**Management of gout by UK rheumatologists: a British Society for Rheumatology national audit**

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**Short running title:** BSR national gout audit

**Abstract**

**Objectives:** To assess the concordance of gout management by UK rheumatologists with evidence-based best-practice recommendations.

**Methods:** Data were collected on patients newly-referred to UK rheumatology out-patient departments over an eight-week period. Baseline data included demographics, method of diagnosis, clinical features, comorbidities, urate-lowering therapy (ULT), prophylaxis and blood tests. Twelve months later, the most recent serum uric acid level was collected. Management was compared to audit standards derived from the 2006 EULAR recommendations, 2007 BSR/BHPR guideline and the NICE febuxostat technology appraisal.

**Results:** Data were collected for 434 patients from 91 rheumatology departments (mean age 59.8 years, 82% male). Diagnosis was crystal-proven in 13%. Of 106 taking a diuretic, this was reduced/stopped in 29%. ULT was continued/initiated in 76% of those with ≥1 indication for ULT. One hundred and fifty-eight patients started allopurinol: the starting dose was most commonly 100mg daily (82%), in those with eGFR<60ml/min the highest starting dose was 100mg daily. Of 199 who started ULT, prophylaxis was co-prescribed for 94%. Fifty patients started a uricosuric or febuxostat: 84% had taken allopurinol previously. Of 44 commenced on febuxostat, 18% had a history of heart disease. By 12 months, serum uric acid levels ≤360μmol/L and <300μmol/L were achieved by 45% and 25% respectively.

**Conclusion:** Gout management by UK rheumatologists concords well with guidelines for most audit standards. However, fewer than half of patients achieved a target serum uric level over 12 months. Rheumatologists should help ensure that ULT is optimised to achieve target serum uric acid levels to benefit patients.

**Key words:**

Gout Management Rheumatology

Audit Urate-lowering therapy Allopurinol

**Introduction**

Gout is the most prevalent inflammatory arthritis [1]. However, despite well-understood pathophysiology, readily available effective medications, and achievable biochemical treatment targets, treatment remains poor. Only one-third of patients with gout in UK primary care received ULT from 1997-2012 and only 38% of these achieve a target serum uric acid (SUA) ≤360µmol/L, despite publication of UK and European management guidelines during this period [1-6]. Poor uptake occurred even though 44% of patients fulfilled criteria for ULT one year after diagnosis and 87% by five years [7]. Yet in a recent proof-of-principle study, 92% of patients reached the target level following nurse-led treatment showing that treatment-to-target is achievable [8].

Less is known about gout management by rheumatologists. A small number of studies from the USA and Europe show that in rheumatology practice, diagnosis is infrequently crystal-proven and initial allopurinol dosing is uncommonly renal function-adjusted whereas prophylactic colchicine is very commonly co-prescribed with ULT [9-11]. A target SUA level ≤360µmol/L was achieved in 78% of patients in a study from Ireland but in fewer than half in Spain and the USA [9,12,13].

This national audit aimed to assess the concordance of out-patient gout management by UK rheumatologists with evidence-based recommendations published by the British Society for Rheumatology (BSR) and European League Against Rheumatism (EULAR) and the National Institute for Health and Care Excellence (NICE) Febuxostat technology appraisal (TA 164) [5,6,14,15].

**Methods**

***Design***

All UK rheumatology units were invited to participate in the audit. Data were collected prospectively on all patients with gout, newly-referred to rheumatology and seen in out-patient clinics over an eight-week period between 06/05/2013 and 28/06/2013. Anonymised data were collected at the time of consultation and entered onto a web-based proforma housed on a secure server. Units were not compensated for participation but reminders were sent during the audit period to maximise participation. The audit was deemed not to require research ethics approval as per guidance from the NHS Health Research Authority [16]. The audit protocol was reviewed and approved by the BSR Standards, Audit and Guidelines Working Group.

***Data collection***

The proforma requested information about demographic details (age, gender), method of diagnosis (clinical, radiographic, microscopy of aspirated synovial fluid/tophaceous material), clinical features (tophi, number of attacks in the preceding year), comorbidities, current and previous ULT, ULT initiated including starting dose, use of prophylactic drugs (non-steroidal inflammatory drugs (NSAID), colchicine, corticosteroids), diuretic use, blood tests (SUA level, serum creatinine, estimated glomerular filtration rate (eGFR)), and follow-up plan. Follow-up data collected 12 months later included the most recent SUA level (where available).

