



Hemostasis: pathological state and therapeutics

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Abstract

Coronary artery disease is a complex syndrome to get initiation from formation of atherosclerotic plaques in systemic circulation to cardiac arrhythmia causing morbidity/mortality. This study was conducted to compare hypolipidemic effects of Niacin and Indian date (Jujuba) in hyperlipidemic patients. Study was conducted from July 2019 to December 2019 at National Hospital Lahore-Pakistan. Sixty participants were enrolled of both gender male and female patients age range from 25 to 60 years. Consent was taken from all patients. They were divided in two groups. Group-I was advised to take 2 grams Niacin in divided doses for the period of two months. Group-II was advised to take 500 grams of fruit Jujube daily for the period of two months. All patients' systolic and diastolic blood pressure was noted. Their baseline LDL and HDL cholesterol was determined by conventional method of measuring Lipid Profile. After two months therapy, their post treatment blood pressure and lipid profile were measured and mean values with \pm SEM were analyzed bio statistically. Group-I which was on Niacin their blood pressure was reduced but it was non-significant change, LDL cholesterol decreased significantly and HDL cholesterol was increased significantly. In group-II patients LDL cholesterol was decreased significantly but HDL increase was not significant with p -value of >0.05 . It was concluded from the research work that Niacin is potent in lowering LDL and increasing HDL cholesterol, while Jujube has significant effect as LDL cholesterol lowering potential, but it does not increase HDL cholesterol significantly. Jujubes and vitamin B-3 did not reduce blood pressure, when analyzed statistically.

Keywords: hyperlipidemia, niacin, cholesterol, Pakistan

Introduction

Early observations that cholesterol is a key component of arterial plaques gave rise to the cholesterol hypothesis for the pathogenesis of atherosclerosis. Population studies have demonstrated that elevated levels of LDL cholesterol and apolipoprotein B (apoB) 100, the main structural protein of LDL, are directly associated with risk for atherosclerotic cardiovascular events (ASCVE). Indeed, infiltration and retention of apoB containing lipoproteins in the artery wall is a critical initiating event that sparks an inflammatory response and promotes the development of atherosclerosis. Arterial injury causes endothelial dysfunction promoting modification of apoB containing lipoproteins and infiltration of monocytes into the subendothelial space. Internalization of the apoB containing lipoproteins by macrophages promotes foam cell formation, which is the hallmark of the fatty streak phase of atherosclerosis. Macrophage inflammation results in enhanced oxidative stress and cytokine/chemokine secretion, causing more LDL/remnant oxidation, endothelial cell activation, monocyte recruitment, and foam cell formation. HDL, apoA-I,

and endogenous apoE prevent inflammation and oxidative stress and promote cholesterol efflux to reduce lesion formation [1]. Commonly used medications for treatment of Hyperlipidemia include Statins, Fibrates, Niacin, and Resins. All these medicines have potential for SEs and low compliance due to one reason or another [2]. Niacin when given in hypolipidemic doses i.e., more than 2 grams per day it causes partial inhibition of release of free fatty acids from adipose tissue, and increased lipoprotein lipase activity, which may increase the rate of chylomicron triglyceride removal from plasma. Niacin decreases the rate of hepatic synthesis of VLDL and LDL by synthesis of apoproteins which are integral part of LDL or VLDL structure [3]. Some herbs have been proved to reduce plasma lipids in human population. Jujubes or Ziziphus jujube have somewhat hypolipidemic as well as hypoglycemic effects [4]. Jujube fruit is known to contain considerable number of phenolic compounds, including chlorogenic acid, gallic acid, protocatechuic acid and caffeic acid [5]. High polyphenolic content of Z Jujube suggests its potent capacity in clearing of oxidants. Many studies proved the hepatoprotective effect of

