Original Article

Factors Affecting the Successful Treatment in Gouty Arthritis Patients at Nongkhai Hospital

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Background: Gout is the most common inflammatory arthritis worldwide, with a prevalence ranging from less than 1% to 6.8% and an incidence of 0.58 to 2.89 per 1,000 cases per year, depending on the study. However, there are still problems in terms of diagnosis and treatment.

Objective: To evaluate 1) the factors affecting the successful treatment in gouty arthritis patients, 2) the prevalence, patients' characteristics, and factors associated with gouty arthritis, and 3) the problems of the diagnosis and treatment of gouty arthritis patients at Nongkhai Hospital, Thailand.

Materials and Methods: The medical records of gouty arthritis patients treated in the outpatient department at Nongkhai Hospital between July 2010 and December 2020 were reviewed. Patients were divided into successfully treated group (STG) and unsuccessfully treated group (UTG) based on target uric acid level throughout the treatment. Factors affecting the successful treatment including address, nationality, age, gender, body mass index (BMI), duration of disease, presence of tophi, alcoholic intake, medical illness, medications, duration of treatment, physicians' specialties, uric acid levels, glomerular filtration rate (GFR), alanine aminotransferase (ALT) before and after treatment, history of drugs discontinuation, and follow up were explored.

Results: Of the 804 patients, 74.3% and 70.3% of patients achieved target uric acid level at one year and throughout treatment, respectively. Factors affecting the successful treatment were GFR before treatment of 60 or more mL/minute/1.73 m^2 (p=0.001), absence of tophi (p=0.023), and physicians' specialties (p=0.001).

Conclusion: The improvement of the physician's education and treatment, close monitoring of patients with tophi, and GFR before treatment will increase the success of treatment and reduce complications.

Keywords: Gout; Gouty arthritis; Tophi; Hyperuricemia; Outcome; Treatment; Predictor

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Gout is the most common inflammatory arthritis worldwide, with prevalence ranging from less than 1% to 6.8% and an incidence of 0.58 to 2.89 per 1,000 cases per year, depending on the study[1]. It is common in Southeast Asia, Pacific Islands, and New Zealand (Maori tribe)[2-4]. In the past 20 to 30 years, there is a tendency to find more cases of gout around the world. The United States has doubled the number of cases of gout in line with economic growth[5,6]. In 2012, there was a 63.9% increase in the prevalence of gout in the United Kingdom[7], as more dramatic rises have been observed in Asia including in China and Thailand. South Korea reported 495,996 new cases between January 1, 2007 and December 31, 2008, and Taiwan reported that every 1 in 16 people have gout[8]. Although gout is a known disease for a long time, there are still problems in terms of diagnosis and treatment. In a retrospective study of 5,942 patients who came from the southeastern United States, Sarawate et al[9] found that more than 80% of allopurinol-treated patients had not checked their serum uric acid levels within 180 days of treatment, and the dosage of allopurinol was not adjusted appropriately in patients with impaired renal function. The same applied to the study by Singh et al[10] of 3,658 patients. Most of them received substandard care, especially for those required senior medical care or frequent hospital stays. A study by Roddy et al[11] collected data from two sources, Consultation in Primary Care Archive (CiPCA) and Prescriptions in Primary Care Archive (PiPCA). In their study, of the 673 patients included, patients received follow-up for co-morbidities but only 5% for lipid levels, 26%

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for blood pressure, 6% for blood sugar, and 21% for kidney function. Only 19% of the patients were prescribed uric acid lowering drugs even though having arthritis. Whereas, in the outpatient department of the Takuatung Hospital Thailand, between August 1, 2013 and July 31, 2015, Chetanananda[12] found that only 13.9% in year 1 and 13.5% in year 2 after the start of treatment, that patients treated had their dosing of uric acid-lowering drugs adjusted until their uric acid level was less than 6 mg/dL. Similarly, the study of Hanvivadhanakul and Wongdet[13] found that of the 139 patients treated in the outpatient department at Thammasat Hospital between January 1 and December 31, 2013, only 33% achieved target uric acid level.

