

Concordance of gout management with European League against Rheumatism recommendations in hospital practice

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Abstract

Aim: To assess the concordance of gout management with the European League Against Rheumatism (EULAR) gout recommendations in hospital practice.

Methods: This was a retrospective review of case notes of patients presenting to rheumatology outpatients between June and December 2009 under the care of 2 consultant rheumatologists. Data collected consisted of demographics, time lag to specialist referral, comorbidities, details about acute and recurrent attacks, lifestyle advice and use of urate lowering therapies. Documented management was assessed for concordance with the EULAR recommendations.

Results: Thirty consecutive patients (27 males, 3 females) attending Rheumatology clinic at Mater Dei Hospital were recruited. Mean age at the time of survey was 59.4 ± 10.7 years, while mean age at diagnosis was 51.1 ± 14 years. Documentation of lifestyle advice was recorded for alcohol reduction (83%), weight loss (43%), diet (13%), and exercise (13%). Adequate control of comorbidities was attained in hyperlipidaemia (71%), diabetes mellitus (55%) and hypertension (30%). Advice about smoking cessation was given to 37%. Uric acid levels below target were achieved in 47%. The mean uric acid level at time of survey was 379 ± 146 $\mu\text{mol/l}$. This was significantly less than that at presentation ($p=0.001$).

Conclusions: Current treatment of gout is poorly concordant with many of the EULAR recommendations. Documentation of lifestyle modifications advice is infrequent except for alcohol reduction. A significant number of patients on allopurinol still have hyperuricaemia implying that more aggressive management is required to improve standard of care. A proforma has been developed to make and help sustain the necessary improvements.

Introduction

Gout is a common inflammatory arthritis affecting about 1-2% of the adult population.^{1,2} The National Health and Nutrition Examination Survey III (NHANES III) estimated the prevalence of gout at 5.1 million in US population from 1988-1994 with 2.7 million being men aged 40 or older.³ Both the incidence and prevalence of gout appear to be increasing significantly.⁴ This is supported by data from New Zealand⁵ as well as from US managed care data which reported an increased prevalence from 2.9 cases per 1000 in 1990 to 5.2 cases per 1000 in 1999.¹ This may be accounted for by changing patterns of risk factors including increased longevity, dietary and lifestyle changes and increased prevalence of co-morbidities.²

Gout is characterised by chronic hyperuricaemia (defined as serum urate levels of >360 $\mu\text{mol/l}$), soft tissue deposition of monosodium urate (tophi) and acute self-limiting bouts of acute arthritis.⁶ Other forms include a chronic erosive inflammatory arthritis as well as uric acid kidney stones.

Various antihyperuricaemic drugs are available including xanthine oxidase inhibitors, uricosurics and uricases targeting production, renal excretion and degradation of uric acid respectively.⁷ The availability of these new effective urate lowering therapies (ULT) has made it possible to attain good disease control in the majority of patients. Despite this, therapeutic targets are still not always achieved.

The European League Against Rheumatism (EULAR) has issued recommendations for diagnosis⁸ and management of gout.⁹ These recommendations highlight the importance of a holistic approach for management of gout incorporating patient education, lifestyle modification and appropriate dose titration of urate-lowering medication. The aim is to achieve a serum uric acid level < 360 $\mu\text{mol/l}$ which is the physiological saturation threshold of urate in the serum.⁶ Various studies have demonstrated that reduction of uric acid levels below 360 $\mu\text{mol/l}$ decreases the likelihood of both acute attacks and crystal load.^{10,11}

Keywords

Gout, audit, hospital

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Gout is largely managed in primary care. However, a number of patients are still referred to secondary care providers usually when there is a problem achieving the primary goals of gout management, i.e. control and prevention of the clinical manifestations or control of urate levels. Little is known about the characteristics, disease control and quality of management of patients attending Rheumatology outpatients.

We carried out a case record survey about management of gout including lifestyle modification advice, use of ULTs and uric acid levels and assessed concordance with the EULAR recommendations for management of gout.

Methods

This was a retrospective review of case notes of patients presenting to rheumatology outpatients between June and December 2009 under the care of two consultant rheumatologists. Data collected consisted of demographics, year and age at diagnosis, time lag to specialist referral, comorbidities, details about acute and recurrent attacks, lifestyle advice and use of ULTs. Lifestyle advice comprised alcohol intake restriction, weight loss and avoidance of red meat and seafood. Biochemical investigations included renal function, HbA_{1c}, lipid profile, uric acid levels and synovial fluid analysis.

