

Effects of allopurinol on ventricular ejection fraction in patients with left ventricular failure

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Abstract

BACKGROUND: Efficiency of xanthine oxidase inhibitors on myocardial contractility is not clearly known. This study was conducted to determine the effects of allopurinol on left ventricular ejection fraction (LVEF) in patients with left ventricular failure.

METHODS: In a randomized, double-blind, placebo-controlled clinical trial, the efficiency of allopurinol in the LVEF status was examined in two groups of patients suffering from class II or III ventricular failure according to the New York Heart Association classification. The intervention group consisted of 16 cases who received allopurinol (100 mg/day on the first three days, 200 mg/day on the second three days, and 300 mg/day (in case the patient could tolerate) for one month until the end of the study). The control group included 15 patients who received the same amount of placebo. LVEF was measured by echocardiography using Simpson's method before the beginning and after the end of the intervention.

RESULTS: The mean LVEF values before and after the intervention in the case group were $38.8\% \pm 9.9\%$ and $41.9\% \pm 9.7\%$, respectively ($P < 0.05$). The corresponding values in the control group were $37.05\% \pm 5.7\%$ and $37.1\% \pm 5.6\%$ ($P > 0.05$). Mean changes related to ventricular ejection fraction in the group treated with allopurinol ($3.1\% \pm 5.6\%$) were significantly higher than those of the placebo group ($0.05\% \pm 0.3\%$) ($P < 0.05$). In addition, LVEF increased by 3.1% of the base level in the intervention group.

CONCLUSION: This study demonstrated that allopurinol prescription can improve LVEF in patients suffering from left ventricular failure to some extent. In fact, its clinical efficacy needs to be approved by more trials in various situations and longer treatment periods.

Keywords: Heart Failure, Left Ventricular Ejection Fraction, Xanthine Oxidase Inhibitors, Allopurinol, Clinical Trial.

ARYA Atherosclerosis Journal 2012, 7(Suppl): S23-S25

Date of submission: 27 Dec 2011, *Date of acceptance:* 18 Feb 2012

Introduction

Left ventricular failure is a costly and highly morbid disease whose frequency is increasing due to aging population and excess of its underlying causes.¹ One of the management objectives in heart failure is to improve the function of cardiac muscle and quality of life along with increasing patient survival. Various solutions and drugs have been used for this purpose.^{2,3} Allopurinol is currently presumed to increase myocardial contractility in patients suffering from heart failure by imposing its inhibitory effect on the xanthine oxidase and improving myocardial contractile power.^{4,5}

In this study, the efficiency of allopurinol on left ventricular ejection fraction (LVEF) was investigated in a group of patients suffering from left ventricular failure.

Materials and Methods

In a randomized, double-blind, placebo-controlled clinical trial, the efficiency of allopurinol in LVEF was investigated in 40 patients suffering from ventricular failure. Patients with left ventricular failure caused by idiopathic or ischemic cardiomyopathy, classified as class II and III according to New York Heart Association classification system were selected for this study. The limit of LVEF was considered as 30-

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50%. Patients who had received one of the non-medical treatments before the study and those for whom allopurinol was prohibited were excluded. Eligible patients who referred to the Heart Clinic of Alzahra Medical Center affiliated to Isfahan University of Medical Sciences (Isfahan, Iran) in 2007 were randomly divided into two groups using the table of random numbers. The participants completed and signed a consent form after the stages of research were precisely explained for them.

After entering the study and before grouping, diagnostic tests including echocardiography to determine ejection fraction, measurement of liver enzymes including aspartate aminotransferase (SGOT) and alanine aminotransferase (SGPT), and renal function tests including blood urea nitrogen (BUN) and creatinine were conducted for each patient. The background information of patients including age, sex, duration of heart failure, and its underlying diseases were recorded. Echocardiography was performed with standard accuracy and using a single technique and echocardiograph. LVEF was calculated by one person (to remove the measurement error caused by several people) by Simpson's method using at least two views of apical 4 chambers and parasternal 2 chamber (to minimize eye measurement error).

After grouping, the first group received 100 mg/day allopurinol (Amin Pharmaceutical Company, Isfahan, Iran) once a day for three days. The dose was then increased to 200 mg/day in two doses for three days and. Afterwards, if the patient could tolerate, three 100 mg doses were administered until the end of the study. The overall course took one month. In the second group, a similar treatment regimen was used with placebo. The basic treatment regimen of the patients continued without any changes during the study.

Patients were excluded from the study in case of death or immigration, necessity of using drugs which interfered with allopurinol (like some antibiotics), adverse effects of or allergy to allopurinol,^{6,7} changes in blood indexes (leukocytosis, leukopenia, increased liver enzymes more than twice as much as the base limit, and kidney failure) caused by allopurinol consumption two weeks after taking the drug, poor echo window in patient's echocardiography, and starting or stopping a medication which impacted preload, afterload, or myocardial contractility during the experiment.

Patients were followed up by weekly phone calls in order to monitor adverse effects, intolerance, and compliance. On the second week after beginning the treatment, complete blood count (CBC) and liver and

kidney function tests were performed and individuals with exclusion criteria were excluded.

At the end of the treatment period, all patients underwent a second echocardiography by the same person who had conducted the first echocardiography (to remove the measurement error caused by several people). He was not aware of the treatment regimen. Finally, LVEF was calculated for all patients. The data was then entered into SPSS (SPSS Inc., Chicago, IL, US) and analyzed by parametric statistical tests using the intention-to-treat method.

Results

Out of the 40 selected participants, 9 were excluded from the study due to different reasons like skin rash (one person), lack of compliance in taking drug or placebo, and being out of reach. Finally, 16 (including 6 women) and 15 (including 5 women) people completed the stages of the study in the intervention and placebo groups, respectively. The mean ages of the studied people in the intervention and placebo groups were 66.1 ± 8.6 years and 63.1 ± 8.8 years, respectively ($P < 0.05$).

The mean LVEF values in the intervention group before and after the study were $38.8\% \pm 9.9\%$ and $41.9\% \pm 9.7\%$ ($P < 0.05$), respectively. The mean values of LVEF in the placebo group before and after the study were $37.5\% \pm 5.7\%$ and $37.1\% \pm 5.6\%$ ($P > 0.05$), respectively. The mean of changes related to LVEF in the group treated with allopurinol ($3.1\% \pm 0.5\%$) was significantly higher than that in the placebo group ($0.05\% \pm 0.3\%$) ($P < 0.05$).

Discussion

Similar to the studies conducted in other countries,⁸⁻¹³ this study showed that xanthine oxidase inhibitors, like allopurinol, can moderately improve LVEF of patients suffering from left ventricular failure.

It is worth mentioning that this study only investigated LVEF changes caused by taking allopurinol. However, the extent to which this medication can be clinically effective requires long-term studies along with follow-up of clinical status of patients. Xanthine oxidase inhibitors can be used in the treatment regimen of patients suffering from heart failure after their efficiency is approved in more trials in various situations and longer treatment periods. Their effects on the incidence of long-term complications and benefits should also be investigated.

Acknowledgments

The Persian version of this article has been previously published in Journal of Isfahan Medical School: 2007, No: 85; 104-108.

Conflict of Interests

Authors have no conflict of interests.

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