

Clinical Practice in Gout Management Among Filipino General Care Practitioners



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ABSTRACT

Title Evidence-based practice guidelines for gout management is widely available. However, management by general care practitioners is still far from ideal.

Objectives This study aims to determine the current trends in the management of gout among general care practitioners.

Methodology Survey questionnaires randomly distributed to the general membership of the Philippine College of Physicians (PCP) and the Philippine Academy of Family Physicians (PAFP).

Results A total of 390 respondents participated, the majority being females (237, 60.8%) with a mean age of 37.32 + 10.22 (20-75) years, half of them holding practice within Metro Manila. The duration of practice was divided into four categories: 72 (18.5%) had <1 year of practice, 138 (35.4%) had 1-5 years of practice, 64 (16.4%) 5-10 years, and 116 (29.7%) had >10 years of practice. Two hundred and twelve (54%) respondents did not attend gout continuing medical education (CME) activities. More than half agreed with synovial fluid examination to confirm gout diagnosis in patients with acute monoarthritis. During a gout flare, 60.5% preferred colchicine while 15.8% prescribed urate-lowering therapies. Colchicine dosing 3x daily was preferred in 30.3% while 17.4% advocated hourly dose until GI toxicity. Urate-lowering therapies (ULT) 1-2 weeks after the gout flare was preferred by

43.3% while 37.4% opted to give it until serum uric acid level (SUA) normalized before discontinuation. Most respondents (60%) chose prophylactic colchicine when starting ULTs. Half of the respondents (49.7%) aimed for SUA level of 6 mg/dL. In chronic tophaceous gout, 46.9% targeted a higher value of 5 mg/dL.

Conclusion Though gout management has improved among general care practitioners, there were still observed inconsistencies and heterogeneous patterns of practice in the community.

Keywords: gout survey, adherence to gout guidelines, Filipino.

INTRODUCTION

Gouty arthritis accounts for millions of outpatient visits annually and its prevalence is still increasing, especially involving the younger age group. Based on the National Nutrition and Health Survey in 2003, it reported an overall prevalence of gouty arthritis in the general population at 1.6%(1). Using data from the National Hospital Ambulatory Medical Care Survey and National Ambulatory Medical Care Survey from 2002, Krishnan et al. found that in comparison to white ethnicity, Asian ethnicity was related to an increased likelihood of gout diagnosis (odds ratio [OR] 2.7, 95% confidence interval [95% CI] 1.1–7.7)(2). Gout is the most prevalent inflammatory arthritis among Filipinos (3,4).

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The pathogenesis of urate crystal deposition is reasonably well understood, accompanied by appropriate urate-lowering therapy (ULT), and lifestyle advice. The objective of gout management is a cure (3). Nonetheless, many patients continue to experience frequent and recurrent episodes of gout and progression of their disease (5). This is because the condition is often misdiagnosed, or diagnosed late, and treatment is frequently suboptimal. Many international and local guidelines have established evidence-based and consensus guidelines that cover the different spectrums of the disease, its diagnosis, and management. However, despite the provision of these guidelines and advancement in the understanding of gout, management of gout continues to be suboptimal. This study aims to determine the current trends in gout management and adherence of general care practitioners to the 2008 Philippine Gout Guidelines.

MATERIALS AND METHODS

Survey questionnaires were randomly distributed during annual conventions and various roundtable discussions involving members of the Philippine College of Physicians (PCP) and the Philippine Academy of Family Physicians (PAFP) as participants. All the members of both societies were eligible to participate in the study and a random sampling method was done to choose the respondents. All valid data from respondents were included in the analysis.

The survey questionnaire used was adapted from the previous study conducted among general care physicians in the Philippines in 2008 (1). The first Philippine Clinical Practice Guidelines in the Management of Gouty Arthritis included allopurinol only as the urate-lowering therapy available at that time. A minor modification in the questionnaire on the choice of urate-lowering therapy includes febuxostat that was introduced in the market in 2010.

Outcomes

To determine the current trends in the management of gout and its concordance with the Philippine Clinical Practice Guidelines and the differences in gout management practice among physicians across the duration of practice and between those who have and have not attended CME activities related to gout. To compare the current trend in gout management

with an earlier survey done in 2008 based on the Philippine Clinical Practice Guidelines on Gout.

