Maturitas 78 (2014) 245–251

Contents lists available at ScienceDirect

Maturitas

journal homepage: www.elsevier.com/locate/maturitas

Review

Gout: Joints and beyond, epidemiology, clinical features, treatment and co-morbidities

Philip C. Robinson (MBChB FRACP)[a,b,*], Simon Horsburgh (PhD)[c]

[a] University of Queensland Diamantina Institute, Princess Alexandra Hospital, Brisbane, Australia
[b] Department of Rheumatology, Gold Coast University Hospital, Gold Coast, Australia
[c] Department of Preventive and Social Medicine, Dunedin School of Medicine, University of Otago, Dunedin, New Zealand

ARTICLE INFO

Article history:
Received 28 April 2014
Accepted 1 May 2014

Keywords:
Gout
Urate
Hypertension
Diet
Diabetes mellitus
Chronic kidney disease

ABSTRACT

Gout is a common inflammatory arthritis precipitated by an inflammatory reaction to urate crystals in the joint. Gout is increasingly being recognised as a disease primarily of urate overload with arthritis being a consequence of this pathological accumulation. It is associated with a number of important co-morbidities including chronic kidney disease, obesity, diabetes and cardiovascular disease.

The prevalence of gout is increasing around the world. Significant progress has been made in determining the genetic basis for both gout and hyperuricaemia. Environmental risk factors for gout have been identified as certain foods, alcohol and several medications. There is, however, little evidence that changing these environmental risks improves gout on an individual level.

Treatment of gout encompasses two strategies: firstly treatment of inflammatory arthritis with non-steroidal anti-inflammatories, corticosteroids, colchicine or interleukin-1 inhibitors. The second and most important strategy is urate lowering, to a target of 0.36 mmol/L (6 mg/dL) or potentially lower in those with tophi (collections of crystalline urate subcutaneously). Along with urate lowering, adequate and prolonged gout flare prophylaxis is required to prevent the precipitation of acute attacks. Newer urate lowering agents are in development and have the potential to significantly expand the potential treatment options. Education of patients regarding the importance of life long urate lowering therapy and prophylaxis of acute attacks is critical to treatment success as adherence with medication is low in chronic diseases in general but especially in gout.

Contents

1. Introduction 246
2. Clinical features and impact of gout 246
3. Epidemiology of gout 246
   3.1. Gout genetics 247
   3.2. Alcohol and dietary influences 247
   3.3. Supplements and medication 247
   3.4. Environmental–genetic interactions 247
4. Treatment overview 247
   4.1. Treatment of acute attacks 247
   4.2. Urate lowering therapy 248
   4.3. Suboptimal adherence to urate lowering therapy 248
   4.4. Prophylaxis against acute gout flares during ULT 248
   4.5. Newer therapeutics 249

* Corresponding author at: University of Queensland Diamantina Institute, Princess Alexandra Hospital, Brisbane, Australia. Tel.: +61 7 3443 6999.
E-mail addresses: philip.c.robinson@gmail.com, philip.robinson@uq.edu.au (P.C. Robinson).

http://dx.doi.org/10.1016/j.maturitas.2014.05.001
0378-5122/

5. Co-morbidities 249
5.1. Hypertension 249
5.2. Renal impairment 249
5.3. Diabetes mellitus 249
5.4. Cardiovascular disease 249
5.5. Optimising therapy 249
6. Conclusions 249
Contributors 249
Competing interest 250
Funding 250
Provenance and peer review 250
Acknowledgements 250
References 250

1. Introduction

Gout is a common inflammatory arthritis associated with important co-morbidities including cardiovascular disease, chronic kidney disease, obesity and type 2 diabetes. Gout is caused by an inflammatory reaction to urate crystals in joints. It is the commonest inflammatory arthritis in men and after the menopause is a common cause of inflammatory arthritis in women [1]. However, while historically gout has been viewed purely as a disease first manifesting as arthritis it is increasingly being recognised as a urate overload disease, often associated with extensive co-morbidities and with inflammatory arthritis being a manifestation of later stage disease [2]. A recent proposal to introduce disease stages is shown in Table 1. Gout has a significant impact on the working age population and impacts on work presenteeism, productivity and physical function [3–5]. Gout is growing in prevalence in developed countries and in addition is poorly recognised and treated [6–9]. This manuscript aims to review the epidemiology of gout, its treatments and highlight its important co-morbidities.

