Comparison of antioxidant property of two antihypertensive drugs amlodipine and Telmisartan in patients of essential Hypertension

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Abstract

Aim: Evaluate the relation of oxidative stress and hypertension and also to evaluate the antioxidant property of two commonly used antihypertensive drugs.

Material and Method: This was an open labeled, comparative, prospective, interventional study involving 30 human patients and 15 human healthy volunteers selected from the outpatient Department of Medicine, Krishna.

Result: ANOVA application to the values of all three groups gave P value of 0.5438 which was also >0.05 and it was not significant. Considering all three parameters we can say that there is no difference among all three groups in the level of oxidative stress before starting treatment.

Conclusion: There is increase in the activity of SOD activity after treatment with Telmisartan for 3 months. There is not much difference in SOD increasing property of Amlodipine and Telmisartan. Both antihypertensive drugs amlodipine and telmisartan are having antioxidant property at least by means of increasing SOD (antioxidant enzyme) activity. But neither of them is better than the other at this.

Keywords: oxidative stress, hypertension

Introduction

Hypertension is one of the most serious concerns of modern medical practice. It is the leading cause of morbidity and untimely death [1]. Hypertension accounts for 6% of deaths worldwide [2]. There are few recognizable and surgically treatable causes of hypertension such as Pheochromocytoma, steroid secreting tumors of adrenal cortex, renal artery stenosis and so on, but most cases involve no obvious cause and are grouped as “essential hypertension”. It is called “essential hypertension” because it was originally, albeit incorrectly, thought that the raised blood pressure was ‘essential’ to maintain adequate tissue perfusion [3]. Oxidative stress describes the injury caused to cells by the oxidation of macromolecules resulting from increased formation of Reactive Oxygen Species (ROS) and/or decreased antioxidant reserve. A variety of antioxidant mechanisms exist in human body, which in normal circumstances remain in balance with oxidative stress. There are two major classes of antioxidants, one is enzymatic and the other one is non enzymatic class of antioxidants (free radical scavengers).

Amlodipine is one of the widely prescribed antihypertensive drugs in essential hypertension patients. Amlodipine is a long acting calcium channel blocker with vascular selectivity [4]. So it can be concluded that in hypertension there is endothelial cell dysfunction and increased level of oxidative stress [5]. And it is also believed that antihypertensive drugs like calcium channel blockers and angiotensin receptor blockers possess antioxidant properties. But there are also studies which are having counterview to this finding and belief. Therefore we thought it worthwhile to evaluate the relation of oxidative stress and hypertension and also to evaluate the antioxidant property of two commonly used antihypertensive drugs [6].

Material and Method

The present study was conducted in a tertiary care centre in Krishna Institute of Medical Sciences (KIMS), Karad. This was an open labeled, comparative, prospective, interventional study involving 30 human patients and 15 human healthy volunteers selected from the outpatient Department of Medicine, Krishna Hospital, Krishna Institute of Medical Sciences Deemed University, Karad and Karad city. Institutional Ethics Committee (IEC) approval was
taken prior to the initiation of the study. Study protocol and Informed Consent Form (ICF) were also approved by the ethics committee. Diagnosis was based on the clinical assessment done by the physician of the respective hospital. Clinical assessment included medical history, physical examination and required laboratory investigations. Blood pressure of the participants was measured with a mercury sphygmomanometer in the sitting position after 5 minutes of rest in a quiet environment following the recommendations of the British Hypertension Society. Mean of 3 readings of systolic blood pressure (SBP) and diastolic blood pressure (DBP) (Korotkoff phase I and phase V, respectively) were taken at 5-minute interval. Persons who fall in the group of stage 1 hypertension according to JNC VII (not stage II/III) were selected as essential hypertensive patients. And controls were also carefully selected so that properly fit into normotensive group (BP value <140/90 mmHg). All the selected participants were asked to come to Krishna hospital phlebotomy room for the collection of blood sample with at least 10 hours of fast (as lipid profile was also to be done). Subjects were asked to rest for 30 minutes before collecting blood sample. Blood was collected in the morning hours; venous blood from the antecubital vein was drawn into a clean dry disposable sterile syringe under all aseptic precautions. About 5 ml of fasting venous blood sample was collected from each patient as well as control subjects. The blood was immediately transferred into two clean and dry test tubes, one with (approximately 1.5ml) and the other without (remaining blood) the anticoagulant. The tube with anticoagulant was centrifuged at 3300 rpm for 10 minutes to separate the red blood cells (RBCs) from the plasma. The plasma transferred to a clean and dry test tube. The serum in test tube with coagulated blood was transferred after centrifugation into another dry test tube. Care was taken to prevent haemolysis. Plasma was used to measure the superoxide dismutase (SOD) activity in blood while serum was used for MDA (Malondialdehyde), TAS (Total Antioxidant Status) and lipid profile measurement. All the biochemical investigations were done in the laboratory of department of Biochemistry, KIMS, Karad. And optical density for all the parameters (MDA, TAS and SOD) was taken on the Chem-5 semiautoanalyser (Erba® Mahaim).

At this point participants with high lipid profile were excluded from the study and remaining was enrolled for the study. Participants who were excluded at this stage were advised to consult the concerned physician for their abnormal lipid profile. At the end of study duration patients (not controls) were again asked to come to the hospital for follow up blood sample which was already explained to them at the start only. Again all the above mentioned parameters were rechecked in each patient except lipid profile. Throughout the study all biochemical evaluations were free for patient. And it was fully funded by Krishna Institute of Medical Sciences, KIMSDU, Karad.

