

Combination of Olmesartan and Amlodipine in Fixed Doses is Effective in Treatment of Hypertensive Patients

Hypertension is a highly prevalent disease that ranges from 30 to 44% and remains under diagnosed and undertreated. Highly effective therapies are therefore required to avoid complications in target organs such as the retina, kidney, brain, and heart. Emerging evidence has shown a significant deficit in the control of



hypertension (blood pressure <140/90 mmHg) among Hispanics or Latinos in about 65%. The combination of olmesartan and amlodipine in fixed doses (FDC) could be an effective choice for the management of hypertension in Hispanic patients. This study aims to determine the efficacy of the combination of olmesartan and amlodipine FDC in Colombian hypertensive patients for the reduction of systolic and diastolic blood pressure values. This was an observational, retrospective, open-label, multi-center, non-comparative study. The primary outcome was a change in systolic and diastolic blood pressure from the baseline to week 12; the secondary outcome was the proportion of patients achieving a target blood pressure of <140/90 mmHg. Safety and tolerability were also

evaluated. For analysis, a student t test was used for paired data, McNemar test, and repeated-measures analysis of covariance (ANCOVA). A total of 428 patients were enrolled from 16 centers in Colombia. At 12 weeks, patients' systolic blood pressure decreased in response to all three doses: by 27.75 ± 20.73 mmHg in 20/5 mg, 31.13 ± 22.23

mmHg in 40/5 mg, and 46.96 ± 20.15 mmHg in 40/10 mg (all $P < 0.001$). Furthermore, the diastolic blood pressure decreased by 14.19 ± 12.89 mmHg in 20/5 mg, 16.25 ± 10.87 mmHg in 40/5 mg, and 24.83 ± 10.41 mmHg in 40/10 mg (all $P < 0.001$). The percentage of patients achieving target blood pressure was 71.31% in 20/5 mg, 70.16% in 40/5 mg, and 63.33% in 40/10 mg. The study concludes that in daily clinical practice in Colombian patients, the FDC of olmesartan/amlodipine provides excellent systolic and diastolic blood pressure control. More than 63% of patients achieved their blood pressure goal—reduced pulse pressure of 13 mmHg—and the medication combination was well tolerated.

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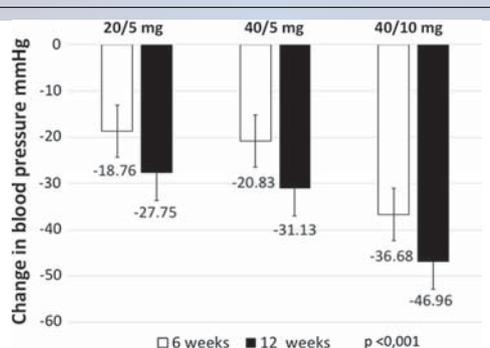


Fig. 1 Reduction of mean systolic blood pressure values at 6 and 12 weeks for each dose of olmesartan and amlodipine FDC

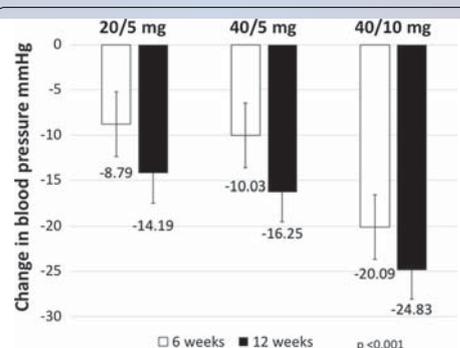


Fig. 2 Reduction of mean diastolic blood pressure values at 6 and 12 weeks for each dose of olmesartan and amlodipine FDC

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Cardiovascular Disease Causes One-Third of Deaths Worldwide

Cardiovascular diseases (CVD), including heart diseases and stroke, account for one-third of deaths throughout the world, according to a new scientific study that examined every country over the past 25 years. "It is an alarming threat to global health," said the researcher. "Trends in CVD mortality are no longer declining for high-income regions and low- and middle-income countries are also seeing more CVD-related deaths." This paper was published in the *Journal of the American College of Cardiology*. In 2015, there were more than 400 million individuals living with CVD and nearly 18 million CVD deaths worldwide. From 1990 to 2010, the age-standardized death rate from CVD dropped globally, driven by improvements in high-income countries, but that progress has slowed over the last five years. In 1990, there were about 393 deaths for every 100,000 people from CVD globally. That fell to 307 deaths per 100,000 in 2010, and, over the next five years, decreased only slightly, to 286 deaths per 100,000. "This paper is the manifestation of two paradoxes," said *JACC* Editor-in-Chief. "First, we keep discussing how much we have progressed among our subspecialty, yet the paradox is that the disease state remains the number 1 killer in the world. The second paradox is that medicine remains very expensive, yet we don't put efforts into promoting health at younger ages, which could be a cost-effective method to preventing the onset of the disease. Instead, we continue to only invest in treating advanced manifestations of cardiovascular disease." The paper is based on the most recent Global Burden of Disease (GBD) study, an international consortium of more than 2,300 researchers in 133 nations. The researcher noted: "High levels of cardiovascular disease can be especially problematic for low-resource countries with limited access to or availability of effective treatments. Many nations are now dealing with a 'double burden' of chronic and infectious disease, which puts additional strain on health systems." Prevalence rates of CVD, including coronary artery disease, atrial



