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SYMPOSIUM PAPER

Effect of blind treatment on stone disease

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Abstract Most of the drugs administered to stone patients appear to be inappropriate and doing more harm than good to the patients. The objective of this paper is to identify the prevalence of blind chemotherapy among the stone patients and find out the real indication for the drugs administered. Patients who attended the stone clinic for the first time were interviewed to find out what drugs they had been taking before the attendance at the stone clinic. 350 patients consuming specific drugs relevant to stone formation at least for a period of 15 days were selected for a detailed assessment. The type of drug consumed, the dose, the duration, the side effects, compliance rate and effect on stone disease were assessed. The biochemical profile of the patients was assessed to identify the role of the therapeutic modalities utilised. Conclusions regarding the utility of drugs in the process of stone formation were made. The values were compared with those of patients not on medication and considering laboratory standards. Of the 350 patients studied, 96 patients were consuming potassium citrate in different doses, 50 were consuming allopurinol, 44 cystone, 27 potassium citrate + magnesium, 25 calcury, 24 rowatinex, 21 ayurvedic drugs, 17 dystone, 17 homeopathic medicines and 17 other drugs. The longest duration of compliance was for cystone—2.5 years. All other drugs were stopped by the patients themselves due to recurrence of symptoms. As much as 93% of the patients did not feel that there was any significant relief of symptoms. The side effects which prompted the patients to stop medicine were gastro intestinal upset, particularly with potassium citrate, rowatinex and potassium citrate + magnesium combination. The relevant biochemical changes noted were increased urinary citrate levels in patients consuming potassium citrate alone or in combination with magnesium. Serum uric acid was within normal limits in patients consuming allopurinol. Urine uric acid levels were also lower in patients on allopurinol. It is concluded that most of the drugs administered blindly were neither indicated nor beneficial for the patients. Metabolic correction has to be based on proper metabolic assessment.

Keywords Urolithiasis · Chemotherapy · Citrate · Allopurinol · Pyridoxine · Ayurvedic drugs · Homeopathic drugs

Introduction

Kidney stones are associated with various biochemical disturbances in blood and urine. Various drugs and dietary changes have been recommended to halt stone recurrence [1]. Several medicines are being prescribed blindly for treatment and prophylaxis of urinary stones all over the world. Medical management for urinary stone disease may be classified as empiric therapy (treatment without doing metabolic studies) and directed medical therapy (based on metabolic assessment). Most of the drugs appear to be out of place and doing more harm than good to the patient.

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This leads to non-compliance of medications, occurrence of side effects and continuation of the process of stone formation. There needs to be a scientific basis for deciding chemotherapy and prophylactic drugs and dosage. Empiric medical therapy has, however, been shown to reduce the stone recurrence rate [2]. The objective of this paper is to identify the prevalence of blind chemotherapy among the patients attending the stone clinic for the first time and finding out the real indication for the drugs administered.

Methods

Patients who attended the urinary stone clinic for the first time during 2007–2008 were interviewed to find out what drugs they had been taking before the attendance at the stone clinic. 350 patients consuming specific drugs relevant to stone formation at least for a period of 15 days were selected for detailed assessment. The prevalence of intake of empirical drugs at the time of presentation was assessed. The type of drug consumed, dose, duration, side effects, compliance rate, clinical relief and effect on stone disease were assessed using a study protocol (Table 1). Compliance was calculated by the duration of the intake of the drug correlated to the duration of treatment advised by the clinician in the original prescription. The biochemical profile of the patients was assessed to identify the role of the therapeutic modalities utilised. Conclusions regarding the utility of the drugs on the disease process were made. The biochemical values namely serum calcium, serum uric acid, urine calcium, urine oxalate and urine uric acid were compared with those of 30 fresh patients not on medications and 30 controls considering the laboratory standards. Analysis of variance was performed to assess the statistical significance of the variation of biochemical values in the different groups.