RESULTS

Demographics

There were 600 questionnaires distributed during conventions and roundtable discussions and a total of 390 (65%) responses were eligible for analysis. Of the 390 respondents who participated in the survey, the majority were females (237, 60.8%) with a mean age of 37.32 ± 10.22 (20-75) years. Almost half of the respondents were practicing in the provinces (49.2%) while 198 (50.8%) were within Metro Manila. The duration of practice was classified into four categories as shown in Table 1. A little more than half of the respondents were in practice for at least 5 years. A similar proportion had not attended any CME activities related to gout. The survey questions covered diagnosis and treatment of gout. Treatment included management of acute gouty arthritis, prophylaxis against gout flares, and management of chronic gout with comorbidities as well as monitoring for drug efficacy.

Statistical Analysis

Tables 2-4 highlighted the distribution of responses to the main questions of this study with comparative responses to the 2008 survey using the One-sample Chi Square Test and the binomial test.

Diagnosis of Gout

Less than three-quarters (64.9%) of the respondents agreed to do the synovial fluid examination in patients suspected to be suffering from acute gouty arthritis, which was similar to the study done by Hamijoyo et al. (8). However, 29.3% in the former study versus 19% in our study would not need synovial fluid examination, while 15.9% in our study admitted having no idea of the procedure versus 7.3% in the former study. Responses in this study were observed to be significantly different from the previous study ($p < 0.001$). Significant differences were also observed across the length of practice ($p = 0.010$). Physicians with 1 to 5 years of experience (71%) and those <1 year in practice (67.5%) agreed to do the synovial fluid exam while 25% of physicians

practicing for more than 10 years admitted having no idea on the procedure. On the other hand, 77.5% who have attended CME activities think that synovial fluid should be examined in a patient who had not undergone crystal analysis in the past, while those who have not attended (22.7%) admitted having no idea of such a procedure ($p < 0.001$).

The majority (67.9%) would examine the synovial fluid specimen only once while 23.1% and 6.9% would have it done at least twice to 5x to as many times as possible, respectively. These responses were similar to the responses in the former study ($p = 0.737$). Higher proportions of those who attended the CME forum would examine the synovial fluid more often versus those who did not attend. On the other hand, there were no differences in responses among physicians across the duration of practice ($p = 0.742$).

Management of Acute Gout

In an otherwise healthy patient, 236 (60.5%) of the respondents will give colchicine, 80 (20.5%) NSAIDs, and 23 (6.02%) oral/intravenous (IV) corticosteroids for acute gouty arthritis while 6.7% will give allopurinol (6.7%), febuxostat (9.2%), and tramadol (3.1%). There was a decrease in the proportion of respondents who advise patients to take allopurinol ($p < 0.001$); while more respondents chose oral corticosteroid ($p < 0.001$) and colchicine ($p < 0.001$) when compared to the former study. Febuxostat ($p = 0.001$) and tramadol ($p = 0.009$), but not colchicine ($p = 0.019$), were the foremost choices among respondents who have been in practice for a longer duration. No significant difference was observed between those who have and have not attended any CME activity.

In a patient with renal insufficiency defined as serum creatinine of 2.2 mg/dL, the majority of respondents (35.1%) chose colchicine, 4.6% NSAIDs, 19.5% oral/IV steroids, and 18.2% tramadol as the drug of choice. When compared with the former study, there was a significant reduction in allopurinol ($p < 0.001$) and NSAID ($p < 0.001$) prescription, and increase in the use of tramadol ($p = 0.001$) and colchicine ($p = 0.023$). There was no difference in prescription among respondents when the duration of practice and attendance to CME fora were compared.

In general, colchicine was prescribed 3x daily in 30.3%, significantly higher when compared to the

former study ($p < 0.001$), 15.9% gave it 2x daily and 5.4% once daily for 3 days. Other management schema included an hourly dose of colchicine until pain relief in 10.5%, colchicine given hourly until abdominal toxicity sets in 16.7%, and until a maximum of 6 tablets was reached in 17.4%. There were no differences in the length of practice and having attended the CME forum or not ($p < 0.066$).

Urate-Lowering Therapy

Most respondents (44.9%) prescribed urate-lowering therapy (ULT) after the first attack of gout, while 52.3% in the former study started ULT in the asymptomatic hyperuricemia phase ($p < 0.001$). Responses vary significantly across the length of practice ($p = 0.001$) wherein most respondents with <1 year experience prescribed urate-lowering drugs (ULD) after the first attack. However, there was no difference among those with or without CME activity ($p < 0.004$).

Optimal Time to Start Urate-Lowering Drugs

Most responders (43.3%) prescribed ULD 1-2 weeks after gout flares, significantly higher than the former study ($p < 0.001$) with 20% each after <1 week and >2 weeks of the attack. Some (15.1%) still practiced giving ULD during acute gout flares. Physicians who have been in practice for long start ULD during an acute flare or less than a week from a flare versus newly practicing clinicians ($p = 0.020$). Majority of the respondents with and without CME attendance initiated ULD 1 to 2 weeks after the gout flare. However, significant differences were evident where more doctors without CME attendance initiated urate-lowering agents 2 weeks after the acute gout attack while more doctors with CME attendance gave it during the attack ($p = 0.004$).