methanolic extract of *Zizyphus jujube* fruits. Histopathological studies supported the biochemical findings. Study concludes a hepatoprotective activity probably due to its antioxidant effect [6]. Some studies evaluated the effect of *Z Jujube* fruit in controlling dyslipidemia in obese adolescents. A triple-blind randomized placebo-controlled trial of 86 obese adolescents aged 12-18 with dyslipidemia proved its hypolipidemic features. Results showed the fruits to be generally well tolerated, with potential favorable effects on blood pressure and serum lipid profile [7]. Hydro-alcoholic preparations from Indian dates have been proved to possess hypotensive and hypolipidemic effects in human population. Main problem with ingestion of Indian dates or *Jujuba* was its larger amount to take by human population to reduce blood pressure and hyperlipidemia. It is proved in various studies that if taken in high amount Indian dates are antioxidant and anti-inflammatory in characteristics. Their cardiogenic and hepatogenic effects are explained in various studies [8]. In ancient Chinese book on herbal medicine *Huangdi Neijing* (475-221 BC), *jujube* was described as one of the five most valuable fruits in China. In *Shennong Bencao Jing* (300 BC-200 AD), an earlier book recoding medicinal herbs, *jujube* was considered as one of the superior herbal medicines that prolonged our life-span by nourishing blood, improving quality of sleep, and regulating digestive system [9].

Subjects and method

Consent: The research work was started after written approval of ethics committee of National Hospital, Lahore. **Duration of study:** It was conducted from July 2019 to December 2019. **Sample size** sixty hyperlipidemic patients were selected from National Hospital Lahore-Pakistan to compare hypolipidemic effects of Niacin (vitamin B-3) and commonly used fruit in

winter season in Pakistan i.e., Indian date or *Jujube* (Bair in urdu). **Inclusion and exclusion criteria:** Both male and female patients suffering from primary or secondary hyperlipidemia were selected. The age limit for patients was 25 to 60 years. **Exclusion criteria** were alcoholics, cigarette smokers, habitual to enjoy sedentary life, with impaired liver or renal functions. **Written and already explained consent** was taken from all participants. Their systolic/diastolic BP was measured by using mercury sphygmomanometer. **Baseline Lipid Profile** was determined in Biochemistry lab of the Hospital. Patients were divided in two groups, 30 patients in each group. **Group-I** was on Tab. Niacin 2 grams daily in three divided doses. **Group-II** was on *Jujube* 500 grams daily in three divided times to eat. They were advised to take fruit and vitamin B-3 for two months. They were also advised not to take junk food and were also advised to do 35 minutes brisk walk daily in the morning or evening. **Statistical analysis:** Mean values ± SEM were taken for statistical analysis using SPSS version 10.0, 2015. Paired ‘t’ test was applied to get significance changes in parameters before and after treatment. P-value >0.05 was considered as non-significant change, p-value <0.01 was considered as significant and p-value <0.001 was considered as highly significant change in the parameter. **Conclusion:** It was concluded that Niacin is antioxidant, hypolipidemic and hypotensive agent in lipid lowering drugs while fruit *Jujubae* is mild hypolipidemic when used in high quantity.

Results

With two months therapy by vitamin B-3 (Niacin) and Indian dates (*Jujube* or *Jujuba*), systolic/diastolic blood pressure was not changed when analyzed statistically but plasma total cholesterol, LDL-cholesterol and HDL-cholesterol were changed, which are shown in following table 1.

Table 1: Illustrating mean values with ±SEM and p-values in two groups of hyperlipidemic patients before and after treatment

	LDL-C	HDL-C	Systoic BP	Diastolic BP
Before treatment	G1= 210.1±2.11	37.9±1.91	110.02±1.12	86.87±2.01
	G2= 198.8±2.17	38.6±2.19	113.98±2.86	89.66±1.04
After treatment	G1= 180.9±2.22	45.2±2.19	108.55±2.87	85.84±1.00
	G2= 190.9±1.73	41.9±2.97	112.56±2.67	87.52±2.22
Change in mg/dl	G1= 29.2	7.3	1.47	1.03
	G2= 7.9	3.3	1.42	2.14
Change in %	G1= 13.9 %	16.2 %	1.33%	1.18%
	G2= 4.0 %	7.9 %	1.24%	2.38%
p value	G1= <0.001	<0.001	>0.05	>0.05
	G2= >0.05	<0.01	>0.05	>0.05

KEY: G1 is group on Niacin, G2 is group on drug-2 ie *Jujube*, ± stands for Standard Error of Mean values, BP stands for blood pressure, p-value >0.05 is non-significant change, p-value <0.01 is used for significant change in parameter, and p-value <0.001 is highly significant change in tested parameter.