fibrillation, heart failure, stroke, and peripheral arterial disease, were highest across sub-Saharan Africa, Eastern and Central Europe, and Central Asia. Some of the lowest rates occurred in high-income Asian countries such as Singapore, Japan, and South Korea, and Southern South American countries, including Chile and Argentina. The highest CVD death rates occurred throughout Central Asia and Eastern Europe, but also in countries such as Iraq, Afghanistan, and many South Pacific island nations. The lowest rates were in Japan, Andorra, Peru, France, Israel, and Spain. Using a measure of development status that combines levels of education, fertility, and income -- the

socio-demographic index (SDI) -- the researchers discovered that, on average, CVD mortality first increased, then declined steeply with increasing SDI, only to plateau in the last few years. Of the cardiovascular conditions studied, ischemic heart disease, also known as coronary artery disease, was the leading cause of health loss in every region of the world except sub-Saharan Africa. In 2015, there were an estimated 7.3 million heart attacks and 110.6 million people living with coronary artery disease. The highest prevalence rates for heart artery disease were found in Eastern Europe, followed by Central Asia and Central Europe, but high rates were also found in some parts of sub-Saharan Africa, the Middle East/North Africa region, and South Asia. Peripheral artery disease was the most prevalent CVD cardiovascular disease worldwide, even though much of it is estimated to be without symptoms. Stroke was the second-leading cause of global health loss. In 2015, there were nearly 9 million first-time strokes. Prevalence rate of coronary artery disease and stroke began increasing as early as age 40, showing that these are not only diseases of the elderly, but also impact younger individuals who are working or caring for family. Other cardiovascular conditions examined include hypertensive heart disease, cardiomyopathy, aortic aneurysm, atrial fibrillation, and rheumatic heart disease.

Preterm Birth Linked to Higher Risk of Heart Failure

Babies born preterm run a higher risk of heart failure during childhood and adolescence than those born at full term, researchers report. The registry-based study was published in *The Journal of the American College of Cardiology (JACC)*. More and more babies survive increasingly preterm births. Babies born prematurely are exposed to life outside the womb at a time when their organs are yet to fully mature and their bodies are not entirely prepared for the radical transition from fetus to neonate. In recent years, scientists have become all the more interested in the consequences of preterm birth on, amongst other things, cardiovascular health in young adults. Complementing previous studies indicating a higher risk of hypertension, stroke and fatal cardiovascular disease, have now uncovered a hitherto unknown connection between preterm birth and heart failure in a registry study of 2.6 million individuals born between 1987 and 2012. "We found that the risk of heart failure was higher for individuals born preterm, and inversely correlated with duration of pregnancy, in that the earlier you're born, the greater the risk," explains lead author. The study shows that children born



before the 28th week are 17 times more likely to suffer heart failure than those born at full term. Individuals born a little later -- in weeks 28 to 31 -- ran just over three times the risk. This correlation held when children with birth defects were excluded from the analysis and other possible determinants, such as birth weight, socioeconomic situation and parental heart conditions, were controlled for. The results corroborate earlier studies indicating abnormal development of the cardiovascular system in people born prematurely. The researchers point out, however, that heart failure is very rare in children and young adults, so the risk of developing the condition at a young age is very small, even for people born prematurely. "It could be the case that the higher risk of heart failure remains when they grow older, in which case more people will be affected as heart failure is much more common in older people," says the researcher. "In general the risk of heart failure can be reduced by adopting a healthy lifestyle, including refraining from tobacco use, keeping physically active, minimizing your alcohol consumption and occasionally checking your blood pressure."