For the above reasons, the present study was performed to assess factors affecting the successful treatment of gouty arthritis patients at Nongkhai Hospital, Thailand. Therefore, the present study could apply the knowledge gained to improve and plan the treatment of the patients to reach the target uric acid level, reduce gout flares, reduce complications, and increase the quality of life.

Materials and Methods

The present study was a retrospective study of gouty arthritis patients (ICD-10 M100-109) treated in the outpatient department at Nongkhai Hospital, Thailand between July 2010 and December 2020. The study was approved by the Research Ethics Committee (REC) at Nongkhai Hospital (No.14/2564). Data were collected onto a medical record form including address, nationality, age, gender, body mass index (BMI), duration of disease, presence of tophi, alcoholic intake, medications, medical illness, duration of treatment, physicians' specialties, uric acid level, glomerular filtration rate (GFR), alanine aminotransferase (ALT) before and after treatment up to the last three follow-up visits, history of drugs discontinuation, and follow-up. The patients were divided into two groups based on whether they achieved target uric acid level throughout treatment. The successfully treated group (STG) were the patients with a serum uric acid of 5.0 mg/dL or less and 5.5 mg/dL or less in patients with or without tophi, respectively. The unsuccessfully treated group (UTG) were the patients with serum uric acid of more than 5.0 mg/dL and more than 5.5 mg/dL in patients with and without tophi. Variable factors were explored between the two groups. Statistical analysis was done by using IBM SPSS Statistics, version 23.0 (IBM Corp., Armonk, NY, USA). Chi-square test or Fisher's exact test were used to analyze between the two groups. Then only statistically significant factors will be further analyzed by the Forward stepwise selection method of multiple logistic regression (p-value of less than 0.05 was considered statistically significant).

Results

One thousand six gouty arthritis patients at Nongkhai Hospital between July 2010 and December 2020 were included in this study. Two hundred two cases had missing data and were ineligible. Therefore, 804 eligible patients were enrolled of which 706 were male (87.8%). The mean age (standard deviation) of patients was 62.8 (12.5) years, females had onset of gout at 63.0 (11.3) years, while males were 54.4 (12.9) years. They often have co-morbidity diseases such as hyperlipidemia, chronic kidney disease, and obesity. Sixteen point six percent of the patients had tophi, 19.3% had a history of alcoholic intake, and 15.7% had a history of herbal medicines used. The patients were treated and monitored by the rheumatologist (72.8%). The median duration of disease and treatment (interquartile range) was 6.0 (2.0 to 11.0) and 3.0 (2.0 to 6.0) years, respectively. Up to 643 patients (80.0%) were diagnosed by clinical and uric acid levels greater than 7.0 mg/dL (Table 1). Mean uric acid levels before and after treatment was 9.3 (1.5), 4.4 (2.0) mg/dL, respectively. The mean GFR before and after treatment was 65.2 (0.9) and 66.4 (0.9) mL/minute/1.73 m^2, respectively. Mean ALT before and after treatment was 31.0 (0.6) and 31.8 (0.9) units per liter, respectively. Mean systolic blood pressure before and after treatment was 129.0 (0.5) and 128.9 (0.5) mmHg, respectively. Mean diastolic blood pressure before and after treatment was 77.4 (0.4) and 76.9 (0.3) mmHg, respectively. Patients lost follow-up was 0.2 (0.01) times per year, with a mean gout flare of 0.3 (0.01) once a year. Most patients were treated with allopurinol 53.7% and allopurinol concomitant with benzbromarone 34.1%. Uric acid-lowering drugs were discontinued by the physician in 2.0% of the cases and by the patient in 16.2% of the cases. Seventy-four-point-three percent and 70.3% of the patients achieved target uric acid levels at 1 year and throughout treatment, respectively. Factors contributing to the successful treatment of gouty arthritis throughout treatment included GFR before treatment of 60 mL/minute/1.73 m^2 or more (p=0.001), absence of tophi (p=0.023), and physicians' specialties (p=0.001) (Table 2, 3).