Prophylaxis for Acute Gout

Prophylaxis for acute gout was sometimes given in 35.1%, often in 13.6%, very often in 8.5%, rarely given in 19.5%, and never given in 22.3%.

For prophylaxis, 60% opted colchicine compared to 33.1% in the former study. NSAID was the choice among 43.2% in the former study ($p < 0.001$). Among those who attended the CME courses, colchicine was their choice while NSAID and steroid were

the choices given by those who had not attended any CME activities ($p = 0.008$).

One to six months duration of prophylaxis was the choice of 30.3%, while 17.8% respondents in the former study discontinued it as soon as serum uric acid normalized ($p < 0.001$).

More than 80% respondents shared that their patients experienced gout attacks when ULD was prescribed, rarely in 39.7%, sometimes in 22.3%, often in 16.9%, and very often in 5.6%, while 12.6% did not have any experience of gout flare in their patients.

Monitoring and Treat-to-Target

Prescription for ULD was given by >50% until SUA normalized and then discontinued. Only a few (16.7%) continued ULD for a year, 10.3% prescribed it for 5 years, while 13.3% gave it for life ($p < 0.001$).

More of those who have been in practice for long prescribe ULD until the SUA normalized compared to younger practitioners who advised using the drug lifelong ($p = 0.008$).

The concept of treat-to-target had been introduced several years ago and it aimed to control gout flares and its complications. In patients without evident tophi, half of the respondents aimed for 6 mg/dL of SUA, while a more stringent level of 5 mg/dL was recommended by 34.9%, and 7 mg/dL by 12.8% respondents. On the other hand, in patients with chronic tophaceous gout, a value of 5 mg/dL was the aim of 46.9% respondents, 6 mg/dL in 35.4%, and 7 mg/dL in 15.1% respondents. No significant difference was observed between those with and without CME activities in the treat-to-target level.

Overall, management of the various clinical phases of gout by general care practitioners has improved through time with some variation across different areas and duration of practice.

DISCUSSION

The Philippine Rheumatology Association (PRA) had published the first evidence-based gout management guidelines (7) with the goal of improving the standards of care for patients. Interestingly, inappropriate management of gout is still a frequent occurrence among physicians.

Over time, several surveys and observational studies have been conducted involving general

practitioners, internists, family physicians, as well as rheumatologists evaluating their clinical practice in dealing with gout, its diagnosis, and treatment and variable treatment strategies being reported (8). In a local survey among Filipino physicians by Hamijoyo et al. in 2008, it showed various inconsistencies in the practice among physicians in the management of gout, and efficient educational programs to improve physician skills, diagnosis, and clinical management of gout was recommended (8).

The gold standard in the diagnosis of gout involves identification of monosodium urate (MSU) crystals under polarized light (3-9). However, crystal identification has received little attention in clinical practice since its introduction (9). Similarly, our study highlighted the inconsistent practice and knowledge of most clinicians in confirming gout diagnosis. Efforts in crystal identification should not be limited to just one or two attempts (9).

Several studies showed that flare control of gout is still far from adequate. Acute gout attacks are best managed using anti-inflammatory agents. In a systematic review, pharmacologic treatments identified with evidence of efficacy for acute gout were colchicine, NSAIDs, corticosteroids (10,11), and animal-derived corticotropin (12).

Choice of treatment for acute attacks should take into consideration comorbidities that will render absolute and relative contraindications mostly, especially NSAIDs. NSAIDs are best avoided and colchicine dose should be adjusted according to renal function. Colchicine has been shown to have better pain relief compared to placebo while six randomized controlled trials compared NSAIDs and corticosteroids and found no statistical difference in pain and effectiveness outcomes and overall adverse effects between the two (12). Among patients with elevated creatinine (2.2 mg/dL), colchicine was the drug of choice in 35%. There was a significant increase in the use of tramadol ($p = 0.001$) and colchicine ($p = 0.023$) in the gout study compared to the former study. Also, 60% of the respondents gave colchicine as prophylaxis compared to NSAIDs (43.2%) in the former study ($p < 0.001$), while 22.3% have never given any prophylaxis.

