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Assessment of awareness about management and drugs used for treatment of gout in Khartoum State, Sudan

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ABSTRACT

The purpose of this study was to evaluate the awareness about management and drugs used for treatment of gout by using questionnaires to collect data from patients who attended the hospitals and health care centers in Khartoum state, Sudan. The results showed that (81.2%) of the patients were males and (18.8%) were females and those of age between 46-60 years represented 46.5%. This study found that (90.1) of the patients were prescribed for allopurinol and (54.5%) of them stopped taking allopurinol when the attack occurred and taking non-steroidal anti-inflammatory drugs (mainly indomethacin 45.45%) to relieve the pain. This study revealed that (86%) of gout patients were advised to avoid certain types of foods such as Red meat, legumes, fatty foods and salt and (31.7%) of them were committed with the advice and (38.6%) sometimes complied with advice while (29.7%) didn't comply. Some medications used to treat concomitant diseases in this study have major drug interactions with allopurinol such as Lisinopril (5%), Aspirin (5%), Amlodipine (10.9%) and Captopril (1.0%).

Keywords: Gout, Allopurinol, NSAIDs, indomethacin, Drug interactions.

INTRODUCTION

Gout is a disease that results from an overload of uric acid in the body, this overload of uric acid leads to the formation of tiny crystals of urate that deposit in tissues of the body, especially the joints, when crystals form in the joints, it causes recurring attacks of joint inflammation (arthritis) [1]. Gout is often classified as primary or secondary, and both forms are associated with hyperuricemia [2]. Gout associated with an inborn error in metabolism or decreased renal excretion without other renal disease is referred to as primary gout, whereas gout associated with an acquired disease or the use of a drug is called secondary gout [3]. Gout is considered a chronic and progressive disease, chronic gout can also lead to deposits of hard lumps of uric acid in the tissues, particularly in and around the joints and may cause joint destruction, decreased kidney function, and kidney stones (nephrolithiasis) [1]. Gout is predominantly a disease of middle-aged men, but there is a gradually increasing prevalence in both men and women in older age groups. In most studies, the annual incidence of gout in men is in the range of one to three per 1,000; the incidence is much lower in women [4].Serum urate levels increase by 1 to 2 mg/dl in males at the time of puberty, but females exhibit little change in urate levels until after menopause, when concentrations approach those seen in males [5]. Gout has been recognized as a familial disorder since the time of Sir Alfred Garrod; about 40% of patients in most series report a family history of gout, and the hereditary component for serum uric acid levels in the general population has been estimated to be approximately 40% [6]. Patients' education is one important area in the management of gout that can be improved. Patients with hyperuricaemia should be told that they need to be cautious about what they eat and drink; Patients need to know that they can manage acute attacks with colchicine or non-steroidal anti-inflammatory drugs; and patients with recurrent gout taking allopurinol to lower their urate concentrations also need to be aware that they should stop use of the drug if they have an acute

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attack; the effective management of gout requires good communication with patients, so that patients can better manage their condition themselves [7]. Lifestyle and dietary recommendations for gout patients should consider overall health benefits and risk, Weight reduction with daily exercise and limiting intake of red meat and sugary beverages would help reduce uric acid levels [7, 8].

The treatments of gout fall into three parts:
(1) Drugs that affect in levels of uric acid: Allopurinol inhibiting uric acid synthesis by inhibition of xanthine oxidase has been lowers the plasma level of uric acid [9,10,11,12]; Probenecid increasing uric acid excretion this by preventing the reabsorption of uric acid by the kidney and increasing its excretion from the body in the urine; Febuxostat is an orally administered, nonpurine selective inhibitor of xanthine oxidase; the drug acts by binding into a channel in the molybdenum center of the enzyme, leading to a very stable and long-lived enzyme-inhibitor interaction with both the oxidized and reduced forms of the enzyme and, as a consequence, a strong inhibition of substrate binding [9].
(2) Non-steroidal anti-inflammatory drugs (NSAIDs): They work by reducing the levels of prostaglandins, chemicals that are responsible for pain, fever, and inflammation; blocks the enzyme that makes prostaglandins (cyclooxygenase), resulting in lower concentrations of prostaglandins; as a consequence, inflammation, pain and fever are reduced. Examples include: diclofenac, Indomethacin, etoricoxib, ketoprofen, naproxen, piroxicam, sulindac [13].
(3) Clochicine: Have anti-inflammatory properties on no dividing cells (like neutrophils) been linked to interference with the cellular organization of labile fibrillar systems concerned with structure and movement; specifically, it prevents the polymerization of tubulin dimers to form microtubules; neutrophils were obvious targets for effects of colchicine, being the major cellular components of synovial fluid during gouty attacks [13].