Results

Of the 350 patients studied, 96 patients were consuming potassium citrate in different doses, 50 were consuming allopurinol, 44 cystone, 27 potassium citrate + magnesium, 25 calcury, 24 rowatinex, 21 ayurvedic drugs, 17 dystone, 17 homeopathic medicines and 17 other drugs—antibiotics, hexasodium hexapotassium hydrogen citrate (Uralyt U), combination of potassium citrate, magnesium and pyridoxine (potrate MB6), sodium citrate (citra soda), pyridoxine, tamsulosin, alfuzosin, hydrochlorothiazide and other diuretics. The compliance rate, clinical efficacy and effect on stone disease process were recorded (Table 2). The longest duration of compliance was for cystone—2.5 years. All other drugs were stopped by the patients themselves due to persistent symptoms. They had, however, restarted the drugs 15 days prior to attendance. As much as 93% of the patients did not feel that there was any significant long term relief of symptoms. About 7% of the patients who had no significant symptoms had been taking cystone. The side effects which prompted the patients to stop medicine were gastro intestinal upset, particularly with potassium citrate, rowatinex and potassium citrate + magnesium combination. The relevant biochemical changes noted in the patients on various drugs (Table 3) were increased urinary citrate levels and decreased urine uric acid levels in patients consuming potassium citrate alone or in combination with magnesium and in patients on allopurinol, analysis of variance of both showing significance of $P < 0.05$. Serum uric acid and urine uric acid levels were within normal limits in patients consuming allopurinol.

Discussion

Identification of stone disease in patients presenting with symptoms related to stone problem is still deficient. Medical management of early stone disease is still in its infancy. Recurrence of urinary stone disease is a significant problem encountered while managing urinary stone disease. As much as 10–20% of the patients develop symptoms of recurrent new stones in one year following an episode of stone disease [3]. Management of recurrent stones with surgery or modern modalities of stone retrieval are very costly. The cost of medical care is estimated to be half to a fourth that of surgical care which entices the common man towards medical treatment [4]. There have been attempts to devise a decision tree model for medical management of stone disease [5, 6]. However, most clinicians are seen to resort to blind chemotherapy, when they encounter patients with suspected stone disease.

Various problems are encountered in administering empirical therapy or blind chemotherapy. When citrate is administered without assessing the urinary citrate level, we are unnecessarily loading citrate into the body. When the oxalate levels are not high, administration of pyridoxine may be unnecessary. This may be the reason for non-compliance by patients reported in the present study. Treatment with pyridoxine administered earlier by several clinicians has been discontinued due to the occurrence of side effects, thanks to the high doses [7–10]. High doses of pyridoxine in patients with low oxalate level may produce intolerance at 120 mg or higher per day. Thus empiric therapy with high dose of pyridoxine may be detrimental to the patients [11, 12]. Even though fair reduction in stone episode rates is reported following empirical or blind chemotherapy, it is not clear whether the chemotherapy as such is responsible for the clinical benefit. Side effects of chemotherapy are not

Table 1 Protocol for assessing blind chemotherapy

Unique No: Date:
Name: Age: Sex:
Diagnosis:

Drug	Dose	Duration	Compliance	Benefit	Side effect	Cost
Potassium citrate						
Allopurinol						
Cystone						
Pot citrate + Mg						
Calcury						
Rowatinex						
Ayurvedic drugs						
Distone						
Homeopathic drugs						
Antibiotics						
Uralyt						
Potrate MB6						
Citra soda						
Pyridoxine						
Tamsulosin						
Alfusin						
Hydrochlorothiazide						
Other diuretics						
Other						

Final opinion

Table 2 Details of the effects of blind chemotherapy

No.	Group	Number	Compliance (%)	Clinical efficacy (%)	Effect on stone (%)
1	Potassium citrate	96	33	15	4
2	Allopurinol	50	56	09	2
3	Cystone	44	68	38	3
4	Potassium citrate + Mg	27	37	34	3
5	Calcury	25	23	10	2
6	Rowatinex	24	36	13	1
7	Ayurvedic drugs	21	78	19	15
8	Dystone	17	63	12	0
9	Homeopathic drugs	17	68	12	12
10	Others	17	35	16	7

reported much because most patients do not consume the drugs for long periods of time. Administration of thiazides blindly has resulted in various adverse reactions including hypotension, gastro intestinal upsets and sexual inadequacies. Allopurinol is usually prescribed in dose of 300 mg/day. At this dose, it produces abnormalities of liver

