is already on such therapy at

the time of the attack, it should not be discontinued.[19] The most commonly used agents for lowering serum uric acid levels are allopurinol (xanthine oxidase inhibitor) and probenecid.

Allopurinol and probenecid

Allopurinol acts by inhibiting the production of uric acid and thereby reducing the deposition of uric acid in joint tissue.[31] This agent is prescribed orally at 100 mg daily, with monthly increments of 100 mg based on the serum levels of uric acid.[28] Probenecid lowers serum uric acid levels by inhibiting the renal tubular transporter in order to increase the excretion of uric acid.[32] It is first prescribed as an oral dose at 250 mg twice daily for one week, and at a maintenance dose of 500 mg twice daily.

Challenges in current treatment of chronic gout

Despite its historical recognition, gout management continues to face numerous challenges. It is essential to consider gout as a chronic condition rather than solely addressing the acute episodes. The perception of gout is that it is an acute disease necessitating treatment solely during acute flares. To address the disease, chronic uric acid-lowering therapy is required to reduce serum uric acid levels below the saturation threshold of 6 mg/dL, alongside chronic anti-inflammatory prophylaxis, particularly during the initiation of uric acid-lowering therapy.[34] Uric acid-lowering therapy effectively manages gout; however, it poses challenges such as the necessity for lifelong adherence, the risk of initial gout flares upon treatment initiation, the requirement for regular uric acid level monitoring, potential drug-drug interactions, and adverse effects.[35] Significant treatment challenges in chronic gout encompass:

Poor medication adherence and health empowerment

Wang et al. reported that the medication adherence rate among gout patients was 59.89%, while the health empowerment score was 24.06%. This study's findings indicate that medication adherence among gout patients is inadequate, underscoring the necessity for clinical intervention. Approximately 60% of patients tend to reduce or discontinue their medication autonomously after experiencing symptom relief. This phenomenon can be attributed to several interrelated factors. Patients' insufficient comprehension of the disease hinders their recognition of the chronic characteristics of gout and its possible complications. Additionally, certain patients, unaware of the need for ongoing medication, erroneously perceive symptom relief as a sign of disease resolution. Gender differences significantly influence adherence, as male patients, who frequently participate in more social activities, are more prone to missing doses.[36] The incidence and prevalence of gout and hyperuricaemia among Black people have surpassed those in White adults, with a disproportionate impact on Black women.[37] This increasing difference can be wholly ascribed to social determinants of health, encompassing elevated obesity and poverty levels in Black women relative to White women, as well as worse renal function and inferior dietary quality among Black males compared to White males. Additionally, Black patients with gout have received inferior gout-related care and have reported elevated levels of healthcare utilisation, particularly among Black women. Black individuals with gout experience a disproportionate burden of the disease and elevated rates of non-adherence, indicating the necessity for culturally customised treatment strategies.[37]

Additional factors contributing to inadequate adherence included insufficient education and comprehension regarding medication administration and its role in disease management. Factors contributing to poor adherence encompassed insufficient financial resources, a deficiency in self-motivation for consistent medication intake, healthcare providers' noncompliance with treatment guidelines, and discrepancies between patients' and providers' views on gout management.[35] Poor adherence results

Table I: Treatment, efficacy, and safety profile overview[29,33]

Treatment	Efficacy measures	Safety profiles
Allopurinol	44.4–80% reach serum uric acid (SUA) < 6 mg/dL	Rash 1.5%; allopurinol hypersensitivity syndrome (AHS) rare; well-tolerated up to 800 mg; no new safety signals in 6-month studies
Febuxostat	48–65% reach SUA < 6 mg/dL (80–120 mg); more effective than allopurinol 300 mg	Similar adverse events to allopurinol; possible increased cardiovascular mortality (as reported in the CARES trial); no dose adjustment for mild-moderate chronic kidney disease (CKD)
Colchicine	38–41% achieve 50% pain reduction at 24 hours; low-dose as effective as high-dose with fewer gastrointestinal adverse events	Gastrointestinal adverse events (diarrhoea 23% low-dose vs. 77% high-dose); severe adverse events rare at low dose
NSAIDs	Effective for acute flares; no significant difference between agents	Gastrointestinal, renal, cardiovascular adverse events; avoid in chronic kidney disease or cardiovascular disease
Corticosteroids	As effective as NSAIDs for acute flares; fewer adverse events	Fewer gastrointestinal adverse events than NSAIDs; short-term use generally safe
Probenecid	Effective for SUA lowering; less effective than benzbromarone	Renal stones, gastrointestinal adverse events; avoid in chronic kidney disease
Benzbromarone	Achieves optimal SUA	Hepatotoxicity risk; not available in all regions
Pegloticase	42% maintain SUA < 6 mg/dL	Infusion reactions, immunogenicity, cardiovascular adverse events
Canakinumab	Superior to triamcinolone for pain/flare reduction; 62% lower flare risk	Infection risk, high cost
Lesinurad	54–76% reach SUA < 6 mg/dL (with xanthine oxidase inhibitor)	Nephrotoxicity risk, especially as monotherapy

in suboptimal outcomes and ongoing disease progression. Non-adherence is associated with an increased frequency of flares and a reduced likelihood of achieving urate targets.[38]