***Audit standards***

Audit standards (AS) were determined *a priori* based on the 2006 EULAR recommendations for the diagnosis and management of gout, 2007 BSR guideline for the management of gout, and NICE TA164 [5,6,14,15]. Standards pertained to diagnosis (AS1, AS2), diuretic cessation (AS3), indications for ULT (AS4), allopurinol starting dose (AS5, AS6), prophylaxis (AS7), use of uricosuric drugs and febuxostat (AS8), use of febuxostat in patients with heart disease (AS9), and whether target SUA levels were achieved (AS10, AS11) (**table 1**).

***Statistical analysis***

Characteristics of the study sample were described using simple descriptive statistics: mean (standard deviation [SD]) or median (interquartile range, IQR) for continuous variables and frequency (%) for categorical variables. The concordance with each audit standard was assessed by calculating the frequency (%) of eligible patients fulfilling each audit standard.

**Results *Baseline patient characteristics***

Data were entered for 434 patients from 91 rheumatology departments across the UK, including teaching and district general hospitals. Mean age was 59.8 years (SD 15.1); 356 (82%) were male. Hypertension, renal disease, hyperlipidaemia and heart disease were common (**table 2**). One hundred and thirty six patients (31%) were taking allopurinol at the time of their rheumatology appointment, few were taking other ULTs. Diuretics were taken by 106 patients (24%). Mean SUA level was 496 (SD 128). Baseline SUA level was ≤360µmol/L in 65 (15%) and <300µmol/L in 36 (8%). Median number of acute attacks of gout in the preceding 12 months was 3 (IQR 1, 5).

***Audit standards - baseline***

*AS1: Clinical diagnosis is acceptable*

*AS2: Definitive diagnosis requires crystal examination*

The diagnosis of gout was made on clinical grounds in 362 (83%). One hundred and eight (25%) had clinically-evident tophi and 56 (13%) had radiographic features of gout. Diagnosis was based on microscopic identification of monosodium urate (MSU) crystals in 57 (13%).

*AS3: In patients on diuretic therapy, this should be stopped or the dose reduced if possible*

Of 106 patients taking a diuretic, this was stopped or the dose reduced in 30 (28%). There were 26 patients taking a diuretic who did not have cardiac or renal failure. Of these, the diuretic was stopped or the dose reduced in 15 (58%).

*AS4: Indications for urate-lowering therapy are ≥2 attacks over 1 year, gouty tophi, radiographic damage, eGFR < 80ml/min, uric acid renal calculi or continuing diuretic treatment*

Of 382 patients with at least one indication for ULT, 291 (76%) either continued or were commenced on ULT. For individual indications, the percentages continuing or commencing ULT were: tophi 81% (87 out of 108), ≥2 attacks in the last year 79% (207/261), eGFR<80ml/min 74% (157/212), continuing diuretic use 71% (56/79), renal calculi 67% (8/12) and radiographic joint damage 66% (37/56).

*AS5: Allopurinol should be started at low dose (50-100mg daily)*

One hundred and fifty-eight patients were commenced on allopurinol. The starting daily dose was 50mg in ten (6%), 100mg in 129 (82%), 300mg in 14 (9%), and unspecified in five (3%).

*AS6: Allopurinol should be started at lower doses in patients with renal impairment*

Of 42 patients with chronic kidney disease (CKD) stages 3-5 (eGFR<60ml/min) who started allopurinol, the starting daily dose was 50mg in seven (17%), 100mg in 33 (79%) and unspecified in two (5%).

Six patients with CKD stages 4 or 5 (eGFR<30ml/min) started allopurinol. Of these, the starting daily dose was 50mg in two (33%) 100mg in three (50%) and unspecified in one (17%).

*AS7: Colchicine or NSAID prophylaxis should be co-prescribed at ULT initiation*

ULT was initiated in 199 patients. Of these, 187 (94%) were co-prescribed prophylaxis. Colchicine was most commonly used (122, 61%) followed by a NSAID (53, 27%), oral corticosteroids (31, 16%) and intramuscular corticosteroids (13, 7%).

*AS8: Following allopurinol intolerance or inefficacy, treat gout with sulphinpyrazone, benzbromarone, probenecid or febuxostat*

Sulphinpyrazone was started in two patients, both had previously taken allopurinol. Of four patients started on benzbromarone, 3 (75%) had previously taken allopurinol. Forty-four patients were commenced on febuxostat. Of these, 37 (84%) had previously taken allopurinol. None were commenced on probenecid.

*AS9: Febuxostat is not recommended for patients with ischaemic heart disease or congestive cardiac failure*

Of 44 patients commenced on febuxostat, 8 (18%) had ischaemic heart disease or congestive cardiac failure.

