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COMPARATIVE USE OF DIFFERENT ANTIHYPERTENSIVE COMBINATIONS AT SAVAR AREA, DHAKA, BANGLADESH

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ABSTRACT: Antihypertensive agents are class of drugs that are used to treat hypertension (high blood pressure) as well as other CVS disorders. Antihypertensive therapy seeks to prevent the complications of high blood pressure, such as stroke and myocardial infarction. Evidence suggests that reduction of the blood pressure by 5 mmHg can decrease the risk of stroke by 34%, of ischemic heart disease by 21%, and reduce the likelihood of dementia, heart failure, and mortality from cardiovascular disease. Single-dose combination antihypertensive therapy is an important option that combines efficacy of blood pressure reduction and a low side effect profile with convenient once-daily dosing to enhance compliance as compared to monotherapy. The survey enabled to monitor 500 prescriptions and found most available combinations at Savar area in Bangladesh among which beta blockers with Ca-channel blockers was used most (89%) and the brand Fixocard of Incepta was the brand leader.

INTRODUCTION: Blood pressure is a measure of the lateral force of the blood pushing against the walls of the arteries. When this force is elevated beyond a normal level, a patient will be diagnosed with either pre-hypertension or hypertension. Hypertension is a major cardiovascular risk factor and a serious problem when left untreated and it frequently in most patients remain asymptomatic for many years. It is a major contributor to cardiovascular disease and a leading cause of stroke, myocardial infarction, heart failure and kidney disease and also affects other organs such as the eyes.

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The prevalence of hypertension increases with age and older patients are more likely to suffer from cardiovascular complications of hypertension [1, 4, 6, 15]. Treating hypertension reduces the rates of myocardial infarction, stroke, and renal disease; however, clinical trial experience suggests that monotherapy is not likely to be successful for achieving goal blood pressure (BP) levels in many hypertensive patients [5]. In multiple recent clinical trials including various subsets of hypertensive patients, the achievement of BP goal has typically required the combination of 2 or more medications, particularly in patients with BP levels>160/100 mm Hg [6, 15].

Multiple medications have been approved for the treatment of hypertension, such as: diuretics, β-blockers, calcium channel blockers, blockers of the renin–angiotensin–aldosterone system, direct vasodilators and centrally acting agents.

Each class of medication has a different mechanism of action and a potentially different side-effect profile [6]. Guidelines on the choice of agents and how to best to step up treatment for various subgroups have changed over time and differ among countries. The majority of people require more than one drug to control their CVS symptoms. The choice between the drugs is to a large degree determined by the characteristics of the patient being prescribed for, the drugs' side-effects, and cost [2, 3, 4, 6].

Tablets containing fixed combinations of two classes of drugs are available and while convenient for the people, may be best reserved for those who have been established on the individual components [6].

Therefore, a study on various brands and choice of combination of CVS drugs was the rationale.

Antihypertensive combination: Antihypertensive combination may be defined as a dosage form that contains two or more different types of medication in the same route. A combination drug most commonly refers to a fixed-dose combination (FDC). In multiple recent clinical trials including various subsets of hypertensive patients, the achievement of BP goal has typically required the combination of 2 or more medications, particularly in patients with BP levels>160/100 mm Hg [5, 10, 11].

Advantages of combination: The fundamental goal of treatment should be the prevention of the important endpoints of hypertension, such as heart attack, stroke and heart failure. Patient age, associated clinical conditions and end-organ damage also play a part in determining dosage and type of medication administered [18, 19].

A target blood pressure of less than 140/90 mm Hg is achieved in about 50 percent of patients treated with monotherapy; two or more agents from different pharmacologic classes are often needed to achieve adequate blood pressure control. Lower doses in combination are as effective as usual higher monotherapy doses but with fewer side effects.

Therefore, the use of two drugs of different classes in low-dose combination has many potential advantages [8, 9, 16, 17].

In experimental models, the combination of a calcium channel blocker with an agent that blocks angiotensin II improves endothelial function, inflammation, ventricular remodeling, and renal function to a greater degree than these drugs given as monotherapy. Several large randomized trials have shown that monotherapy is ineffective in reducing BP to a predetermined target range. For instance, in the Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack (ALLHAT) trial, only 27% of 42,418 participants achieved the goal BP (140/90 mmHg) on monotherapy, from a baseline mean systolic BP of 146 mmHg and 156 mmHg for previously treated and untreated patients, respectively. The JNC-7 guidelines recommend initiating therapy with two antihypertensive agents in patients with Stage 2 and higher levels of BP. The European Society of Hypertension also recommends initial combination antihypertensive therapy in patients at high cardiovascular risk [12, 13, 14, 15].

MATERIALS AND METHODS: The methodology involved was to collect randomized representative samples. 500 prescriptions were collected from patients of local government and non-government hospitals prescribed by physicians or registered medical practitioners. The survey was conducted for 6 months (September 2012 to February 2013).

Some confidential information was collected orally. Two sources were basically used to collect the data. Primary data was collected from the representative drug house, hospital and direct interview of patient. Secondary data was collected from several books, literature, other publication and internet.

Microsoft Office Excel (2007) was used as a tool for statistical analysis to evaluate the collected data.

RESULT AND DISCUSSION: The aim of study was to assess the recent CVS drug market, brand leaders of various classes and matters relating to the near future to other new CVS agents.

