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Pitfalls in management of acute gouty attack, a qualitative research conducted in Makah Region – Saudi Arabia



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KEYWORDS

Acute gouty attack;
Allopurinol;
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Guidelines

Abstract Objective: To probe doctors' attitudes and reveal wrong perception in the management of acute gouty attacks.

Design: A descriptive study using a designed questionnaire that was completed through face to face interviews in hospitals, health units and polyclinics in the Makah Region.

Method: This is a qualitative study of treatment by 99 doctors conducted in the second half of 2012. The sample included orthopedists, rheumatologists, general practitioners and family physicians.

Results: 72 (72.7%) doctors started treatment of acute attacks with mono-therapy. 58 doctors (58.6%) started with NSAIDs. Indomethacin was the most frequent prescribed NSAIDs. 18 doctors (18.2%) prescribed Allopurinol as the first drug of choice.

42 doctors (43.8%) started Allopurinol "2 weeks after acute attack". 31 doctors (32.3%) mentioned that they used 100 mg daily dose. 41 doctors (42.7%) mentioned that the starting dose depends on the patient's condition. Allopurinol was prescribed once daily by 37 doctors (38.9%). 53 doctors (55.8%) used Allopurinol as prophylaxis.

The most frequent test requested was a 24-h urine test for uric acid. In case patients were already on Allopurinol and presented with an acute attack of gout; 33 doctors (34.7%) tended to "increase the dose".

The most important factor in adjusting the Allopurinol dose is Serum Uric Acid Level. 37 doctors (39.4%) mentioned that they ask for Serum Uric Acid Level every 3–4 weeks.

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Conclusion: There were common pitfalls that need a training program to increase awareness of doctors with general guidelines and recommendations. The most critical pitfalls include prescribing Allopurinol in acute gouty attacks and ignoring the Renal Function Test.

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1. Introduction

Gout is a pathological and clinical disorder which is mainly characterized by hyperuricemia; which is an increase in serum urate levels of 7.0 mg/dl in men or greater than 6.0 mg/dl in women.^{1,2} Tophi are a pathognomonic feature of gout detectable by physical examination and/or by imaging approaches and pathology examination.^{3–5} Typically, the disease initially presents as acute episodic arthritis then manifests as chronic arthritis of one or more joints.^{1,2}

Gout is one of the most common rheumatic diseases of adulthood, with a self-reported prevalence. In USA it was recently estimated as 3.9% of adults (~8.3 million people).⁶ In Saudi Arabia, 8.42% of the study population had hyperuricemia but no case of gout was found.⁷ Compared with women, men have a four- to nine-folds increased risk of developing gout.⁸

1.1. Treatment of acute attacks

The choice mainly depends on whether the patient has concomitant health problems or not (e.g.: peptic ulcer or renal insufficiency). There are various treatment options, such as corticosteroids, NSAIDs, ACTH and colchicine. Colchicine is now rarely used. An intra-articular steroid injection is preferred when an easily accessible large joint is involved and when comorbid conditions exist limiting the use of colchicine and NSAIDs. Reasonably septic arthritis must be excluded.^{9–11}

Patients with no underlying health problems and having an acute gouty attack, are usually prescribed with NSAIDs as drugs of choice. Most NSAIDs can be used, however, indomethacin is the NSAID conventionally chosen for acute gout. An agent with a quick onset of action is selected. Aspirin is not recommended since it can lengthen and strengthen the acute attack, since it can change Uric Acid Levels.

1.2. Colchicine

Is now less commonly used than NSAIDs, due to its narrow therapeutic window and risk of toxicity. Although, it was once the treatment of choice for acute gout.^{12,13}

1.3. Combination therapy

If the patient does not have an adequate response to initial therapy with a single drug, guidelines advice that adding a second appropriate agent is acceptable. Using combination therapy from the start is appropriate for an acute, severe gout attack, particularly if the attack involves multiple large joints or is poly-articular.¹⁴

1.4. Treatment of chronic gout

As first line pharmacological approach, guidelines recommend either Allopurinol or febuxostat with xanthine oxidase inhibitor therapy with gout patients who have renal disease.

Guidelines advice, however, state that mono-therapy in patients with creatinine clearance less than 50 mL/min with probenecid is not a first line choice,¹⁵ since probenecid may also cause drug interactions.

