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Original Article

Different duration of Colchicine for preventing recurrence of Gouty arthritis

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ABSTRACT

Background: Gout is a Common recurrent clinical syndrome characterized by increased serum uric acid and recurrent attacks of acute arthritis. Colchicine is used for Prophylaxis against recurrence of arthritis, but the duration of its administration has mentioned variable. In this study, optimal duration of prophylactic colchicine for prevention of gouty arthritis was assessed.

Methods : In a clinical trial 190 patients with gouty arthritis divided randomly to group 1,2and 3 and received colchicine for 3 to 6, 7 to 9 and 10 to 12 months then colchicine discontinued and the patients followed one year for recurrence of arthritis. Result assessed by survival analysis with Kaplan –Meier method.

Results: The probability of recurrence of arthritis (in order of duration of colchicine prophylaxis) was 54%, 27.5% and 23%, respectively. The difference between group one and others was statistically significant, but between group 2 and 3 was not statistically significant.

Conclusion: The most suitable duration of colchicine prophylaxis that accompanied with lower recurrence rate was 7-9 months, which seems more cost -effective than 10-12 months regimen.

Key words: Gout, Colchicine, Arthritis, Recurrence

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Gout is a common recurrent clinical syndrome, which affects at least one percent of men in western population, with a male to female ratio ranging from 7-9/1 [1, 2]. For preventing recurrence of arthritis and progression, the management of gout involves not only treating acute arthritis but also lowering urate level [2]. Current therapies for acute gouty arthritis consist of colchicine, NSAIDs and glucocorticoids [4, 5, 6], and most patients need urate lowering agents for preventing it [2, 3, 4].

Normal upper limit of serum uric acid is 7 mg/dl in men and 6 mg/dl in women [1, 3]. Change in serum uric acid level is one of the predisposing factors for recurrence of acute gouty arthritis which is frequently prevented by NSAIDs and colchicines.

Data supporting the use and duration of NSAIDs or colchicine are sparse [6, 7], but a low dose of colchicine (1 mg/d orally) plus anti-hyperuricemic therapy is a standard practice for preventing recurrence of arthritis [4, 6 - 8].

Prophylaxis with colchicine apparently reduces the rate of recurrent acute attacks, whether or not the serum urate concentration is normal [8, 9], but the duration of prophylaxis with colchicine isn't defined and it continued for 3 months [10], for six months [1], and for one year after last episode of gouty arthritis [2, 11, 12].

In present study, patients received colchicine in three different durations and followed for recurrence of acute arthritis till one year later.

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Subjects and Methods

This clinical trial performed on 229 patients with gout that referred to rheumatology clinic of AL-Zahra hospital in Isfahan during 2000-2005.

Inclusion criteria contains patients with gouty arthritis that more than one year elapsed from diagnosis and had at least one indication of long-term treatment with urate–lowering agents [2,4,5]. The results of careful history and physical examination including; demographic data, duration of disease, number of attacks in previous year , history of other disorders , renal stone ,tophi , drug, previous laboratory data (such as serum uric acid , SGOT , SGPT , CBC , BUN, Cr, uric acid of 24 hours urine) were collected.

All patients were treated with allopurinol, and randomly divided into three groups, receiving colchicine (1 mg/day) for 3-6 months (group 1), for 7-9 months (group 2) and for 10 -12 months (group 3). At least every 3 months, the patients were visited and drugs consumption was evaluated. Laboratory examinations included CBC , Serum Uric acid , BUN , Cr , SGOT , SGPT and were repeated every three months.

Colchicine discontinued in all groups, and the patients followed one year for any evidence of recurrence of gouty arthritis. If patients relapsed before the end of one year, exclude from study and treated for acute gouty arthritis.

For detecting probability of recurrence of acute arthritis, we used survival analysis and Kaplan - Meier method from SPSS 11.5. Survival curves of three groups compared with Log – Rank test.

Results

In this study, 190 patients completed follow up. Table 1 shows characteristics of the patients in each group.

For detecting similarity between patients of each group, they were divided to two subgroups; with recurrence of arthritis or without any episode of arthritis, and mean level of serum uric acid and age were compared (T–test). The difference was not significant ($p > 0.05$).

In the end of sixth months; the probability of recurrence of occurred attack was 46 %, 11% and 6% in group 1,2,3, and in the end of one year; was 54 %, 27.5 % and 23 % in group 1,2,3, respectively. Log –Rank test showed significant differences between group 1 and others ($p < 0.001$) and no difference between group 2 and 3 ($p = 0.1$)(Figure 1).