Table and figure show the class of combined cardiovascular drugs available in the current market in Bangladesh. In most of the classes in cardiovascular therapy combination therapy was applied. The recent trend in therapy is much more preventive.

So, it is coming in practice the use of combination products. Their use is increasing day by day.

Among all, beta blockers with Ca-channel blockers were used most and the brand Fixocard of Incepta was the brand leader whereas amdocal plus of Beximco was at second position.

Diuretics with ACE inhibitors took 77% and Angilock plus of Square were the brand leader. In the thrombolytic class Ecospirin plus (Acme) was the brand leader.

In the market, combined diuretics are more available to avoid electrolyte imbalance, nephrotoxicity, hypovolaemia impotency etc. Among the diuretics class thiazide was used in high quantity, 40.81% and potassium sparing took 30.62% indapamide possessed 38% and hydrochlorothiazide 62%. In potassium-sparing class spironolactone possessed 46.66% and triamterene and amiloride possess 26.67%. Loop diuretic frusemide found in 55.42% quantity. In the Losartan and Hydrochlorothiazide combination osartil of Incepta was the brand leader.

Miscellaneous combination took place 11% of total use.

MOST AVAILABLE ANTIHYPERTENSIVE COMBINATIONS IN BD MARKET [20, 21, 22]

Drug Category	Combinations
Beta blockers with Ca-channel blockers.	Atenolol 50 mg + Amlodipine 5 mg (tablet). Atenolol 25 mg + Amlodipine 5 mg (tablet). Atenolol 50 mg + Nifedipine 20 mg (Capsule).
Beta blockers with thiazide diuretics.	Atenolol 50 mg + Chlorthalidone 25 mg (tablet). Atenolol 100 mg + Chlorthalidone 25 mg (tablet).
ACE-inhibitors with Ca-channel blockers.	Benazepril 10 mg + Amlodipine 5 mg (Capsule). Benazepril 10 mg + Amlodipine 5 mg (Capsule). Benazepril 20 mg + Amlodipine 10 mg (Capsule).
ACE-inhibitors with thiazide diuretics.	Ramipril + Hydrochlorothiazide.
Ang-II receptor antagonists with thiazide diuretics.	Candesartan 8 mg + Hydrochlorothiazide 12.5 mg. Irdesartan + Hydrochlorothiazide. Tamlesartan + Hydrochlorothiazide (40 mg+12.5 mg) and (80 mg + 12.5 mg). Losartan + Hydrochlorothiazide (50 mg +12.5 mg) and (100 mg + 12.5 mg). Valsartan + Hydrochlorothiazide.
Ang-II receptor antagonists with Ca-channel blockers.	Valsartan + Amlodipine.
Anti-platelets and thrombolytic.	Clopidogrel + Aspirin.

Comparative use of different classes of combinations:

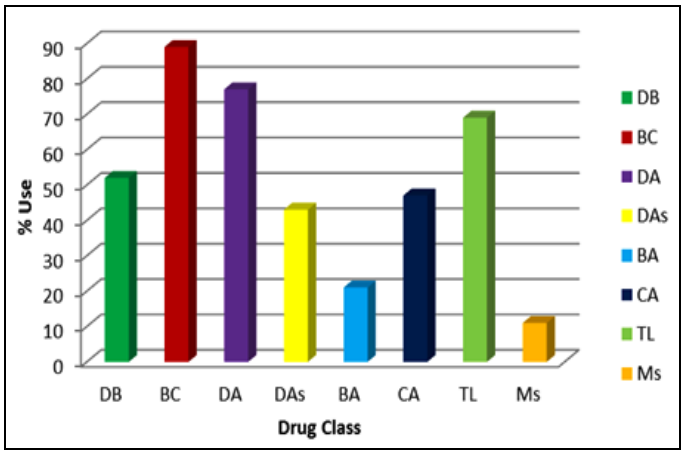

FIGURE 1: COMPARATIVE USE OF DIFFERENT COMBINATIONS AT SAVAR AREA AND AVAILABLE IN BD MARKET. [DB=Diuretics + Beta blockers, BC = Beta blockers+ Ca-channel blockers, DA = Diuretics + ACE inhibitors, DAs = Diuretics + ARBs, BA = Beta blockers + ARBs, CA = Ca-channel blockers + ACEI, TL = Thrombolytics and Ms = Miscellaneous.]

CONCLUSION: There were many anti-hypertensive combinations available to use at Savar area and used to improve overall efficacy and tolerability. Antihypertensive FDCs may provide significant advantages over high-dose monotherapy, such as improved BP-lowering efficacy, reduced adverse event frequency, improved patient compliance, potentially lower treatment costs, and better control to BP within shorter time.

Combination therapy has been recommended as potential first-line therapy in recent consensus guideline statements, especially for higher-risk patients such as those with stage 2 hypertension.

The current study suggests that, the combination of beta blockers with Ca-channel blockers, diuretics with Ca-channel blockers, diuretics with angiotensin receptor antagonists, thiazide diuretics with potassium sparing diuretics or /and loop diuretics as well as ARBs and antiplatilets with thrombolytics have yet to be proved more efficacious than either agent alone. These combinations provides synergy with regard to BP lowering and have demonstrated beneficial effects on hard end points, reducing cardiovascular morbidity and mortality and inhibiting the development and progression of type 2 diabetes mellitus and the progression of renal disease.

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