Statistical Analysis
At the end of the study statistical analysis was done using Paired & Unpaired Student’s T test and ANOVA.

Result
Intergroup Comparison was done by using student’s unpaired ‘t’ test and ordinary ANOVA statistical tests. And P value < 0.05 was taken as a level of significance. Group C and Group A values were compared using unpaired ‘t’ test. Which gave P value: 0.5560 which is >0.05. So it was not considered as significant. And there is no difference between two groups (C and A). Group C and Group T values were compared using unpaired ‘t’ test. Which gave P value: 0.1659 which is >0.05. So it is not considered as significant.

Discussion
The present study was undertaken to evaluate the relationship between oxidative stress and hypertension. It was also aimed to study and compare the antioxidant property of two drugs Amlodipine and Telmisartan in patients of essential hypertension. It was randomized, prospective, open labeled, comparative and interventional kind of study [7]. A large number of methods have been used to assess oxidative stress in biological systems. The methods used in the present study analyzed the bioavailability of the most important antioxidant mechanisms including SODs and TAS together with the oxidation byproduct MDA. All are well established for measuring oxidative stress in blood and cells, with a low coefficient of intra-assay variability [8]

Unlike the findings in animal models, the association between oxidative stress and hypertension in humans is less consistent. There is growing evidence that increased oxidative stress and associated oxidative damage are mediators of vascular injury in cardiovascular pathologies, including hypertension, atherosclerosis, and ischemia-reperfusion. Oxidative stress is associated with hypertension; however, it is unclear whether ROS initiate the development of hypertension, or if they are a consequence of the vascular damage observed in hypertension [9].

Present study failed to elucidate increased production of MDA (lipid peroxidation byproduct) in hypertensive groups as compared to control group. There was also no difference in antioxidant parameters (TAS and SOD) in both groups in current study. This was inconsistent with the finding in studies by Raedon et al. and study by H.D.Khanna They all found significant increase in lipid peroxidation product like MDA and also significant decrease in SOD and other antioxidant parameters in hypertensive individuals than controls. Results of present study were also not in line with Labios et al. Study. Here they found increase in lipid peroxidation parameter and also significant increase in antioxidant parameters like SODs and GPx in hypertensive individuals than normal controls [10].

Our study did not find increase in oxidative stress or change in antioxidant status in untreated hypertensive groups. This may be because we included only stage 1 (JNC 7) hypertensive patients who are newly diagnosed of hypertension. Therefore it can be said that there was not enough time for oxidative stress to develop. All the above mentioned studies also included

[143]
moderate to severe hypertensive patients in their study. We did not include stage 2 or stage 3 hypertensive patients in our study because the protocol of treatment followed in our hospital, which is in line with the JNC 7 guidelines, generally does not recommend the use of monotherapy in stage 2 and stage 3 hypertension (JNC 7). We required patients on monotherapy of amlodipine or telmisartan as we had to compare the antioxidant property of both drugs.

But our results are in full agreement with the results of following studies. Study done by Cracowski et al. [11] did not find significant difference in oxidative stress parameters in hypertensive groups compared to normal control group. Even Ward et al. [11] have recently demonstrated no difference in either plasma or 24-h urinary F2-isoprostanes (oxidative stress parameter) in treated or untreated hypertensive subjects compared with normotensive control subjects. Tse et al. did not find differences in levels of some antioxidants between hypertensive patients and normal control subjects. And they suggested that oxidative stress is not implicated in pathogenesis of hypertension at least in early stages [11].

Even few animal studies found to have no significant causative association of oxidative stress with hypertension. Zhang et al. study indicates that oxidative stress might not have a major contribution to the hypertensive responses elicited by the vasoconstrictors in rats. Similarly, Elmarakby et al. showed in Sprague-Dawley rats that two antioxidants, tempol and apocynin, prevented an endothelin-1–mediated increase in plasma 8-isoprostane, an indicator of oxidative stress, and aortic superoxide production, but failed to attenuate blood pressure rise [12].

So our finding is that amlodipine and telmisartan both are having some antioxidant property at least by means of increasing SOD activity if not decreasing MDA level. Study limitations should also be considered before real interpretation. Present study was undertaken in 30 hypertensive individuals and 15 healthy normal volunteers. And each group consisted of only 15 subjects. So sample size was statistically not enough to get some conclusive inference.

Second thing we did not measure the blood pressure of patients at the time follow up (after 3 months of therapy) so we could not establish the relationship of blood pressure and change in oxidative stress parameter. Third thing we could not measure all the parameters for oxidative stress like F2-isoprostane level, catalase and glutathione peroxidase activity due to non feasibility.

Inspite of all these limitations present study surely suggests that amlodipine (CCB) and telmisartan (ARB) are having SOD increment activity which in itself is an antioxidant property. But we did not find anyone of two better than the other at this property when compared in between.

Conclusion

Based on findings from present study following conclusion can be drawn:

There is no increase in Total antioxidant status after treatment with Telmisartan for 3 months.

There is significant increase in the activity of SOD (superoxide dismutase) after treatment with Amlodipine for 3 months.

There is increase in the activity of SOD activity after treatment with Telmisartan for 3 months.

There is not much difference in SOD increasing property of Amlodipine and Telmisartan.

Both antihypertensive drugs amlodipine and telmisartan are having antioxidant property at least by means of increasing SOD (antioxidant enzyme) activity. But neither of them is better than the other at this.

Conflicts of interest: No conflict of interest

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References