Difficulty achieving target uric acid levels

Gout management encompasses two primary components: the treatment of gout flares for immediate symptomatic relief and long-term urate-lowering therapy (ULT) aimed at reducing serum uric acid levels to prevent future gout flares and the formation of tophi. However, achieving and maintaining target serum uric acid levels presents challenges, and the clinical benefits of ULT require time to manifest.[39] The objective is generally to keep serum uric acid levels under 6 mg/dL; however, numerous patients find it challenging to achieve and sustain these levels due to various factors, such as insufficient monitoring, treatment disruptions, and the presence of chronic kidney disease comorbidities.[40] The administration of ULT without reaching the uric acid target suggests that crystal deposits will persist, placing the patient at risk for adverse medication-related events.[41]

Paradoxical flare initiation

Flare represents the primary characteristic of gout, resulting from the inflammatory response to monosodium urate crystals. Thus, the prevention of gout flares should be the principal objective of gout management. Nonetheless, the paradoxical rise in flare risk after the commencement of ULT poses significant challenges for demonstrating the anticipated long-term advantages of flare prevention in clinical trials. The paradoxical deterioration observed at the initiation of treatment may dissuade patients and complicate management strategies.[42]

Treatment resistance and refractory cases

Certain patients experience chronic refractory gout that exhibits inadequate response or resistance to conventional treatments. Chronic refractory gout is characterised by persistent hyperuricaemia accompanied by recurrent flares, tophi, and/or chronic gouty arthritis. This condition occurs when conventional therapy fails to normalise serum uric acid levels, and when signs and symptoms remain inadequately managed despite the use of oral xanthine oxidase inhibitors at the maximum medically appropriate dosage, or when these medications are not tolerated or are contraindicated. Patients with chronic refractory gout present significant treatment challenges, and available therapeutic options are limited, underscoring the necessity for innovative strategies in complex cases.[43]

Advances in the treatment of chronic gout

The challenges in current treatment highlight the need for innovative therapies and personalised approaches. Recent advancements in the treatment of chronic gout indicate a notable evolution in therapeutic strategies, influenced by a deeper understanding of the disease and the creation of new targeted therapies.[44] The field is progressing due to the emergence and implementation of advanced biological therapies, an increasing focus on personalised medicine, and advancements in genetic research.[45]

Nanoparticles delivery systems approach

Advancements in nanotechnology present promising novel strategies for enhancing gout therapy. The advent of nanotechnology has generated new prospects for improving the pharmacological characteristics and clinical efficacy of medication formulations. Numerous nanostructured delivery systems, such as polymeric nanoparticles, liposomes, solid lipid nanoparticles (SLNPs), and nanoemulsions, have significantly advanced through the integration of traditional herbal remedies, providing superior attributes and accurate targeting abilities. Nanoparticles possess considerable potential to enhance drug delivery systems, mitigate inflammation, and alter the behaviour of urate crystals. They facilitate the precise administration of medications directly to the afflicted joint, enhancing therapy efficacy and reducing systemic adverse effects. Contemporary therapies, including anti-inflammatory and uric acid-lowering medications, sometimes encounter obstacles such as inadequate solubility, rapid elimination, and restricted absorption, which may diminish their therapeutic effectiveness. Nanoparticles present a viable option by augmenting drug bioavailability via enhanced solubility, safeguarding against premature degradation, and facilitating targeted distribution to inflamed joints. This can decrease necessary dosages, mitigate systemic adverse effects, and provide prolonged therapeutic results, hence reducing administration frequency and enhancing patient adherence.[44]

Emerging novel therapies

Pozdeutinurad (AR882) signifies a novel category of dual-pathway inhibitors that may provide benefits compared to current treatments.[46] In the trial including AR882, 42 patients with refractory gout with at least one subcutaneous tophus were randomised to receive either 75 mg AR882, 50 mg AR882 in conjunction with allopurinol, or allopurinol monotherapy. This study indicated that long-term administration of AR882, either alone or in conjunction with allopurinol, for the management of tophaceous gout patients was well tolerated, exhibited a comparable safety profile, and showed superior efficacy compared to allopurinol alone. The findings endorse AR882 as a secure therapeutic alternative for gout patients, encompassing those with both overt and subclinical crystal deposition.[46]