1.5. Prophylaxis

Some drugs can alter the levels of tissue and serum uric acid, causing acute attacks of gout, such as probenecid, Allopurinol and febuxostat. Accordingly low dose NSAID or colchicine is given for 6 months at least in order to decrease this unfavorable effect. Low doses of prednisone are sometimes given when the patients cannot take either colchicine or NSAIDs.

1.6. Allopurinol

It should be started at a low dose of 100 mg per day, but can be titrated to 800 mg per day as necessary for a patient to achieve the target SUA level of 6.0 mg/dl.^{16–18} It has been recommended that patients with renal impairment should receive lower doses. Allopurinol can be used in combination with probenecid. Stopping Allopurinol is not recommended during acute attacks.¹⁹

Aim of the study to probe doctors' attitudes and reveal wrong perception in the management of acute gouty attacks.

2. Methodology

This is a qualitative research in which 99 physicians were face-to-face interviewed through a structured questionnaire. Physicians were from the Makah Region – Saudi Arabia and essentially involved in gout management. Interviews were conducted in the second half of 2012.

The objective of the study is to describe physicians' prescribing habits in the treatment of gout and whether or not matching the general guidelines and recommendations.

The sample included orthopedists, rheumatologists, general practitioners and family physicians withdrawn from hospitals, health units and polyclinics.

3. Results

99 doctors were asked 17 questions about their experience with acute gout attack.

Table 1 shows treatment of choice; mono vs. combined therapy, first line of choice and first NSAID of choice.

The most common indication of initiating urate lowering agents in patients with acute gouty attack is Serum Uric Acid Level, mentioned by 67 doctors (68.4%) followed by the presence of Tophi (44–44.9%), history of Renal Stones (41–41.8%) and history of 2 or more severe attacks (36–36.7%). Less frequent indications are history of renal failure (28–28.6%),

24 h urine uric acid level (20–20.4%), Joint X-ray changes (19–19.4%), age (15–15.3%), history of co-morbid diseases (14–14.3%) and history of severe single attack (13–13.3%). The least frequent indications were sex, thyroid disease, specific indication and race. Each doctor mentioned an average of 3.2 indications.

Table 2 shows the use of ULT; Treatments used as a prophylaxis to prevent recurrent attacks, when doctors start ULT, Starting Dose of ULT (Allopurinol) and Frequency of using ULT per day.

Table 3 shows tests that doctors like to order in following up patients.

In case the patient was already on Allopurinol and presented with an acute attack of gout, 33 doctors (34.7%) tend to “increase the dose”, 30 doctors (31.6%) tend to “stop it and continue after the attack”, 23.2% tend to “continue on the same dose”, 5.3% “decrease the dose” and 5.3% will stop it completely.

The most important factor in adjusting Allopurinol dose is the Serum Uric Acid Level, mentioned by 76 doctors (79.2%), Renal Function (serum creatinine) mentioned by 56 doctors (58.3%), “number of attacks” mentioned by 27 doctors (28.1%) and “24-h Urine Uric Acid Level” mentioned by 25 doctors (26%). Each doctor mentioned an average of 1.91 answers.

Frequency of serum uric acid test; 1 doctor (1.1%) “every 1–2 weeks”, 37 doctors (39.4%) mentioned “every 3–4 weeks”, 19 doctors (20.2%) “every 5–6 weeks”, 29 doctors (30.9%) “every 7–8 weeks” and 8 doctors (8.5%) mentioned that they do not use it for follow up.

The most important precipitating factors that doctors consider are Alcohol (mentioned by 60 doctors 62.5%), obesity (53–55.2%), thiazide or lasix (48–50%) and low dose of aspirin (18–18.8%).

Factors which are considered when prescribing uricosuric agents are; Renal Function Tests (mentioned by 73 doctors – 76%), History of Renal Stones (57–59.4%), Measuring 24-h Urine Uric Acid (39–40.6%) and age (31–32.3%). Each doctor mentioned an average of 2.15 answers.

4. Discussion

A sample of 99 doctors from the Makah Region were face-to-face interviewed to describe their attitudes in the management of acute gouty attacks and to find out whether doctors follow general guidelines and recommendations or not.