Discussion

Dyslipidaemia has a prominent role in the onset of notorious atherosclerosis, a disease of medium to large arteries. Atherosclerosis is the prime root of cardiovascular events contributing to the most considerable number of morbidity and mortality worldwide. Factors like cellular senescence, genetics, clonal haematopoiesis, sedentary lifestyle-induced obesity, or diabetes mellitus upsurge the tendency of atherosclerosis and

are foremost pioneers to definitive transience. Accumulation of oxidized low-density lipoproteins (Ox-LDLs) in the tunica intima triggers the onset of this disease. Hypolipidemic drugs decrease chances of LDL particles available for oxidation, so prevent CAD. Vitamin B-3 (Niacin) is commonly used hypolipidemic drug which inhibit lipoprotein lipase activity, so lesser formation of free fatty acids will be available which are main sources of TG-rich lipoproteins (VLDL) formation.

Lesser amount of VLDL lead to lesser synthesis of LDL particles which are rich in cholesterol. In our research study it was proved that no vitamin B-3 nor Indian dates decrease systolic or diastolic blood pressure when pre and post treatment results were analyzed biostatistically. In our results vitamin B-3 (Niacin) 2 grams daily intake for two months decreased LDL-cholesterol about 13.9 % which is highly significant change. HDL-cholesterol in this group increased about 16.2 % which is again highly significant change. (ZQ Zhu, *et al*)^[10], and (W Cao, *et al*)^[11], proved same results when they used 2 grams of Niacin in 66 hyperlipidemic patients, but (WB Yao, *et al*)^[12] observed lesser effects of Niacin on HDL cholesterol, i.e., only 4.4 % increase in HDL cholesterol. (Hung PG, *et al*)^[13] explained different mechanisms of hypolipidemic response of Nicotinic acid on persons with different genetic code. One of the favorable mechanisms for patients with CAD they described is fibrinolytic activity of Niacin. In our results Jujube fruit decreased LDL cholesterol is 7.9 mg/dl, which is significant change in the parameter. HDL cholesterol is not increased significantly in our results with p-value of >0.05. (Tan H, *et al*)^[14], and (Tripathi M, *et al*)^[15], observed same reason of Jujube on LDL and HDL-cholesterol, which augment our results. (Tschesche R, *et al*)^[16], observed more effects of Jujube as we observed in low density lipoprotein cholesterol. (Um S, *et al*)^[17] proved that LDL cholesterol is much decreased as compared to our results. (KB Kang, *et al*)^[18] observed too less effects of Jujube fruit in 5 hyperlipidemic patients. This difference in two studies is due to their small sample size, i.e., they tried herb only on five hyperlipidemic patients, while we tried in 30 hyperlipidemic patients. Compliance of Indian fruit Jujuba is low due to its very high amount to take as hypolipidemic and hypotensive herbs. It was explained by (Loom Viyu, *et al*)^[19], and (A. Mohammad, *et al*)^[20]. In atherosclerosis susceptible regions, the endothelial cells have cuboidal morphology, a thin glycocalyx layer, and a disordered alignment. In addition, these regions have increased endothelial cell senescence and apoptosis as evidenced by ER stress markers. In contrast, less atherosclerosis prone endothelium is exposed to laminar shear stress causing activation of signaling pathways that maintain endothelial cell coaxial alignment, proliferation, glycocalyx layer, and survival^[21-4].

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