The usual dose of Allopurinol is between 200 and 400 mg daily (depending on uric acid levels and renal function) given in divided doses; the regimen most often prescribed is 100 mg to be taken 3 times a day. It would, however, be more convenient for the patient if the drug could be administered in a single daily dose, especially since treatment is usually required for the rest of the patient's life [14].

The goals of therapy for patients with gout include termination of the acute attack, prevention of further attacks during the Intercritical period, assessment for associated and contributing factors, and consideration of long-term hypouricemic therapy [15]. Each aspect of therapy should be considered separately, and there should be no confusion between efforts to suppress inflammation in acute attacks and efforts to lower serum urate levels, decrease the frequency of attacks, and prevent complications in the future [16].

Justification: Patients suffering from gout may have low awareness about the drugs used for treating gout, possible side-effect, drug-drug interactions and drug-food interactions; therefore the aim of this study is to evaluate the patients' awareness about their disease (gout) and how to deal with both acute attack and the asymptomatic period of the disease.

MATERIALS AND METHODS

Methodology:
Study design: This is a cross sectional study conducted in 101 of gout patients attended at hospitals and Healthcare centers in Khartoum state, Sudan during July 2012. All information has been collected using questionnaire after the ethical approval and patient's agreement.

RESULTS

As shown in table (1) below, 81.2% of gout patients were males and 18.8% were females. Table (2) describes the percentage age groups of gout patients. Patients with their ages between 31-45 represented 26.7% of the whole sample, those of between 46-60 years represented 46.5%, those of between 61-75 years constituted for 22.8%, those patients between 76-90 years constituted 3% while the remaining 1% was constituted by those patients with their ages above 91years. As shown in table (3) below, 87.1% of gout patients were advised to take the medications at a certain time during the day. As shown in table (4), 61.4% of gout patients in this study adhered to their medications regularly, 19.8% of patients did not comply with timely use of their medications while 18.8% were between these two, sometimes complying with timely use of their medications while ignoring other times. Table (5) indicates that most of gout patients in the study used allopurinol constituting 90% of the whole patients. As shown in table (6) below, 54% of patients in the study stopped taking the medication (allopurinol) when the attack occurred while 45.5% of them continued taking medications. As indicated in table (7) indomethacin was administered to 45.45% of patients who had intervention therapy after stopping medication as a result of the attack while other medications had been administered for the majority of gout patients constituting 54.5% of

patients. As shown in Table (8), 94.44% of gout patients who were pregnant or breast-feeding were not advised by physicians and pharmacists to stop medication. As shown in Table (9), 86.1% of gout patients were advised to avoid certain types of foods while the remaining 14% were not given advice about their foods. As shown in Table (10), 13% of gout patients were advised to avoid certain types of medications.

DISCUSSION

Gout is a disease that results from an overload of uric acid in the body, this overload of uric acid leads to the formation of tiny crystals of urate that deposit in tissues of the body, especially the joints, when crystals form in the joints, it causes recurring attacks of joint inflammation (arthritis) [1].

This study revealed that the percentage of males (81.2%) was higher than females (18.8%). This result agrees with the results reported by *Mikuls TR, Farrar JT, Bilker WB* (2005) who said that Gout is predominantly a disease of middle-aged men, but there is a gradually increasing prevalence in both men and women in older age groups. In most studies, the annual incidence of gout in men is in the range of one to three per 1,000; the incidence is much lower in women [4].

The age group of gout patients between 46-60 yrs in this study, represented (46.5%). This result agrees with the results reported by *Choi HK, Atkinson K, Karlson EW* (2004) who reported that the prevalence of gout increases in direct association with age; therefore, the increased longevity of populations in industrialized nations may contribute to a higher prevalence of gout through the disorder's association with age-related diseases and treatments for aging-related diseases. Moreover, the prevalence of the clinical manifestations of gout increases with the duration of hyperuricemia. Thus, elderly patients with longstanding hyperuricemia are more likely to present with the signs and symptoms of gout [5].