Patients were included in the survey if the diagnosis of gout was based on the presence of monosodium urate (MSU) crystals from joint aspiration, a history of acute arthritis of the 1st metatarsophalangeal joint (MTPJ), a typical history (defined as severe pain, swelling and erythema of a joint developing over 6-12 hours) or the presence of tophi. Patients with hyperuricaemia but without any of the characteristics mentioned above were excluded from the study.

The EULAR 2006 recommendations for management of gout⁹ consist of 12 key evidence based recommendations focusing on the general, acute and chronic management of gout. They incorporate both pharmacological and non-pharmacological treatments and cover various aspects including adverse lifestyle modification, treatment of associated co-morbidities and risk factors.

A minimum standard of 60% was set for each EULAR recommendation given the circumstances and after discussion and consensus with other team members.

Results

Thirty patients (27 males, 3 females) attending Rheumatology clinic at Mater Dei Hospital were recruited. Mean age at the time of survey was 59.4 ± 10.7 years, while mean age at diagnosis was 51.1 ± 14 years. The mean weight was 86.2 ± 15.7 kg. The mean follow up time was 14 years (Table 1).

Diagnosis was made by a rheumatologist in 73% while in 27% it was done by the General Practitioner. In 64% diagnosis was based on a history of arthritis involving the 1st MTPJ, while in 26% this was based on a typical history as explained above. None of the patients were initially diagnosed after finding of MSU crystals in the joint. The time lag from onset of symptoms to specialist referral was 6 months (range 2 months-20 years). The median serum uric acid level at time of referral was 512 (range 231-811) µmol/l. The median serum creatinine was 97.5 (range 68-221) µmol/l. Four patients had a history of uric acid stones. None of the patients had a history of joint sepsis.

EULAR Recommendation 1

Optimal treatment of gout requires both non-pharmacological and pharmacological modalities and should be tailored according to:

- a) specific risk factors (levels of serum urate, previous attacks, radiographic signs)*
- b) clinical phase (acute/recurrent gout, intercritical gout, and chronic tophaceous gout)*
- c) general risk factors (age, sex, obesity, alcohol consumption, urate raising drugs, drug interactions, and comorbidity)*

All patients had a serum uric acid measurement at baseline. The mean uric acid level at time of referral was 512 (range 231-811) µmol/l. Eighty-three percent were reported to have recurrent attacks. The median frequency of attacks in the previous year was 2 (range 0-9) while median duration

Table 1: Characteristics of patients with gout

Age (years): mean (SD)	59.4 (10.7)
Male gender: n (%)	27 (90)
Weight (kg): mean (SD)	86.2 (15.7)
Age at diagnosis (years): mean (SD)	51.1 (14)
Serum urate at diagnosis (µmol/l): mean (range)	512 (283 - 811)
Current serum urate (µmol/l): mean (range)	379 (92 - 671)
Current serum creatinine (µmol/l): mean (range)*	97.5 (68 - 211)
Medication use: n (%)	
- on thiazide diuretics prior to first attack	8 (27)
- on allopurinol	28 (93)

*Normal range 60 – 120 µmol/l

of attack was 5 (range 2-12) days. Forty percent admitted to drinking alcohol (43% not recorded) the median amount of units per week was 4.5 (range 1-98) while 17% denied alcohol intake. The type of alcohol was specified in 20% only (13% beer, 7% wine). Twenty-seven percent were smokers (40% not recorded). The average number of cigarettes smoked was 16.5 ± 9.5 per day. 26.5% suffered from diabetes mellitus (47% not recorded), 67% from hypertension (30% not recorded), 43% had hyperlipidaemia (50% not recorded) and 23% ischemic heart disease (67% not recorded). Two patients were on thiazide diuretics at presentation. Radiographic data was not collected in our survey.

EULAR Recommendation 2

Patient education and appropriate lifestyle advice regarding weight loss if obese, diet, and reduced alcohol (especially beer) are core aspects of management.

Documentation of lifestyle advice was recorded for alcohol reduction (83%), weight loss (43%), diet (13%), and exercise (13%) (Figure 1).

EULAR Recommendation 3

Associated comorbidity and risk factors such as hyperlipidaemia, hypertension, hyperglycaemia, obesity, and smoking should be addressed as an important part of the management of gout.