Table 1. Baseline characteristics of study patients (total n=804)

Characteristics	n (%)
Address	
Nong Khai	592 (73.6)
Others	212 (26.4)
Nationality	
Thai	784 (97.5)
Foreigner	20 (2.5)
Sex	
Male	706 (87.8)
Female	98 (12.2)
Age (years)	
<60	300 (37.3)
≥60	504 (62.7)
Duration of disease (years)	
<5	331 (41.2)
≥5	473 (58.8)
Presence of tophi	133 (16.6)
Alcoholic intake	155 (19.3)
History of herbal medicine	126 (15.7)
BMI (kg/m^2)	
<18.5	58 (7.2)
18.5 to 22.9	210 (26.1)
23.0 to 24.9	170 (21.1)
25.0 to 29.9	274 (34.1)
>30.0	92 (11.4)
CKD stage	
Stage 1 (≥90.0 mL/minute/1.73 m^2)	140 (17.4)
Stage 2 (>60.0 to 89.9 mL/minute/1.73 m^2)	325 (40.4)
Stage 3 (>30.0 to 59.9 mL/minute/1.73 m^2)	265 (32.9)
Stage 4 (>15.0 to 29.9 mL/minute/1.73 m^2)	56 (7.0)
Stage 5 (>10.0 to 14.9 mL/minute/1.73 m^2)	7 (0.9)
Stage 6 (≤10.0 mL/minute/1.73 m^2)	11 (1.4)
Pre-treatment	
Uric acid <8.0 mg/dL	162 (20.1)
Pre-treatment (continued)	
GFR ≥60.0 mL/minute/1.73 m^2	465 (57.8)
ALT <40.0 units/L	656 (81.6)
Medical illness	
DLP	658 (60.3)
CKD	552 (48.0)
HT	519 (42.8)
DM/IFG	491 (46.0)
Fatty liver	83 (9.1)
Renal stones	79 (7.8)
CVA	57 (5.2)
IHD	46 (4.2)
Medications	
Aspirin	153 (19.0)
Diuretics	44 (5.5)
Losartan	175 (21.8)
Fenofibrate	6 (0.8)
Physicians' specialties	
Rheumatologist	585 (72.8)
Internal medicine	199 (24.8)
Nephrologist	13 (1.6)
General practitioner	7 (0.9)
Uric lowering drugs	
Allopurinol	432 (53.7)
Benzbromarone	63 (7.8)
Febuxostat	9 (1.1)
Allopurinol + Benzbromarone	274 (34.1)
Allopurinol + Sulfinpyrazone	2 (0.3)
Febuxostat + Benzbromarone	23 (2.9)
Febuxostat + Sulfinpyrazone	1 (0.1)
Duration of treatment <5 years	503 (62.6)
Drugs discontinuation	146 (18.2)
Loss follow up	308 (38.3)

BMI=body mass index; CKD=chronic kidney disease; GFR=glomerular filtration rate; ALT=alanine aminotransferase; DLP=dyslipidemia; HT=hypertension; DM=diabetes mellitus; IFG=impaired fasting glucose; CVA=cerebrovascular disease; IHD=ischemic heart disease

Discussion

Eight hundred four eligible patients were enrolled in this study. Six hundred forty-three (80.0%) patients were diagnosed with clinical uric acid levels greater than 7.0 mg/dL, and only 33 cases (4.1%) were diagnosed by arthrocentesis, although the definite diagnosis of gouty arthritis was the detection of monosodium urate crystals in synovial fluid or tophi[2,3,9]. This may be due to a large number of outpatients, which was about 70 to 80 cases per day, and patients that may have received initial treatment before being referred to Nongkhai Hospital. Patients were given a mean dose of allopurinol 418.8 mg/case, benzbromarone 97.2 mg/case, febuxostat 78.8 mg/case, and combined uric lowering drugs in 36.8% (p=0.058, adjusted OR 1.791). This is consistent with the previous studies suggesting that the physicians should gradually increase the dose of allopurinol (dose escalation)[14-18] greater than 300 mg[19,20], or consider concomitant allopurinol with benzbromarone in patients unresponsive to a single drug[21-23] to achieve targeted uric acid levels. In other studies, febuxostat has been effective in reducing uric acid levels to the target with fewer side effects compared to allopurinol[20,24-26], but only 33 patients were enrolled in the present study. This is because