This study showed that most of the patients (about 90%) in Khartoum state took allopurinol for treatment of gout and also used nonsteroidal anti-inflammatory drugs (54%) specially indomethacin (45.45% from NSAIDs) and Diclofenac sodium (25.45% from NSAIDs) for treatment of gout attack. 87.1% of gout patients were advised to take the medications at a certain time during the day, and about 44.6% of the gout patients were taking the medication after breakfast, and about 61.4% of gout patients adhered to drugs regularly. The study found that 54.5% of gout patients stopped taking allopurinol when the attack occurred and used nonsteroidal anti-inflammatory drugs in place of allopurinol and about 45.45% of gout patients were taking indomethacin**,** this result agrees with the results reported by *Fam AG* (2002) who mentioned that the NSAIDs are useful in most patients with acute gout and remain the agents of choice for young, healthy patients without comorbid diseases. Indomethacin has been the most widely used agent over the years; it usually begins to provide relief within hours after the initial oral dose. NSAIDs with a high specificity for cyclooxygenase-2 (e.g., celecoxib) should be useful in treating acute gout in patients at risk for gastrointestinal toxicity from the currently available NSAIDs and also said that the Patients remain at increased risk for another attack of gout for several weeks after resolution of the initial attack; prophylaxis with small doses of colchicine or NSAIDs should be used for most patients. The reason for stop taking the medication (allopurinol) because the NSAIDs are useful for relive pain of gout attack [17].

The study revealed that 18.8% of gout patients had Hypertension and 5% had Diabetes mellitus while 4% had Hypertension and Diabetes mellitus together. This result agrees with the results reported by *Johnson RJ, Kang DH, and Feig D* (2000) who stated that the relationship between hyperuricemia and hypertension is notable, because a higher serum urate level is known to be associated with hypertension. As many as 50% of untreated hypertensive persons have hyperuricemia, which often precedes hypertension, and even among children hyperuricemia has been shown to correlate with blood pressure. In the Normative Aging Study, gout was found to be more common among hypertensive individuals, with a strong association with thiazide diuretic use. The association of gout and hyperuricemia has been attributed to such factors as obesity, insulin resistance [18].

Some medications used to treat concomitant diseases in this study have major drug interactions with allopurinol such as Lisinopril (5%), Aspirin (5%), Amlodipine (10.9%) and Captopril (1.0%).
The study also discovered that 94.44% of gout patients who were pregnant or breast-feeding (n= 18) were not advised by physicians and pharmacists to stop medication.

The results indicated that the types of foods not recommended for gout patients included: Red meat, legumes, fatty food, sardine and salt. This result agrees with the results reported by *Lawrence RC, Felson DT, Helmick CG* (2007) who concluded that red meat intake as it is associated with higher uric acid levels and increased future risk of gout and Seafood intake has been linked to higher serum

uric acid levels and increased future risk of gout, which is likely due to its high purine contents the recent healthy eating pyramid recommends 1–3 times daily consumption of nuts and legumes, which appears readily applicable among patients with gout or hyperuricemia [8].

This study showed that the patients were advised by physicians or pharmacists not to take aspirin (10.9 %) or diuretic (2%). This result agrees with the results reported by Seegmiller, J. E., laster, L. and Howell, R. R. (1963) who stated that Aspirin (low dose) and other salicylates inhibit tubulat secretion of uric acid when give in low dose and Diuretics (except spironolactone) may cause hyperuricemia this occure either via volume depletion which in turn increase proximal tubular reabsorption or via impaired tubular secretion of uric acid.The study revealed that 65.3% of gout patients in Khartoum state seek for physicians help upon disease recurrence [19].

CONCLUSION

Gout is a common arthritis caused by deposition of monosodium urate crystals within joints after chronic hyperuricaemia. In this study the age group of patients with the highest incidence of gout was between 46-60 years and represented (46.5%), indicating the prevalence of gout increases in direct association with age.

This study showed that allopurinol was the common drug used for treatment of gout patients (about 90%) in Khartoum state and also used nonsteroidal anti-inflammatory drugs (54%) specially indomethacin (45.45% from NSAIDs) for treatment of gout attack.

The study revealed that 54.5% of gout patients stopped taking the medication when the attack occurred and used nonsteroidal anti-inflammatory drugs in place of allopurinol and about 45.45% of gout patients were taking indomethacin.

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Conflict of interest: None to declare.

Table 1: Description of gender participation in this study

Gender	Frequency	Percentage
Male	82	81.2
Female	19	18.8
Total	101	100

Table 2: Shows patient age groups considered in this study

Age	Frequency	Percentage
31 – 45	27	26.7
46 – 60	47	46.5
61 – 75	23	22.8
76 – 90	3	3.0
91+	1	1.0
Total	101	100.0

Table 3: The advice that was given to the patients by the pharmacists or Physicians about taking the medications at a certain time during the day

Advice	Frequency	Percentage
Yes	88	87.1
No	13	12.9
Total	101	100.0

Table 4: Shows how the patients take their medication at regular times

Regular times	Frequency	Percentage
Yes	62	61.4
No	20	19.8
Sometimes	19	18.8
Total	101	100.0