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Systolic, Diastolic Blood Pressures may have Different Effects on Different Types of Cardiovascular Diseases

Raised systolic and diastolic blood pressures may have different effects on different types of cardiovascular diseases at different ages, according to new research involving 1.25 million patients from primary care practices in England published in the journal *The Lancet*. The new findings suggest that individuals with higher systolic blood pressures have a greater risk of intra-cerebral hemorrhage, subarachnoid hemorrhage, and stable angina, whereas raised diastolic blood pressure is a better indicator of abdominal aortic aneurysm risk. "Our findings do not support the widely held assumptions that systolic and diastolic pressure have similar strong associations with the occurrence of all cardiovascular diseases across a wide age range", explains lead investigator. The study is the first to explore the effects of blood pressure on the risk of 12 different cardiovascular conditions in various age groups as a first presentation of cardiovascular disease. Researchers examined blood pressure data using the electronic health records of 1.25 million patients without cardiovascular disease, aged 30 years and older, who were followed for a median 5.2 years to record the first cardiovascular event. They also calculated the lifetime risks of developing specific cardiovascular diseases linked with high blood pressure at age 30 through to 80 years of age. The findings show that despite modern therapy, the lifetime burden of hypertension remains substantial. For example, in a 30 year old with hypertension (blood pressure $\geq 140/90$ mm Hg), the lifetime risk of developing cardiovascular disease was 63% compared with 46% in an individual with healthy blood pressure, and they devel-

oped cardiovascular disease 5 years earlier. Stable and unstable angina accounted for almost half of the loss of time free from cardiovascular disease at this age, whereas heart failure contributed to nearly a fifth of the years lost in individuals 80 years and older. According to the researcher, "With lifetime risks, the need for new blood pressure lowering strategies is paramount. Our estimates provide vital new information that can be used to improve patient counseling and decision making for people with hypertension, which are currently based mainly on the risks of heart attack and stroke, and will help to focus guidelines and doctors to the cardiovascular conditions that might be more common and in which screening and treatments are more likely to have an effect." Writing in a linked Comment, the researcher says, "Although the efficacy of anti-hypertensive drug therapy is undisputed, observational studies suggest that few patients reach target blood pressure. Several steps therefore need to be taken to improve antihypertensive treatment and control: the assessment of global cardiovascular risk in individual patients; improving caregiver organization, support, and education; increasing drug compliance and treatment persistence to prescribed treatment; expanding the use of home blood pressure monitoring and 24 h ambulatory blood pressure monitoring; considering secondary forms of hypertension in difficult to treat patients; and referring patients with remaining uncontrolled hypertension to a specialist hypertension centre."

World Hypertension Day 2017



World Hypertension Day (WHD) is an international event dedicated to promoting public awareness of hypertension, encouraging citizens of all countries to prevent and control this silent killer. Every year, May 17th is dedicated to WHD. For the five-year period 2013-2018, the theme of WHD will be 'Know Your Numbers' with the goal of increasing high blood pressure awareness in all populations around the world. Beximco Pharmaceuticals Ltd. has celebrated the day this year with the following activities:

- A Public Awareness Rally on WHD, 17th May 2017 which was held on Sheikh Abu Naser Medical College Hospital, Khulna. In this rally all the doctors, students, nurses and all other employees and also the employees of Beximco Pharmaceuticals Ltd. took part. There was also a patients counseling program on the same day.
- Continuing medical education (CME) on management of hypertension was held on Khulna Medical College Hospital (KMCH) in this day, which was organized by Beximco Pharmaceuticals Ltd. All specialized doctors of cardiology, medicine, nephrology and neurology of KMCH has participated the program.

Angiotensin-converting Enzyme Inhibitors and Angiotensin Receptor Blockers Equally Effective in Diabetics



For patients with diabetes and hypertension, guidelines recommend angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) over other anti-hypertensives.

But few studies have compared the efficacy of these drugs in diabetic patients. Researchers find ACE inhibitors and ARBs produce similar outcomes in analysis of more than 100,000 diabetic patients. To compare ACE inhibitors with ARBs, researchers carried out a network meta-analysis including data from published and unpublished randomized controlled trials and subgroup data on patients with diabetes from larger trials. The analysis included 103,120 participants. The team found that ACE inhibitors and ARBs were equivalent with regards to major cardiovascular outcomes and risk of progression to renal disease over a median follow-up of 3.2 years. Combining both treatments did not provide any benefit over monotherapy. Writing in the journal *PLoS Medicine*, the researchers say prescribers should weigh up the benefits, costs and potential harms of the drugs for individual patients with diabetes.