Table 2. Factors affecting the successful treatment of gouty arthritis

Factors	STG (n=565)	UTG (n=239)	Crude OR (95% CI)	p-value
Address				
Nong Khai	399 (49.6)	193 (24.0)	0.573 (0.396 to 0.829)	0.003*
Others	166 (20.6)	46 (5.7)		
Nationality				
Thai	549 (68.3)	235 (29.2)	0.584 (0.193 to 1.766)	0.335
Foreigner	16 (2.0)	4 (0.5)		
Sex				
Male	498 (61.9)	208 (25.9)	1.108 (0.703 to 1.747)	0.659
Female	67 (8.3)	31 (3.9)		
Age (years)				
<60	209 (26.0)	91 (11.3)	0.955 (0.699 to 1.304)	0.771
≥60	356 (44.3)	148 (18.4)		
Duration of disease (years)				
<5	183 (22.8)	148 (18.4)	0.295 (0.215 to 0.404)	0.001*
≥5	382 (47.5)	91 (11.3)		
Absence of tophi	459 (57.1)	212 (26.4)	0.551 (0.351 to 0.867)	0.009*
No alcoholic intake	434 (54.0)	215 (26.7)	0.370 (0.232 to 0.589)	0.001*
No history of herbal medicine	454 (56.5)	224 (27.9)	0.274 (0.156 to 0.481)	0.001*
BMI (kg/m^2)				
≤25.0	317 (39.4)	120 (14.9)	1.268 (0.936 to 1.716)	0.125
>25.0	248 (30.8)	119 (14.8)		
Pre-treatment				
Uric acid <8.0 mg/dL	127 (15.8)	35 (4.4)	1.690 (1.122 to 2.545)	0.011*
GFR ≥60.0 mL/minute/1.73 m^2	347 (43.2)	118 (14.7)	1.632 (1.203 to 2.214)	0.002*
ALT ≤40.0 units/L	452 (56.2)	204 (25.4)	0.686 (0.454 to 1.038)	0.073
Medical illness				
No DLP	80 (10.0)	66 (8.2)	0.432 (0.299 to 0.625)	0.001*
No CKD	179 (22.3)	73 (9.1)	1.055 (0.760 to 1.463)	0.751
No HT	221 (27.5)	64 (8.0)	1.757 (1.260 to 2.449)	0.001*
No DM/IFG	195 (24.3)	118 (14.7)	0.540 (0.397 to 0.735)	0.001*
No fatty liver	492 (61.2)	229 (28.5)	0.294 (0.149 to 1.580)	0.001*
No renal stones	502 (62.4)	223 (27.7)	0.572 (0.323 to 1.012)	0.052
No CVA	523 (65.0)	224 (27.9)	0.834 (0.453 to 1.535)	0.559
No IHD	531 (66.0)	227 (28.2)	0.826 (0.420 to 1.623)	0.578
Medications				
Non-prescribed aspirin	461 (57.3)	190 (23.6)	1.143 (0.782 to 1.671)	0.489
Non-prescribed diuretics	538 (66.9)	222 (27.6)	1.526 (0.815 to 2.855)	0.184
Prescribed losartan	138 (17.2)	37 (4.6)	1.764 (1.183 to 2.631)	0.005*
Prescribed fenofibrate	3 (0.4)	3 (0.4)	0.420 (0.084 to 2.096)	0.370
Physicians' specialties				
Rheumatologist	529 (65.8)	56 (7.0)	48.019 (30.583 to 75.398)	0.001*
Others	36 (4.5)	183 (22.8)		
Uric lowering drugs				
Combine	272 (33.8)	24 (3.0)	8.316 (5.287 to 13.081)	0.001*
Single	293 (36.4)	215 (26.7)		
Duration of treatment (years)				
<5	326 (40.5)	177 (22.0)	0.478 (0.342 to 0.667)	0.001*
≥5	239 (29.7)	62 (7.7)		
No drugs discontinuation	461 (57.3)	197 (24.5)	0.945 (0.636 to 1.403)	0.779
No loss follow-up	327 (40.7)	169 (21.0)	0.569 (0.411 to 0.787)	0.001*