Our study has shown the practice of administering colchicine at hourly doses until GI toxicity sets in. Standard references (16,14) used the following regimen in giving colchicine during acute gouty arthritis: one tablet (0.5 mg or 0.6 mg) given every

hour until relief of symptoms or gastrointestinal toxicity occurs or a total of 4 to 10 tablets are achieved. The dose should be adjusted based on renal function and avoided in patients with gastrointestinal side effects or toxicity (15). However, in recent guidelines to avoid commonly associated abdominal and other related adverse effects, a dose of 0.5 mg BID-QID is being recommended (7,10-11).

Less than 20% initiate the ULD during an acute flare among physicians who have been in practice for long using febuxostat or allopurinol. Evidence showed that any attempt to alter the level of SUA (either initiating or withholding ULD) will further prolong the acute attack. Sudden fluctuations in serum urate levels may tend to precipitate and make an inflammatory reaction already in progress substantially worse by a major change in the serum urate concentration (7). In a recent study of Xin Feng et al. in 2015, patients started on allopurinol during an attack exhibited higher attack rates compared to those started later (18). Nevertheless, the recently published 2016 European League Against Rheumatism (EULAR) Task Force for Gout stated that some patients chose not to take prophylaxis but did not experience flare (10). Two small trials have suggested that allopurinol initiation during an acute gout attack did not prolong the duration of flares nor worsen its severity as compared with delayed initiation (17).

In a national survey involving primary care physicians from the US, a little less than 50% of the responders in clinical practice showed an inappropriate dose of medications in the setting of renal disease and lack of prophylaxis in initiating ULT accounted for much of the lack of compliance with treatment recommendations (8).

The best way to control recurrent flares of acute gout is that the management should focus on keeping SUA levels low enough to deplete the body urate pool. To achieve this, the SUA must be reduced below the saturation point of MSU under physiological conditions (18). This has been recognized in recent evidence-based recommendations from the EULAR Task Force for Gout, which recommends that the SUA should be reduced to a target of 6 mg/dL (360 mol/l) (10). Recommendations pointed out that the target SUA level should be linked to the saturation level of MSU rather than to the normal laboratory range which can vary between facilities and with

time. The British Society for Rheumatology (BSR) has also published guidelines for the management of gout and these recommend a stricter SUA target of <5 mg/dL (<300 mol/l) (19). In patients without evident tophi, half of the respondents (49.7%) would aim for 6 mg/dL of serum uric acid level, while a more stringent level of 5 mg/dL was seen in 34.9% and 7 mg/dL in 12.8% of the respondents. On the other hand, in patients with chronic tophaceous gout, a sterner target value of 5 mg/dL was aimed at by 46.9%, 6 mg/dL by 35.4%, and a more lenient 7 mg/dL by 15.1%.

The optimal time to start ULT after an acute gout flare varied (20). Most respondents making up 44.9% prescribed ULT after the first attack versus 52.3% in the former study who initiated ULT during a symptom-free period ($p < 0.001$). The recent EULAR Guidelines for Gout recommended early initiation of ULT that is close to the first attack (10).

Early initiation of ULT decreased the time to attain the target, lowered the incidence of chronic kidney disease (CKD) (20), and certainly improved outcomes, and contained cost (18). Whichever form of therapy used to achieve a goal range of SUA resulted in near elimination of gout flares and improved tophus status over time (5).

There is still a significant variability among clinicians in managing gout despite available clinical practice guidelines aimed at providing optimal health care to gout patients (21). Inadequate management of hyperuricemia and gout leads to long-term complications and increases morbidity. In the US National Health Survey, an improvement in gout management has been shown to be due to increased awareness on the part of the physician and patient (2). Our study showed inconsistencies in the practice of physicians who have either attended continuing medical educational forums on gout or not.

CONCLUSION

Overall, this study showed that general care practitioners manage gout in accordance to the 2008 Philippine Clinical Practice Guidelines. Gout management has significantly improved in some but not all aspects. However, focused educational fora might still serve as a very helpful approach to general care practitioners to engage in optimal healthcare delivery in the community.