72 doctors (72.7%) started the treatment of acute gouty attacks with mono-therapy which matches to general guidelines and recommendations.¹⁵

58 doctors (58.6%) started treatment with NSAIDs which matches the guidelines. 34 doctors (34.3%) use Oral Colchicine which is the second choice of general guidelines and recommendations. 18 doctors (18.2) use Allopurinol which is not recommended by the guidelines in acute attacks and is considered a big mistake in the management of acute attacks and 14 doctors (14.1%) use steroids which is the third choice of the guidelines.¹⁵

Indomethacin is the most frequent prescribed NSAID, mentioned by 41 doctors (41.8%) followed by Profen and Diclofenac by 21 doctors (21.4%) for each of them followed by Meloxicam by 10 doctors (10.1%) and Celecoxib & Naproxen by 6 doctors (6.1%) for each of them (Table 1).

Table 1 Treatment of choice of acute gouty attacks; mono vs. combined therapy, first line of choice and first NSAID of choice.

	Number	%
<i>Choice of mono vs. combined therapy</i>		
Mono-therapy	72	72.7
Combined therapy	27	27.3
Total	99	100
<i>First treatment of choice^a</i>		
NSAIDs	58	58.6
Oral Colchicine	34	34.3
Allopurinol	18	18.2
Steroid	14	14.1
Uricosuric Agent	7	7.1
IV Colchicine	6	6.1
None	1	1.0
Total	138.00	139.4
<i>First NSAID of choice^b</i>		
Base	99	
Indomethacin	41	41
Profen	21	21
Diclofenac	21	21
Meloxicam (Mobic)	10	10
Celecoxib	6	6
Naproxen	6	6
Piroxicam	2	2
Others	2	2
Total Responses	109	110

Others include; Paracetamol and colchicine.

^a Each doctor mentioned an average of 1.39 treatments.

^b Each doctor mentioned an average of 1.10 NSAIDs.

Only 53 doctors (55.8%) used Allopurinol as prophylaxis to prevent recurrent attacks which matches with guidelines. 22 doctors (23.2%) use uricosuric agents, 16 doctors (16.8%) Colchicine and 12 doctors (12.6%) use NSAIDs.^{16–18}

42 doctors (43.8%) started Allopurinol 2 weeks after acute attack which matches with guidelines. On the other hand, 12 doctors (12.5%) started Allopurinol 4-weeks later, 29 doctors (30.2%) started Allopurinol “Immediately” which is also a common mistake and does not match the guidelines.^{16–18}

General guidelines and recommendations advise that the dosage of Allopurinol should be started at a low dose of 100 mg per day.^{16–18} Only 31 doctors (32.3%) mentioned that they started with a 100 mg dose while 9 doctors (9.4%) started with 200 mg and 18 doctors (18.8%) started with 300 mg/day. 41 doctors (42.7%) refused to recommend a certain dosage as a starting dose as it depends on the patient’s condition.

Allopurinol is prescribed once daily by 37 doctors (38.9%), which matches with guidelines. BID is reported by 16 doctors (16.8%) and TID by 6 doctors (6.3%). 33 doctors (34.7%) mentioned that it depends on the case while 3 doctors (3.2%) do not use Allopurinol.

Only 44 doctors (45%) consider the Serum Creatinine (Renal Functions) test as a very important test in Allopurinol dose adjustment (Table 3).

Guidelines advise not to stop Allopurinol in case the patient is presented by an acute attack of gout and is already on Allopurinol.¹⁹ However, in our study the results have

Table 2 The use of urate lowering therapy.

	Number	%
<i>Treatments used as a prophylaxis to prevent recurrent attacks^a</i>		
Base	95	
Allopurinol (ULT)	53	56
Uricosuric agent	22	23
Colchicine	16	17
NSAID	12	13
None	9	9
Other	4	4
Total responses	116	122
<i>When doctors start ULT^b</i>		
Base	99	
Immediately	29	29
2 weeks later	42	42
4 weeks later	12	12
Other	14	14
Don't use ULT	2	2
Total responses	99	100
<i>Starting dose of ULT (Allopurinol)^c</i>		
Base	99	
100 mg	31	31
200 mg	9	9
300 mg	18	18
Depend on the case	41	41
Total responses	99	100
<i>Frequency of using ULT per day</i>		
Base	95	
Once daily	37	39
Two times daily	16	17
Three times daily	6	6
Depend on the case	33	35
Don't use ULT	3	3
Total Responses	95	100

^a Each doctor mentioned an average of 1.22 treatments. Others include; diet and according to urine uric acid levels.