STG=successfully treated group; UTG=unsuccessfully treated group; OR=odds ratio; CI=confidence interval; BMI=body mass index; GFR=glomerular filtration rate; ALT=alanine aminotransferase; DLP=dyslipidemia; CKD=chronic kidney disease; HT=hypertension; DM=diabetes mellitus; IFG=impaired fasting glucose; CVA=cerebrovascular disease; IHD=ischemic heart disease

* Statistically significant

Table 3. Factors affecting the successful treatment of gouty arthritis

Factors	Adjusted OR (95% CI)	p-value
Absence of tophi	2.138 (1.110 to 4.117)	0.023*
Pre-treatment: GFR ≥60.0 mL/minute/1.73 m^2	2.740 (1.613 to 4.652)	0.001*
Physicians' specialties: rheumatologist	69.787 (35.954 to 135.457)	0.001*

OR=odds ratio; CI=confidence interval; GFR=glomerular filtration rate

* Statistically significant

febuxostat has only been used in the last 2 to 3 years in the present study hospital. In addition, 74.3% and 70.3% of patients achieved target uric acid levels at 1 year and throughout treatment, respectively. The patients had a mean gout flare of 0.3 (0.01) times per year throughout treatment, which is better than other studies[13,27-30]. This may be because the patients were treated by rheumatologists. Consistent with other studies, serum uric acid levels below 6 mg/dL and colchicine prophylaxis were associated with reduction of gouty attack[31-42].

From the current study, the factors affecting the successful treatment of gouty arthritis throughout treatment are GFR before treatment of 60 mL/minute/1.73 m² or more (p=0.001), absence of tophi (p=0.023), and physicians' specialties (p=0.001). GFR before treatment of 60 mL/minute/1.73 m² or more achieved a target uric acid level of 74.6% and an adjusted odds ratio of 2.740, consistent with other studies[43,44]. The American College of Rheumatology clinical practice guidelines 2020 and other studies recommend that the physicians should adjust the uric acid-lowering doses based on GFR before treatment, and slowly increase the dose later until the target uric acid level is achieved[45-49]. Likewise, patients without tophi achieved target uric acid levels of 57.1% and adjusted odds ratio of 2.138, consistent with other studies[13,50-52]. Furthermore, patients treated by rheumatologists had the target uric acid level of 90.4% and the adjusted odds ratio was 69.787, which was not different from other studies[12,13,45,52-58]. Because most rheumatologists adjusted uric acid lowering drugs to meet the target uric acid level, in a treat-to-target strategy, close monitoring of patients as well as blood tests frequencies are different from other physicians' specialties.

The present study has limitations due to missing and incomplete data. Patients were from a single center. The observational nature and lack of control group do not allow causal inferences. Finally, other potential factors influencing treatment outcomes could not be assessed such as the difference in the education among physicians, patients' lifestyle modifications, and diet control.

Conclusion

The current study identified the factors affecting the successful treatment of gouty arthritis throughout treatment, which are GFR before treatment of 60 mL/minute/1.73 m² or more, absence of tophi, and physicians' specialties. Therefore, the improvement of the physician's education and treatment, close monitoring of patients with tophi, and GFR before treatment will increase the success of the treatment and reduce the complications.

What is already known on this topic?

Adherence to treatment of gout is commonly low, declining with time on prescription. Non-adherence was the main cause of failure to achieve serum uric acid.

What this study adds?

The physicians' specialties and the adherence of treatment of patients are the key factors contributing to the success of gouty arthritis treatment.

Conflicts of interest

The authors declare no conflict of interest.

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