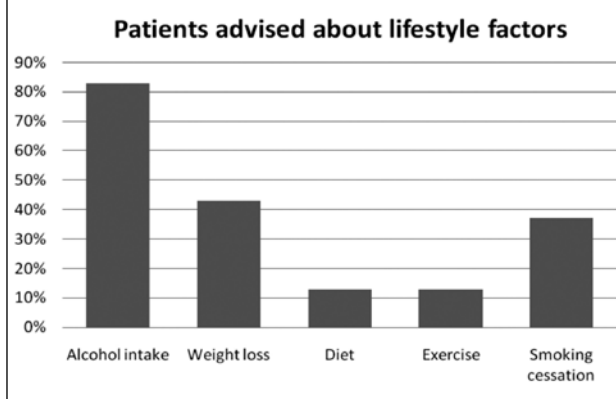
Adequate control of comorbidities was attained as follows: hyperlipidaemia (71%), diabetes mellitus (55%), hypertension (30%). Advice about smoking cessation was given to 37%.

EULAR Recommendation 4

Oral colchicine and/or NSAID are first line agents for systemic treatment of acute attacks; in the absence of contraindications, an NSAID is a convenient and well accepted option.

During an acute attack NSAIDS were prescribed in 50% while colchicine in 10%. The type of drug used was not reported in the remaining cases.

Figure 1: Advice about lifestyle factor modifications



EULAR Recommendation 5

High doses of colchicines lead to side effects, and low doses (for example, 0.5 mg three times daily) may be sufficient for some patients with acute gout.

The highest dose of colchicine used did not exceed 0.5mg three times daily (100% concordance).

EULAR Recommendation 6

Intra-articular aspiration and injection of long acting steroid is an effective and safe treatment for an acute attack.

Only 2 patients were given intra-articular steroid injections during an acute attack.

EULAR Recommendation 7

Urate lowering therapy is indicated in patients with recurrent acute attacks, arthropathy, tophi, or radiographic changes of gout.

Urate lowering therapy was started in view of recurrent attacks (70%), presence of gouty tophi (17%), urate stones (10%) and renal insufficiency (3%). ULT was initiated in line with the above recommendations in all patients (100% concordance). 30% still reported two or more acute attacks despite taking ULT.

EULAR Recommendation 8

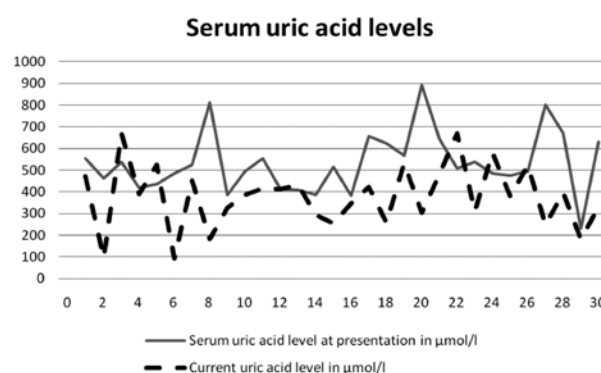
The therapeutic goal of urate lowering therapy is to promote crystal dissolution and prevent crystal formation; this is achieved by maintaining the serum uric acid below the saturation point for monosodium urate ($360 \mu\text{mol/l}$).

The mean uric acid level at time of survey was $379 \pm 146 \mu\text{mol/l}$. This was significantly less than that at presentation ($p=0.001$). However, only 47% achieved uric acid levels below target.

EULAR Recommendation 9

Allopurinol is an appropriate long term urate lowering drug; it should be started at a low dose (for example, 100 mg daily) and increased by 100 mg every 2–4 weeks if required; the dose must be adjusted in patients with renal impairment; if allopurinol

Figure 2: Serum uric acid levels at first presentation and at last visit



toxicity occurs, options include other xanthine oxidase inhibitors, a uricosuric agent, or allopurinol desensitisation (the latter only in cases of mild rash).

All patients except one were on allopurinol. The median dose at time of survey was 300 (range 100-600) mg/day. One patient experienced a hypersensitivity reaction manifested as widespread erythematous rash. Allopurinol desensitisation was carried out and the patient did not experience any further adverse events.

In over 88% of patients allopurinol was started once the acute attack was over, the mean time being 13 weeks after the attack.