2. Clinical features and impact of gout

The first attack (or 'flare') of gout commonly, although not universally, occurs in the first metatarsophalangeal joint and is referred to as 'podagra'. Some individuals may only have one to two attacks of gout, or have extremely intermittent attacks months apart, but the majority will suffer from increasingly frequent attacks. Subsequent attacks commonly involve additional joints such as the knee and as gout progresses it can cause polyarticular attacks and tophus development, although tophi can also be the first presentation of disease. Gout can eventually progress to a chronic phase whereby there is persisting inflammation in joints.

The characteristic of attacks is a rapid onset (over 12–24 h) of acute pain, which can be associated with overlying joint erythema and swelling. Attacks can mimic septic arthritis, cellulitis or systemic infection because extensive or polyarticular attacks can cause fever. As the differential diagnosis includes septic arthritis joint aspiration for diagnostic purposes is necessary if at all possible. Other sequelae of persistent hyperuricaemia and chronic gout include urate renal stone development and gouty nephropathy.

The impact of gout on the life of patients and their families can be substantial if gout flares cannot be controlled. The intense pain of a flare can be debilitating, leading to gout patients to isolate themselves from those around them to limit possible physical contact, as well as reduced self-efficacy in personal care [5,10]. The pain associated with recurrent flares can also lead to reduced participation in social and recreational activities as patients seek to minimise the chance of precipitating a flare or being caught away from home when one occurs [10]. Gout can also dramatically affect occupational functioning. Gout patients take a mean of 4.6 more days off work per year than non-gout patients [4], although some have found this figure to be closer to 25 days [5]. Modification of work activities to accommodate flares and mobility issues can also occur. It is not surprising then that patients with chronic gout score poorly on health-related quality of life measures [10]. Together, these highlight that the impact of gout goes beyond just joints – contrary to the traditional view, gout can have a substantial impact on the lives of patients and their families if not controlled with appropriate treatment.

3. Epidemiology of gout

Fundamentally gout is a urate overload disease, historically the mechanism of overload was divided into over production or under excretion [2]. Recently, the intestinal excretion of urate by the transporter ABCG2 has been identified as very important [11]. This has led to the proposal of new classification system for hyperuricaemia, see Table 2.

Clinical gouty arthritis is strongly linked to the level of serum urate, with increasing levels of hyperuricaemia leading to a progressively increasing risk of gout [12,13]. However, it should be noted that only a minority of those with hyperuricaemia develop gout. For example, the prevalence of gout in the US in 2007–2008 was 6% but the prevalence of hyperuricaemia was 21% [14]. The reason that only a minority of those with hyperuricaemia develop clinical gouty arthritis is not clear.

Table 1
Proposed staging system for gout.

Gout stage	Symptomatology	Description
A	Asymptomatic	At risk of gout but without MSU crystal deposition
B	Asymptomatic	MSU crystal deposition but without signs or symptoms of gout
C	Symptomatic	MSU crystal deposition with prior or current episodes of gout flares
D	Symptomatic	Advanced gout requiring specialised interventions

Source. Adapted from Ref. [2].
Note. Patients can move from stage B directly to stage D.
MSU – monosodium urate.

Table 2
Proposed new classification of the pathophysiology of hyperuricaemia.

Type	Subtype
A. Renal overload type	A1. Over production type A2. Extra-renal under excretion type[a]
B. Renal under excretion type	

Source. Adapted from Ref. [11].
[a] Due to genetic ABCG2 dysfunction. *Note*. An individual patient may have more than one cause for their hyperuricaemia.