***Planned clinic follow-up appointment***

A follow-up appointment in rheumatology was proposed for 316 patients (73%). Ninety-two patients (21%) were discharged to primary care. Follow-up was left “open”, to be arranged according to the patient’s need, in 23 (5%).

***12-month follow-up***

Twelve-month follow-up data were received for 219 patients (50%). These patients had tophi at baseline more frequently than those without follow-up data (29% versus 21%) but did not differ by age, gender, number of attacks in the 12 months preceding baseline, previous allopurinol use, or baseline SUA or renal function.

***Audit standards – 12-month follow-up***

*AS10: Target serum uric acid level is ≤360μmol/L*

*AS11: Target serum uric acid level is <300μmol/L*

Of 219 patients with 12-month follow-up data, a follow-up SUA level was available for 157 (72%) and not performed in 40 (18%). Whether or not a follow-up SUA had been checked was unknown in 22 (10%). Of the 197 patients in whom it was known whether a follow-up SUA level was performed, target SUA levels of ≤360μmol/L and <300μmol/L were achieved by 89 (45%) and 50 (25%) respectively.

**Discussion**

In this first national audit of gout management by UK rheumatologists, ULT initiation in patients with indications (AS4), allopurinol starting dose and renal-adjustment (AS5, AS6), use of prophylaxis when initiating ULT (AS7), and use of uricosurics and febuxostat (AS8, AS9) concorded well with guidelines [5,6,14,15]. Few patients were diagnosed by MSU crystal identification (AS2). Cessation or reduction of diuretics (AS3) was infrequently recommended, even amongst patients without cardiac or renal failure. Our most important finding is that target SUA levels ≤360μmol/L (AS10) and <300μmol/L (AS11) were achieved by only 45% and 25% of patients respectively. This audit could not ascertain why target levels were infrequently reached but reasons could include patients being discharged, rheumatologists not up-titrating ULT, poor adherence, patient non-attendance for appointments or blood tests, or treatment side-effects.

Our finding that gout diagnosis was based upon crystal identification in only 13% of patients (AS2) is similar to studies undertaken in Spain (26%) and France and Greece (6%) [9,11]. Most patients initiating allopurinol were dosed appropriately for renal function (AS5, AS6) contrasting with Spain where 52% of patients receiving allopurinol were initiated at low-dose (≤100mg daily) [9] and the USA where 92% of patients with moderate-severe kidney disease starting allopurinol commenced at a dose >50mg daily [11]. However, renal-adjusted dosing often fails to achieve target SUA levels and a recent randomised trial supports the effectiveness and safety of higher doses [17,18]. In our study, 94% of patients who commenced ULT were co-prescribed prophylaxis (AS7) similar to the USA (90%) and France and Greece (70%) [10,11]. The proportion who achieved a target SUA≤360µmol/L was similar to studies from Spain (41%) and the USA (35%) but lower than a rheumatology sub-specialty gout clinic in Ireland (78%) [9,12,13]. Compared to audits of management in UK primary care [3,4], rheumatologists more frequently initiated ULT when tophi were present (81% versus 20%), started low-dose allopurinol (88% versus 62%), and co-prescribed prophylaxis with ULT (94% versus 25%), however, GPs more commonly recommended diuretic cessation/reduction (28% versus 36%). Most importantly, the proportion who achieved a target SUA level ≤360μmol/L was only slightly higher than that achieved in primary care (38% of those treated with allopurinol) [4].

 Strengths of this audit include the national setting and sample size. Patients were entered from most UK rheumatology units. Data were entered at the time of consultation making accurate recording likely. However, clinicians’ awareness of the audit could have influenced clinical behaviour, potentially overestimating guideline concordance. Caveats regarding data collection include not ascertaining whether rheumatologists were trainees or fully-trained or use of ultrasonography or dual-energy CT in diagnosis. Provision of dietary and lifestyle advice was not assessed because many rheumatology units do not routinely quantify dietary intake and body mass index and clear thresholds for intervention are lacking [5,6,14], preventing assessment of the appropriateness of such advice. We asked about renal calculi and radiographic features of gout, rather than specifying uric acid calculi and radiographic damage, potentially under-estimating how many people with these indications received ULT (AS4). Renal calculi (67%) and radiographic damage (66%) were the indications with the lowest proportions receiving ULT. Twelve-month follow-up data were available for only half of the baseline sample, although these differed from those lost-to-follow-up only by having more frequent tophi.