Table 3 Biochemical profiles of patients on blind chemotherapy

No.	Group	Serum calcium (mg %)	Serum uric acid (mg %)	Urine calcium (mg/day)	Urine oxalate (mg/day)	Urine uric acid (mg/day)	Urine citrate (mg/day)
1	Potassium citrate	8.9	6.4	278	84	547	896
2	Allopurinol	8.7	4.3	267	76	467	367
3	Cystone	9.2	6.1	287	84	614	346
4	Potassium citrate + Mg	9.5	4.9	257	74	547	798
5	Calcury	10.6	6.4	254	48	677	267
6	Rowatinex	11.5	6.3	286	63	745	278
7	Ayurvedic drugs	9.6	5.8	248	59	594	256
8	Dystone	9.7	6.4	306	69	614	310
9	Homeopathic drugs	10.5	6.4	273	76	646	352
10	Others	10.5	5.9	311	75	593	267
11	Fresh stone patients	9.9	6.7	308	69	638	257
12	Controls	9.3	5.4	279	43	548	167
	Anovar	NS	NS	NS	NS	$P < 0.05$	$P < 0.05$

enzymes and even Steven Johnson syndrome. Most of the patients do not require this dose of allopurinol for reducing the uric acid level and also reducing the stone incidence rates. Potassium citrate may be used to control moderately high levels of uric acid [13]. It has been noted that uric acid may promote calcium oxalate stone formation. This is believed to be due to the monosodium urate which promotes calcium oxalate crystallisation [14].

Quite often, it is very difficult for the clinicians to assess the role of chemoprophylaxis as the patient might not have developed a recurrence even without the consumption of the prophylactic medications. It is believed that a patient acts as his own control as far as the effect of medical management is concerned. Naturally, the assessment of the effect of chemotherapy has to be based on the occurrence of symptoms, presence of blood cells or different types of crystals in the urinary deposits or formation of new stones. Radiologically recognised reduction in the size of the stones or those reported by ultra sound studies are deficient in scientific value and should not be considered as scientific basis for reporting improvement in calculogenic status of the individuals. Dietary modifications are always restrictive in value, as it is very difficult to assess the extent of restrictions imposed by the patients upon their diet based on advice. Not all patients respond to dietary restrictions uniformly. To give appropriate dietetic advice for the individual patients, the response of the patients to specific dietary exaggerations or restrictions will have to be studied.

Blind chemotherapy further presents the problems of cost effectiveness. The dose of medications should be prescribed depending upon the minimum needs for individual patients. Administering higher doses of medications would result in high cost of treatment and higher chances of adverse reactions. There is an argument against metabolic evaluation, because of the cost involved. It is agreed that proper metabolic assessment is costly, but a scientific decision making cannot be made without a total metabolic assessment. It may not be possible to perform metabolic assessment repeatedly during follow up to study the effect of chemoprophylaxis routinely, because of the cost factor involved. However, the reduction of severity of symptoms, presence and extent of RBCs, pus cells or crystals, their sizes and presence of aggregation and clumping may be assessed without significant cost to the patients at regular intervals. Most of the papers on empirical chemotherapy have not reported on the basic assessment patterns of the urine deposit when followed up for long periods of time. These deficiencies restrict the value of the reports on empirical chemotherapy and chemoprophylaxis for single or recurrent stone formers.

The duration of medical management and assessment of compliance are problems because the patient may return after few months or few years and may report that he has been taking the drugs regularly. Only when the relevance of the observation is made known to the patient will he come forth with truth about actual compliance, irregularity of treatment and stoppage of treatment. Any study to assess the effect of dietetic or drug therapy will have to consider possible irregularities in the statement made by the patients as far as the duration and dose of the drugs are concerned. Stone clinic effect is basically awareness of the pathology of stone nucleation and growth. Dietetic advice and increased intake of fluids will form the major part of the stone clinic effect.

Conclusion

It is concluded that most of the drugs administered blindly were neither indicated nor beneficial for the patients. Such

unscientific medications will be detrimental to patient care. Metabolic correction has to be based on proper metabolic assessment.

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