EULAR Recommendation 10

Uricosuric agents such as probenecid and sulphinpyrazone can be used as an alternative to allopurinol in patients with normal renal function but are relatively contraindicated in patients with urolithiasis; benzbromarone can be used in patients with mild to moderate renal insufficiency on a named patient basis but carries a small risk of hepatotoxicity.

One patient was on benzbromarone in view of renal impairment.

EULAR Recommendation 11

Prophylaxis against acute attacks during the first months of urate lowering therapy can be achieved by colchicine (0.5–1 mg daily) and/or an NSAID (with gastro-protection if indicated).

Seventy-nine percent were documented to have received adequate cover with NSAIDs or colchicine as prophylaxis against an acute attack during the first month of starting ULT.

EULAR Recommendation 12

When gout associates with diuretic therapy, stop the diuretic if possible; for hypertension and hyperlipidaemia consider use of losartan and fenofibrate, respectively (both have modest uricosuric effects).

Sixty-seven percent were documented to have hypertension, 10% of these were on losartan, 23% were on ACE inhibitors (perindopril and enalapril) 7% were on a thiazide diuretic, 17% were on a loop diuretic and in 10% treatment was unrecorded. No patients were on fenofibrate.

Discussion

Better understanding and advancements in treatment have made cure of gout arthropathy an achievable goal. Despite this, the management of chronic gout has been generally found to be suboptimal and poorly concordant with the EULAR recommendations.⁵

Numerous factors may contribute to this outcome. These include lack of interest in the disease due to unavailability of new therapeutic agents, poor compliance with ULT, and lack of disease awareness by patients and doctors. Patients often have multiple co-morbidities so gout is seen as a less important disease.

Indications about when and how to start treatment and achievement of uric acid thresholds have changed over the years and may have lead to confusion among clinicians. Some clinicians would start ULT after the first attack with the presumption that early treatment should result in easier control and possibly cure, while others would start therapy if attacks are frequent. Patients who were on Allopurinol for hyperuricaemia despite having never had any manifestations of gout were not included in our study.

Gout is mainly managed at a primary care level. However a number of patients are referred to secondary care. These include patients in whom there is a problem achieving the primary goals of gout management whether this is control and prevention of the clinical manifestations or control of serum urate levels.

Our cohort is more likely to represent this group of patients who have more resistant or difficult gout. Difficult gout is often avoidable. However some cases of difficult gout occur because of limitations of current therapies. Acute attacks are very painful and patients are likely to seek immediate help from their general practitioner or self-medicate.

Once a patient is diagnosed with gout an individualised long term management plan based on the patient's characteristics and expectations incorporating both pharmacological and non pharmacological therapies is warranted.

The aim of ULT is to achieve cure by reducing the overall tissue levels of uric acid, dissolve existing crystals and stopping new monosodium urate crystals formation. Compliance with ULT is known to be poor and long term adherence and persistence is required to achieve a good outcome. The benefit obtained is independent of disease severity.¹² Evidence of effect has been demonstrated for both pharmacological^{13,14} and non pharmacological therapies.¹⁵

In the majority of patients advice about alcohol reduction was documented in the case notes. However, documentation about advice given regarding weight loss, diet and exercise was less consistent. Few studies have looked at the provision of advice about coexistent risk factors in gout. In a general practice study less than 30% of patients were given advice regarding alcohol and diet¹⁶ while recall of advice about alcohol reduction was only found in 40% in another study.⁵ There is a broad consensus that education about lifestyle modifications, adherence and efficacy improve outcomes across many chronic diseases, although long term benefits have not been studied. Alcohol is an independent risk factor for gout¹⁷ while the association of purine rich foods¹⁸ and weight reduction^{19,20} with gout have also been demonstrated.