 Frequent suboptimal gout management in UK primary care is replicated in rheumatology clinics. Further research should investigate reasons for suboptimal management in rheumatology and examine how best to configure services to facilitate optimum evidence-based ULT. Our experience is that follow-up of patients with gout in rheumatology is very variable, with some rheumatologists anecdotally reporting local commissioning arrangements preventing follow-up of patients with gout. This suggests that our findings reflect suboptimal management in both rheumatology and primary care, indicating that rheumatologists should improve management in secondary care but also work with primary care colleagues to develop better systems to treat gout across the health economy. Subsequent audits should compare against recently updated EULAR and BSR recommendations [19,20]. Our findings and these new guidelines’ recommendation that ULT should be offered to all patients with gout at first diagnosis should serve as a “call-to-arms” to all rheumatologists to take gout seriously and ensure that ULT is initiated, escalated and monitored appropriately to achieve target SUA levels to benefit patients.

**KEY MESSAGES**

* Most aspects of gout management concorded well with published guidelines.
* Fewer than one-half of patients achieved the target serum uric acid level.

**CONFLICT OF INTEREST STATEMENT**

All authors declare no competing interests.

**FUNDING STATEMENT**

We have no funding to declare.

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**Table 1 Audit Standards (AS)**

|  |  |
| --- | --- |
| **Audit standard (AS)** | **Guideline** |
| AS1: Clinical diagnosis is acceptable | EULAR |
| AS2: Definitive diagnosis requires crystal examination | EULAR |
| AS3: In patients on diuretic therapy, this should be stopped or the dose reduced if possible | EULAR |
| AS4: Indications for urate-lowering therapy are: * ≥ 2 attacks over 1 year
* Gouty tophi
* Radiographic damage
* eGFR < 80ml/min
* uric acid renal calculi
* continuing diuretic treatment
 | BSR/BHPRBSR/BHPR and EULAREULARBSR/BHPRBSR/BHPRBSR/BHPR |
| AS5: Allopurinol should be started at low dose:* 50-100mg daily
* 100mg daily
 | BSR/BHPREULAR |
| AS6: Allopurinol should be started at lower doses in patients with renal impairment | BSR/BHPR and EULAR |
| AS7: Colchicine or NSAID prophylaxis should be co-prescribed at ULT initiation | BSR/BHPR and EULAR |
| AS8: Following allopurinol intolerance or inefficacy treat gout with:* Sulphinpyrazone
* Benzbromarone
* Probenecid
* Febuxostat
 | BSR/BHPR and EULARBSR/BHPR and EULAREULARNICE TA 164 |
| AS9: Febuxostat is not recommended for patients with ischaemic heart disease or congestive cardiac failure | NICE TA 164 |
| AS10: Target serum uric acid level is ≤360μmol/L | EULAR |
| AS11: Target serum uric acid level is <300μmol/L | BSR/BHPR |
| AS, Audit Standard; BHPR, British Health Professionals in Rheumatology; BSR, British Society for Rheumatology; eGFR, estimated glomerular filtration rate; EULAR, European League Against Rheumatism; NICE, National Institute for Health and Care Excellence; NSAID, non-steroidal anti-inflammatory drug; TA, Technology appraisal |

Table 2 Patient baseline characteristics

|  |  |
| --- | --- |
|  | **n (%)a** |
| Age, years; mean (SD)  | 59.8 (15.1) |
| Male gender | 356 (82) |
| Hypertension | 214 (49) |
| Diabetes mellitus | 59 (14) |
| Renal disease | 119 (27) |
| Hyperlipidaemia | 115 (27) |
| Renal calculi | 12 (3) |
| Renal transplant | 5 (1) |
| Ischaemic heart disease | 86 (20) |
| Cardiac failure | 34 (8) |
| Current diuretic use | 106 (24) |
| Serum uric acid, μmol/l; mean (SD) | 496 (128) |
| Serum uric acid ≤360μmol/l | 65 (15) |
| Serum uric acid <300μmol/l | 36 (8) |
| Serum creatinine, μmol/l; mean (SD) | 104 (45) |
| CKD stage≥3 (eGFR<60ml/min) | 128 (30) |
| Number of attacks in last 12 months, median (IQR) | 3 (1,5) |
| Current urate-lowering therapy |  |
|  | Allopurinol | 136 (31) |
|  | Febuxostat | 6 (1) |
|  | Sulfinpyrazone | 1 (1) |
|  | Probenecid | 1 (1) |
|  | Benzbromarone | 0 |
|  | No urate-lowering therapy | 289 (67) |
| CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; IQR, inter-quartile range; SD, standard deviationa data are n(%) unless otherwise stated |