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Statin was Associated with Improved Outcomes in Heart Failure Patients

The positive effect of statin use in patients with ischemic heart disease (IHD) is well documented. The major benefits include not only reduced risk of myocardial infarction and cardiovascular mortality but also reduced utilization of health resources and positive cost-effectiveness. It has been discussed whether statins also have effects on the systemic inflammatory response and whether this could partially explain the beneficial effects. This anti-inflammatory effect of statins has also been linked to reduced mortality in other diseases, such as chronic obstructive pulmonary disease and diabetes mellitus. The pathophysiology of heart failure with preserved ejection fraction is poorly understood, but may involve a systemic pro-inflammatory state. Therefore, statins might improve outcomes in patients with heart failure with preserved ejection fraction defined as $\geq 50\%$. Of 46 959 unique patients in the prospective Swedish Heart Failure Registry, 9140 patients had heart failure and ejection fraction $\geq 50\%$ (age 77 ± 11 years, 54.0% women), and of these, 3427 (37.5%) were treated with



statins. Propensity scores for statin treatment were derived from 40 baseline variables. The association between statin use and primary (all-cause mortality) and secondary (separately, cardiovascular mortality, and combined all-cause mortality or cardiovascular hospitalization) end points was assessed with Cox regressions in a population matched 1:1 based on age and propensity score. In the matched population, 1-year survival was 85.1% for statin-treated *versus* 80.9% for untreated patients (hazard ratio, 0.80; 95% confidence interval, 0.72–0.89; $P < 0.001$). Statins were also associated with reduced cardiovascular death (hazard ratio, 0.86; 95% confidence interval, 0.75–0.98; $P = 0.026$) and composite all-cause mortality or cardiovascular hospitalization (hazard ratio, 0.89; 95% confidence interval, 0.82–0.96; $P = 0.003$). The study concludes that in heart failure with ejection fraction $\geq 50\%$, the use of statins was associated with improved outcomes. The study was published in the journal *Circulation: Heart Failure*.

Impact of Statin Use After Heart Transplantation

Heart transplantation is a life-saving treatment option for carefully selected end-stage heart failure patients. Posttransplant care consists primarily of immunosuppression and treatment of hypertension. Statin therapy immediately after cardiac transplant has become an integral part of post-cardiac transplant care. The molecular mechanisms responsible for the beneficial effects of statins extend beyond cholesterol-lowering action. Pleiotropic properties of statins include promotion of apoptosis, inhibition of angiogenesis, down regulation of circulating cytokines, and reduction of circulating monocytes. These pleiotropic properties may contribute to reduction in the incidence of cardiac allograft dysfunction in heart transplant recipients.



Terminal malignancy is an important cause of death late after heart transplantation. Statins, through inhibition of 3-hydroxy-3-methylglutaryl-coenzyme A reductase enzyme, decrease the production of farnesyl pyrophosphate, geranylgeranyl pyrophosphate, and other molecules involved in tumor cell proliferation, angiogenesis, and cell differentiation. This molecular mechanism suggests that statins might decrease the incidence of cancer in heart transplant recipients. However, statins also enhance the production of regulatory T cells, which impairs antitumor immune response and consequently promote the development of cancer. Although various studies revealed the beneficial effects of statins in post-cardiac transplant patients, these were relatively small and low-powered studies. A meta-analysis of published studies was performed to evaluate the role of statins in

post-cardiac transplant patients, specifically examining the effects on hemodynamically significant/fatal graft rejection, coronary vasculopathy, terminal cancer, and overall survival.

Search was made of PubMed, Cochran CENTRAL, and Web of Science databases using the search terms “cardiac transplant” or “heart transplant,” and “statin” for a literature search. A random-effects model with Mantel-Haenszel method was used to pool the data. Ten studies was identified, 4 randomized controlled trials, and 6 non-randomized studies, which compared outcomes in heart transplant recipients undergoing statin therapy to statin-naïve patients. A pooled analysis of 9 studies reporting mortality

revealed that the use of statins was associated with significant reduction in all-cause mortality (odds ratio, 0.26; 95% confidence interval, 0.20–0.35; $P < 0.0001$). Statins also decreased the odds of hemodynamically significant/fatal rejection (odds ratio, 0.37; 95% confidence interval, 0.21–0.65; $P = 0.0005$), incidence of coronary vasculopathy (odds ratio, 0.33; 95% confidence interval, 0.16–0.68; $P = 0.003$), and terminal cancer (odds ratio, 0.30; 95% confidence interval, 0.15–0.63; $P = 0.002$). The evidence from a pooled analysis suggests that statins improve survival in heart transplant recipients. Statins may prevent fatal rejection episodes, decrease terminal cancer risk, and reduce the incidence of coronary vasculopathy. Additional prospective studies are needed to further investigate and explain this association. The study was published in the journal *Circulation: Heart Failure*.

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