Gout has been linked with diabetes, hypertension and hyperlipidaemia.²¹ These are all important modifiable risk factors for cardiovascular disease together with smoking. Good quality care needs to address and manage all these co-morbidities. Hypertension and smoking were the least risk factors to be addressed. Choice of drugs is another important issue. Losartan and fenofibrate have both been shown to moderately reduce uric acid levels apart from their blood pressure lowering^{22,23} and lipid lowering effects respectively.²⁴

The therapeutic goal of a serum urate level below 360 µmol/l was achieved in less than half of our cohort. Possible reasons could be resistant gout, inadequate attention to modifiable lifestyle changes, poor compliance with ULT, concern about hypersensitivity reactions to allopurinol and failure to increase the allopurinol dose as needed. In our study compliance was not assessed but poor adherence to ULT has been shown in a number of earlier studies.^{25,26} Allopurinol hypersensitivity syndrome (AHS) is a rare but potentially life threatening disease characterised by an erythematous desquamating rash, fever, hepatitis, eosinophilia and worsening renal function. AHS may be barrier to use of ULT. In one of our patients, AHS was limited to a skin reaction and allopurinol desensitisation was effective (Farrugia *et al*; unpublished data). Allopurinol 300mg was the most common prescribed dose, similar to other studies.^{16,27} However, the allopurinol dose should be increased till serum uric acid levels fall below the target threshold given that a number of patients persist in having high serum uric acid levels despite treatment with 300mg daily.

No patients were on alternative uricosuric therapy such as probenecid and sulphinyprazole while benzbromarone was used in one patient who had impaired renal function. The new selective xanthine oxidase inhibitor febuxostat or the recombinant urate oxidase pegloticase are currently not available in Malta. The awareness of the sparse local availability of alternatives to allopurinol could be another reason why patients with difficult gout are not being referred to secondary care by general practitioners. Another reason could be that patients with renal impairment are being managed directly by nephrologists without referral to the rheumatologists.

A major limitation in our study was the small number of patients recruited. The reasons for such small numbers given the known prevalence of gout are likely to be multifactorial. These include prevalent management of gout in primary care as well as by other specialist in hospital practice such as nephrologists, internists and orthopaedic surgeons. Additionally, patients were recruited on an ongoing basis as and when they presented to rheumatology clinic. Lack of a patient database of patients attending Rheumatology clinic may have led to ascertainment bias with a number of cases being missed. Finally, the retrospective nature and reliance on documentation may not necessarily give the complete picture as advice may well have been given although not documented. There was no mention whether written advice/leaflets were given which might help patients to remember the information given.

For audits to be successful it is imperative to create the right environment where audit is an integral part of clinical risk management, quality control and ultimately clinical governance. Organisations must recognise the need for appropriate funding and support for this to happen. The most common barriers to successful audit include lack of resources, lack of expertise, problems between groups and inadequate protected time for health care team to participate.²⁸ Setting up of a central clinical audit office as found in many countries would be very helpful to

provide a structured audit programme, coordinate activity and improve the quality of healthcare.

Successful audits require improvements to be made and sustained so as to close the audit cycle. For this reason as part of this audit a data collection proforma has been formulated for use in clinical practice encompassing the EULAR recommendations and made available on the Mater Dei Hospital intranet (KURA). Suggestions to improve the quality of care for patients with gout include increasing awareness and education programmes to doctors about the need for tighter control, and earlier referral of difficult gout. EULAR recommendations need to be disseminated to primary care physicians where most of the management of gout clearly takes place. Patients should be provided with written information and referred to allied health professionals if needed for lifestyle modification advice. Future plans include reauditing to assess whether further improvement are needed and monitoring to sustain improvements.

Conclusions

Current treatment of gout is unsatisfactory and below par with the EULAR recommendations. Documentation of lifestyle modifications advice is infrequent except for alcohol reduction. A significant number of patients on allopurinol still have hyperuricaemia implying that more aggressive pharmacological and non-pharmacological management is required to improve the standard of care.

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Bayer-Schering Pharma prize in obstetrics & gynaecology

The Bayer-Schering Pharma Prize in Obstetrics & Gynaecology for the academic year 2009-10 was awarded to Dr. André Zammit, who obtained the highest aggregate mark in the speciality during the final examinations of the Medicine and Surgery course. The prize was hotly contested by the three other student candidates who were also awarded a distinction grade during these examinations – Dr. Lorna Attard, Dr. Christina Azzopardi, and Dr. Marija Farrugia. Their achievement has been rewarded by a small book token. Congratulations are due to all these candidates. In the accompanying photograph, Dr. Zammit is seen receiving a cheque for €250 from Professor Charles Savona-Ventura, Head of Obstetrics and Gynaecology at the Medical School with Mr. Simon Delicata, representing Bayer-Schering Pharma who sponsored the prize. Bayer Schering Pharma AG is an international healthcare company that is committed to sustainable development in various fields of healthcare including Gynaecology.