The mean time of recurrence was 8 months (7 – 9 , CI 95 %) in group, 11 months (10 – 11 , CI 95 %) in group2, and 11 months (11 – 12 , CI 95 %) in group 3 . Log –Rank test showed significant difference between group 1 and others ($p < 0.001$) and no difference between group 2 and 3($p = 0.09$). The effect of age, serum level of uric acid was evaluated by Cox-Regression test and none of them have significant effect on recurrence of arthritis.

Livers enzymes raised less than two folds normal in three patients of group one, 5 patients of group two and 6 patients of group three. Rising was transient and enzyme level reduced to normal despite of drug continuation. In group three, one patient affected with neuromyopathy and serum creatinin raised in one patient. The prevalence of drug side-effect was not different among 3 groups, when compared with Chi–Square test ($p = 0.2$).

Discussion

The duration of colchicines for preventing recurrence of gouty arthritis is variable [4, 10], and without recurrence rate of arthritis after discontinuation of colchinine. In our study, colchicine therapy for 3 to 6 months had higher recurrence rate than others. Colchicine consumption for more than 6 months accompanied lower rate of recurrence. For the patients used colochicine for 10-12 months, the rate of recurrence was lower than for 7-9 months, without significant difference.

For longer period, colchicine increased probability for drug side effects, but the difference was not significant.

The most common side effect was mild transient rising of liver enzymes. In other studies also, low dose of colochicine (1 mg/day) had few side effects [5, 6].

Previous studies in western population may be different from Iranians in spite of race, culture and diet. It seems that the most suitable duration of colchicine prophylaxis against recurrence of gouty arthritis is 7 to 9 months in our population.

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Table 1. The patient's characteristics

Groups	Age (years)	Number		Mean uric acid (mg/dl)	
		Male	Female	Before Treatment	During Treatment
Group1; 3-6 months follow up	8 ± 48.8	61	2	8.3	6.2
Group2; 7-9 months follow up	8.2 ± 45.1	60	2	8.3	6
Group3; 10-12 months follow up	8.5 ± 44.8	62	3	8.8	6.1
Total	8.1 ± 46.6	183	7	8.5	6.1

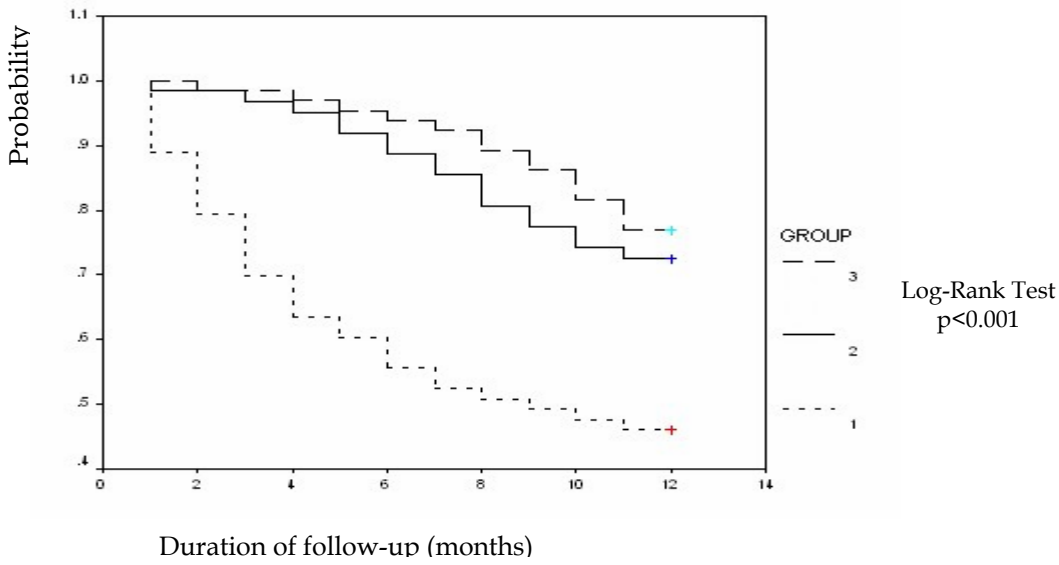

Figure1. Recurrence functions of gout (Kaplan- Meier curve)

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