^b Others include; 2 or more severe attacks according to 24 h urine uric acid, according to Uric Acid Level, after 6 months, after stabilization in hospital, after the acute attack subsided, depends on the case, 3 weeks later.

^c Each doctor mentioned an average of 1.05 answers.

Table 3 Tests used to follow up.

	Number	%
Base	97	
24 h urine uric acid	62	64
Joint X-ray	49	51
Serum creatinine (Renal Functions)	44	45
Urine analysis	36	37
CBC	27	28
Liver function tests	20	21
Ca level	15	15
ECG	3	3
Others	12	12
None of them	6	6
Total responses	274	282

Each doctor mentioned an average of 2.82 tests.

Others include; serum uric acid, joint fluid, ESR and urine.

shown that 23.2% of the doctors “continue on the same dose”, 34.7% tend to “increase the dose”, 31.6% tend to “stop it and continue after the attack”, 5.3% “decrease the dose” and 5.3% will “stop it completely”. Renal Function Tests and serum uric acid are important factors in adjusting the Allopurinol dose. Only 79.2% of the doctors reported the Serum Uric Acid Level, 58.3% mentioned Renal Function (creatinine), 28.1% mentioned “number of attacks” and 26% mentioned “24-h urine Uric Acid Level”.¹⁵

Guidelines recommend testing the Uric Acid Level every 3–4 weeks to adjust the Allopurinol dose. Only 37 doctors (39.4%) mentioned “every 3–4 weeks”, 19 doctors (20.2%) “every 5–6 weeks”, 29 doctors (30.9%) “every 7–8 weeks” and 1 doctor (1.1%) “every 1–2 weeks”. 8 doctors (8.5%) mentioned that they do not use it for follow up.¹⁹

Factors which are considered when prescribing uricosuric agents are; Renal Function Tests (mentioned by 73 doctors – 76%), History of Renal Stones (57–59.4%), measuring 24-h urine uric acid (39–40.6%) and Age (31–32.3%), which does not match with general guidelines and recommendations.^{16–18}

5. Conclusion

A considerable number of doctors do not follow general guidelines and recommendations in managing acute gouty attacks. There were common pitfalls that need a training program to increase the awareness of doctors with the general guidelines and recommendations.

Common pitfalls were

- Management of acute attacks:
 - **ULT (Allopurinol) should not be given in acute gouty attacks:** 18% of doctors reported that their first drug of choice in acute attack is Allopurinol and 29% reported that they use Allopurinol immediately in acute attacks.¹⁵
 - **Mono-therapy is recommended to start with in acute gouty attacks.** 27% of doctors start with combined therapy in acute attacks.¹⁵
- Prophylaxis therapy:
 - **ULT (Allopurinol) is the drug of choice in prophylaxis against recurrent acute attacks.** After the resolution of the acute attack, only 53 doctors (56% of doctors) reported that they use Allopurinol as prophylaxis.^{16–18}
 - **Allopurinol therapy (ULT) should be started 2-weeks after acute attack as a prophylaxis therapy to prevent recurrence.** Only 44% started Allopurinol “2-weeks after acute attack”.^{16–18}
 - **Allopurinol should be started at a low dose of 100 mg/day.** Only 32% of doctors mentioned that the starting dose of Allopurinol is 100 mg daily.^{16–18}
 - **Allopurinol should be given once daily (OD).** Only 39% of doctors reported that they prescribe Allopurinol once daily.¹⁹
- Allopurinol and recurrent attacks:
 - **In case the patient was already on Allopurinol and presented with an acute attack of gout, Allopurinol should be “continued in the same dose”.** Only 23% of doctors mentioned that they will “continue in the same Dose”.^{16–18}

- Follow up and Allopurinol dose adjustment:
 - **Serum uric acid is essential in Allopurinol dose adjustment.** Only 79% of doctors asked for Serum Uric Acid Level to adjust the dose of Allopurinol.¹⁵
 - **Serum Uric Acid Level testing should be repeated “every 3–4 weeks”.** Only 39% of doctors mentioned that they repeat Uric Acid Level testing “every 3–4 weeks” to adjust the dose of Allopurinol in order to achieve the targeted Uric Acid Level (less than 6mg/dl).¹⁹
 - **Renal Function Test is essential in Allopurinol dose adjustment.** Only 58% of doctors asked for Renal Function Tests to adjust the dose of Allopurinol.^{16–18}

Recommendations

Increase the level of awareness, by doing seminars and printing brochures to correct these misconceptions and pitfalls. Further studies are recommended.