Table 5: The frequencies and their respective percentages of patients using xanthine oxidase inhibitors (allopurinol)

Allopurinol	Frequency	Percentage
Yes	91	90.1
No	10	9.9
Total	101	100.0

Table 6: The frequency and percentage of gout patients who stopped taking the medication when the attack occurred

Patients stopped taking allopurinol during attack	Frequency	Percentage
Yes	55	54.5
No	46	45.5
Total	101	100.0

Table7: Therapy intervention in gout patients who stopped taking their medication when the attack occurred

Therapy intervention	Frequency	Percentage
Peroxidol	3	5.45
Indomethacin	25	45.45
Mefenamic acid	4	7.27
Naproxen	3	5.45
Ibuprofen	3	5.45
Diclofenac sodium	14	25.45
Ketoprofen	1	1.81
Piroxicam	1	1.81
Meloxicam	1	1.81
Total	55	100.0

Table 8: Advice given by physicians or pharmacists to stop the medication in pregnant or breast-feeding patients with gout

Given advise(s)	Frequency	Percentage
Yes	1	5.555
No	17	94.445
Total	18.0	100.0

Table 9: Advice given by physicians or pharmacists about patient food type

Physician advice	Frequency	Percentage
Yes	87	86.1
No	13	14
Total	101	100.0

Table 10: Advice given by physicians or pharmacists to avoid certain type of medications

given Advice	Frequency	Percentage
Yes	13	12.8
No	88	87.2
Total	101	100.0

REFERENCES

1- Bieber JD, Terkeltaub RA. Gout: On the brink of novel therapeutic options for an ancient disease. Arthritis Rheum 2004; 50 (8):2400-14.
2- Bruce N Cronstein, Robert Terkeltaub. The inflammatory process of gout and its treatment. Arthritis Research & Therapy 2006; 8(Suppl 1):S3 (doi:10.1186/ar1908).
3- Rott KT, Agudelo CA. Gout. JAMA 2003; 289 (21):2857-60.
4- Mikuls TR et al. Gout epidemiology: results from the UK General Practice Research Database, 1990-1999. Ann Rheum Dis 2005; 64:267-272.
5- Choi HK et al. Purine-rich foods, dairy and protein intake, and the risk of gout in men.N Engl J Med 2004; 350 (11):1093-103.
6- Wilk JB et al. Segregation analysis of serum uric acid in the NHLBI Family Heart Study. Hum Genet 2000; 106 (3):355-9.
7- Harrold L R et al.: Sex differences in gout epidemiology: evaluation and treatment. Ann Rheum Dis. 2006; 65 (10):1368–1372.

8- Lawrence RC et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. Arthritis Rheum 2008; 58:26–35.
9- Okamoto K et al. An extremely potent inhibitor of xanthine oxidoreductase. Crystal structure of the enzyme-inhibitor complex and mechanism of inhibition. *J. Biol. Chem.2003*; 278:1848–1855.
10- CHALMERS RA et al. A comparative study of the xanthine oxidase inhibitors allopurinol and oxipurinol in man. Clin Sci. 1968; 35 (2): 353-62.
11- Feigelson P et al. PYRAZOLOPYRIMIDINES AS INHIBITORS AND SUBSTRATES OF XANTHINE OXIDASE. J. Biol. Chem. 1957; 226:993-1000.
12- Rundles RW et al. Effects of a xanthine oxidase inhibitor on thiopurine metabolism, hyperuricemia, and gout. Trans. Ass. Amer. Phycns.1963; 76:126

13- Baum C et al. Utilization of nonsteroidal anti-inflammatory drugs. Arthritis Rheum 1985; 28(6):686-92.
14- LOEBL WY et al. Withdrawal of allopurinol in patients with gout. Ann Rheum Dis. 1974; 33(4): 304–307.
15- Terkeltaub RA. Clinical practice. gout. N Engl J Med. 2003; 349(17):1647-55.
16- Zhang W et al. EULAR evidence based recommendations for gout. Part II: Management. Report of a task force of the EULAR standing committee for international clinical studies including therapeutics (ECISIT). Ann Rheum Dis 2006; 65(10):1312-24.
17- Fam AG. Treating acute gouty arthritis with selective COX 2 inhibitors. BMJ 2002; 325(7371):980-981.
18- Johnson RJ et al.: Is there a pathogenetic role for uric acid in hypertension and cardiovascular and renal disease? Hypertension 2003; 41(6):1183-90.
19- SEEGMILLER JE et al. Biochemistry of uric acid and its relation to gout. (1963): N Engl J Med.1963; 268: 712-6 contd.