Other novel medicines, including IL-1 inhibitors (canakinumab, anakinra, rilonacept), present additional alternatives for the management of gout attacks, but some remain unapproved by the Food and Drug Administration (FDA).[44]

Breakthrough biological therapies

The most notable advancement has been the creation of biological treatments, specifically pegloticase. Biological pharmaceuticals like pegloticase are transforming the management of chronic and severe gout, especially for individuals unresponsive to

conventional therapies. This PEGylated uricase enzyme offers a potent alternative for refractory instances where standard therapies have been ineffective.[43] Recent studies have improved the efficacy of pegloticase via combinatorial strategies. Findings from this extensive observational registry indicate that concurrent immunomodulatory medication therapy enhances the persistence of pegloticase, resolving prior issues related to treatment durability.[47]

Personalised medicine approaches

Treatment is progressively being personalised, with genetic studies guiding therapeutic choices. Clinicians may now more accurately anticipate patient responses to certain medications and customise therapies accordingly, departing from the conventional trial-and-error methodology. Implementing pharmacogenomic (PGx) testing helps identify predisposed individuals to benefit from specific treatments, enhance medication adherence, and diminish pill load.[48] Individuals possessing the HLA-B*58:01 allele are at an elevated risk of severe and perhaps fatal dermatological responses when treated with allopurinol. Moreover, racial inequalities in the prevalence of HLA-B*58:01 necessitate genetic screening in high-risk populations, particularly some Asian subgroups and African Americans. Individuals with G6PD deficiency may get haemolytic anaemia and methemoglobinaemia after using pegloticase and probenecid. Individuals possessing the less active variant of the drug-metabolising enzyme CYP2C9 exhibit an elevated risk of NSAID-induced upper gastrointestinal haemorrhage.[45]

Future perspectives in gout treatment

The future of gout management is increasingly shaped by a multifaceted research landscape, with novel drug classes, immunomodulation, gene-based therapies, and personalised treatment paradigms that together promise more effective and patient-centred care. There are several ULTs under investigation. For example, lesinurad and verinurad are novel selective uric acid reabsorption inhibitors that act on the Urate Transporter 1 (URAT1) transporter in the kidney. They provide a targeted approach to enhance uric acid excretion.[49] Beyond uric acid lowering, emerging research into immunomodulatory therapies targeting specific inflammatory pathways involved in gout pathogenesis offer the potential for more precise and less toxic interventions compared to broad anti-inflammatory drugs.[2]

Additional innovative trends in gout management include the repurposing of sodium-glucose co-transporter 2 (SGLT2) inhibitors, which not only reduce gout flares but also lower mortality and address associated cardiometabolic comorbidities.[50] Cutting-edge gene therapies using mRNA and CRISPR-Cas9 hold promise for addressing the genetic predispositions underlying hyperuricaemia and chronic gout, contribution to the possibility of long-term disease control or even curative approaches by correcting specific mutations affecting uric acid metabolism.[6] These strategies promise more precise, effective and potentially curative approaches.

Conclusion

Gout remains amongst diseases with high prevalence owing to lifestyle patterns, metabolic syndrome, and certain medications. Moreover, the high prevalence of comorbidities such as hypertension, diabetes, chronic kidney disease and the frequent use of uric acid-raising medication like thiazide diuretics complicate the management of gout in local practice. The limited, inaccessible, and non-specific detection and monitoring strategies hinder gout management, as early detection could be central to gout prognosis. The increased understanding of uric acid metabolism offers unique pharmacological interventions that could accelerate the elimination and excretion of uric acid. Treat to target serum urate below 6 mg/dL remains the main strategy to prevent recurrent flares and joint damage. Allopurinol is the most commonly used ULT due to it being widely available and cost effective. In resource-limited settings, patient education and adherence support are important particularly where follow-up and lab monitoring is inconsistent. Through these strategies, gout management strategies could shift towards targeting the root cause, instead of only treating complications or alleviating symptoms. Harnessing advancements in drug formulation strategies and pharmacogenomics could be pivotal in reducing side-effect of anti-gout drugs, improving their efficacy profile (primary and secondary endpoints), and patient compliance. Whilst the above represent exciting innovative avenues, patient education and counselling should also be considered as an integral instrument in gout management practices.

ORCID

Unami Sibanda https://orcid.org/0000-0002-0159-3536

Angel-Alberta Zhou https://orcid.org/0000-0001-7101-7609

Omobolanle Omoteso https://orcid.org/0000-0003-3059-7381

Siyabonga Melamane https://orcid.org/0009-0006-2383-9847

Ntethelelo Sibiya https://orcid.org/0000-0001-5894-8935

Bonginkosi Ndzamba https://orcid.org/0000-0002-1015-341X

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