Disclosure

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- (2) Disclosure of competing interest: Not Applicable.
- (3) Disclosure of sponsorship: Not Applicable.

References

1. Neogi T. Clinical practice: gout. *N Engl J Med* 2011;**364**:443, 52.
2. Terkeltaub R. Update on gout: new therapeutic strategies and options. *Nat Rev Rheumatol* 2010;**6**:30, 8.
3. Dalbeth N, Aati O, Gao A, et al. Assessment of tophus size: a comparison between physical measurement methods and dual-energy computed tomography scanning. *J Clin Rheumatol* 2012;**18**:23, 7.
4. Dalbeth N, Clark B, Gregory K, et al. Mechanisms of bone erosion in gout: a quantitative analysis using plain radiography and computed tomography. *Ann Rheum Dis* 2009;**68**:1290, 5.
5. Desai MA, Peterson JJ, Garner HW. Clinical utility of dual-energy CT for evaluation of tophaceous gout. *Radiographics* 2011;**31**:1365, 75.
6. Zhu Y, Pandya BJ, Choi HK. Prevalence of gout and hyperuricemia in the US general population: the National Health and Nutrition Examination Survey 2007–2008. *Arthritis Rheum* 2011;**63**:3136, 41.
7. Al-Arfaj AS. Hyperuricemia in Saudi Arabia. *Rheumatol Int* 2000;**20**(2):61, 4.
8. Annemans L, Spaepen E, Gaskin M, et al. Gout in the UK and Germany: prevalence, comorbidities and management in general practice 2000–2005. *Ann Rheum Dis* 2008;**67**:960–6.
9. Reber P, Crevoisier X, Noesberger B. Unusual localisation of tophaceous gout. A report of four cases and review of the literature. *Arch Orthop Trauma Surg* 1996;**115**(5):297–9.
10. Schapira D, Stahl S, Izhak OB, et al. Chronic tophaceous gouty arthritis mimicking rheumatoid arthritis. *Semin Arthritis Rheum* 1999;**29**(1):56–63.
11. Shogan CP, Folio CL. Tophaceous gout and rheumatoid arthritis awareness. *J Am Osteopath Assoc* 2008;**108**(7):352, 3.
12. Medsafe Pharmacovigilance Team. Colchicine: lower doses for greater safety Publishing; 2005. www.medsafe.govt.nz/profs/puar-ticles/colchdose.htm (Accessed November 2005).
13. Nuki G. Colchicine: its mechanism of action and efficacy in crystal-induced inflammation. *Curr Rheumatol Rep* 2008;**10**:218–27.
14. Khanna D, Khanna PP, Fitzgerald JD, et al. 2012 American College of Rheumatology guidelines for management of gout. Part 2: Therapy and anti-inflammatory prophylaxis of acute gouty arthritis. *Arthritis Care Res* 2012;**64**(10):1447, 61.
15. Khanna D, Fitzgerald JD, Khanna PP, et al. 2012 American College of Rheumatology guidelines for management of gout. Part 1: Systematic non pharmacologic and pharmacologic therapeutic approaches to hyperuricemia. *Arthritis Care Res* 2012;**64**(10):1431, 46.
16. Chao J, Terkelatub R. A critical reappraisal of Allopurinol dosing, safety and efficacy for hyperuricemia in gout. *Curr Rheumatol Rep* 2009;**11**:135–40.
17. Reinders MK, Haagsma C, Jansen TL, et al. Arandomised controlled trial on the efficacy and tolerability with dose escalation of Allopurinol 300–600 mg/day versus benzobromaron 100–200 mg/day in patients with gout. *Ann Rheum Dis* 2009;**68**(6):892–7.
18. Arrol B, Bennett M, Dalbeth N, et al. More Allopurinol is needed to get gout patients <0.36 mmol/l: a gout audit in the form of a before-after trial. *J prim Health Care*. 2009;**1**(4):315–8.
19. Harris H. Consultant Rheumatologist Review approved on behalf of NHS Fife by the Fife Area Drugs & Therapeutics Committee. *BPJ* 2011;**37**:34–40.