REFERENCES

1. Li-Yu J. Relationship of Gout and Hyperuricemia in Cardiovascular and Renal Morbidity: 2003 National Nutrition and Health Survey (NNHeS), *Phil J. Internal Medicine*. 2008;46(Nov-Dec):279-285.
2. 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 & Rheumatism*. 2011;63(10):3136-3141. Available from: doi:10.1002/art.30520.
3. Prasad P, Krishnan E. Filipino Gout: A Review. *Arthritis Care and Research*. 2014;66(3):337-343. doi:10.1002/acr.22118.
4. Torralba TP, Bayani-Sioson P. The Filipino and Gout. *Seminars in Arthritis and Rheumatism*. 1975;4:307-320.
5. Becker MA, Schumacher Jr HR, MacDonald PA, et al. Clinical Efficacy and Safety of Successful Long-Term Urate-Lowering With Febuxostat or Allopurinol in Subjects With Gout. *J Rheumatol*. 2009;36(6):1273-82. Available from: doi:10.3899/jrheum.080814.
6. Hamijoyo L, Li-Yu J, Torralba T. A Survey on the Clinical Management of Gout Among Filipino Physicians. *Phil J Internal Medicine*. 2008;46(Mar-Apr);51-55.
7. Li-Yu J, Salido EO, Manahan S, Lichauco JJ, Lorenzo, JP, Torralba KT, et al. Philippine Practice Guidelines for the Management of Gout. *Phil J Internal Medicine*. 2008;46:165-173.
8. Doherty M, Bardin T, Pascual E. International Survey on the Diagnosis and Management of Gout. *Ann Rheum Dis*. 2007;66(12):1685-1686. Available from: doi:10.1136/ard.2007.071530.
9. Pascual E, Silvera F, Andres M. Synovial Fluid Analysis for Crystals. *Curr Opin Rheumatol*. 2011;23(2):161-169. Available from: doi:10.1097/BOR.0b013e328343e458.
10. Richette P, Doherty M, Pascual E, Barskova V, Becce F, Castaneda-Sanabria J, et al. 2016 Updated EULAR Evidence-Based Recommendations for the Management of Gout. *Ann Rheum Dis*. 2016(0):1-14. Available from: doi:10.1136/annrheumdis-2016-209707.
11. Khanna D, Fitzgerald JD, Khanna PP, Bae S, Singh MK, Neogi T, et al. 2012 American College of Rheumatology Guidelines for the Management of Gout. Part 1: Systematic Nonpharmacologic and Pharmacologic Therapeutic Approaches to Hyperuricemia. *Arthritis Care & Research*. 2012;64(10):1431-46. Available from: doi:10.1002/acr.21772.
12. Shekelle PG, Newberry SJ, Fitzgerald JD, Motala A, O'Hanlon CE, Tariq A, et al. Management of Gout: A Systematic Review in Support of an American College of Physicians Clinical Practice Guideline. *Ann Intern Med*. 2017;166(1):37-51. Available from: doi:10.7326/M16-0461.
13. Wortmann RL, Kelley WN. Gout and Hyperuricemia. In: Harris ED, Budd RC, Firestein GS, et al. Editors. *Kelley's Textbook of Rheumatology*. 7th ed. Elsevier Saunders. Philadelphia 2005:1402-1429.
14. Reginato A. Gout and Other Crystal Arthropathies. In: Kasper DL, Fauci AS, Braunwald E, Hauser SL, et al. Editors. *Harrison's Principles of Internal Medicine*. 16th ed. McGraw-Hill Companies. New York 2005:2046-2050.
15. Terkeltaub RA. Gout. *New Engl J Med*. 2003;349(17):1647-1655. Available from: doi:10.1056/NEJMc030733.
16. Xin Feng, Yao Li, Wei Gao. Significance of the Initiation Time of Urate-Lowering Therapy in Gout Patients: A Retrospective Research, *Joint Bone Spine* 2015;82(6):428-31. Available from: <https://doi.org/10.1016/j.jbspin.2015.02.021>.
17. Hill EM, Sky K, Sit M, et al. Does Starting Allopurinol Prolong Acute Treated Gout? A Randomized Clinical Trial. *J Clin Rheumatol*. 2015;21(3):120-125. Available from: doi:10.1097/RHU.000000000000235.
18. Perez-Ruiz F. Treating to Target: a Strategy to Cure Gout. *Rheumatology*. 2009;48(2):ii9-ii14. Available from: doi:10.1093/rheumatology/kep087.
19. Jordan KM, Cameron JS, Snaith M, Zhang W, Doherty M, Seckl J, et al. British Society of Rheumatology and British Health Professionals in Rheumatology Guideline for the Management of Gout. *Rheumatology*. (Oxford) 2007(8);46:1372-1374. Available from: doi:<https://doi.org/10.1093/rheumatology/kem056a>.
20. Perez-Ruiz F, Naredo E. Imaging Modalities and Monitoring Measures of Gout. *Curr Opin Rheumatol*. 2007;19(2):128-33. Available from: doi:10.1097/BOR.0b013e32801450b7.
21. Harrold L, Mazor K, Negron A, et al. Primary Care Providers' Knowledge, Beliefs and Treatment Practices of Gout: Results of Physician Questionnaire. *Rheumatology*. (Oxford) 2013(9);52:1623-29. Available from: doi:<https://doi.org/10.1093/rheumatology/ket158>.



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