BETA BLOCKERS (BISOPROLOL) IN THE MANAGEMENT OF CARDIOVASCULAR DISEASE
HYPERTENSION, HEART FAILURE AND CAD

Dike Ojji
MBBS, PhD, FWACP, FACP, FESC
Department of Medicine, Faculty of Health Sciences,
University of Abuja & University of Abuja Teaching Hospital, Gwagwalada, Abuja
Outline

• Background on beta blockers (beta-1-selective agents)

• Sympathetic overdrive in CVD

• Bisoprolol in the treatment of hypertension

• Bisoprolol in the treatment of CHF

• Bisoprolol in the management of CAD

• Summary
Heterogeneity of Beta Blockers

• Heterogeneous in terms of their pharmacologic and hemodynamic properties

• Some exhibit higher selectivity for beta-1 adrenoceptors (heart)

• Some higher selectivity for beta-2-adrenoceptors (bronchi)

• Others block alpha receptors, found on vascular smooth muscle, as well as b-adrenoceptors
Beta Receptors

• B1
  • Heart
  • Kidneys
  • Fat cells

• B2
  • Lungs
  • Skeletal Muscles
  • Liver/Pancreas
Main Factors Contributing to Heterogeneity Within the β-blocker Class

- $\beta_1/\beta_2$ Selectivity
- Vasodilation Properties
- Side effects
- Efficacy
- Metabolic profile
### Classification of beta-blockers according to their beta\textsubscript{1}-selectivity

<table>
<thead>
<tr>
<th>Relative beta\textsubscript{1}-selectivity</th>
<th>Non-selective</th>
<th>Beta\textsubscript{1}-selective</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Atenolol</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Metoprolol</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Bisoprolol</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Betaxolol</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Esmolol</td>
</tr>
<tr>
<td></td>
<td>Bupranolol</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Propanolol</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Timolol</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Labetalol</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Carvedilol</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Alprenolol</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Pindolol</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Oxprenolol</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Carteolol</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Bucindolol</strong></td>
</tr>
<tr>
<td>Intrinsic sympathomimetic activity (ISA)</td>
<td></td>
<td>Acebutolol</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Celiprolol</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nebivolol*</td>
</tr>
<tr>
<td></td>
<td>Alprenolol</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pindolol</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Oxprenolol</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Carteolol</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bucindolol</td>
<td></td>
</tr>
<tr>
<td>Hydrophilicity</td>
<td>Nadolol</td>
<td>Atenolol</td>
</tr>
<tr>
<td></td>
<td>Sotalol</td>
<td>Celiprolol</td>
</tr>
</tbody>
</table>

*Although nebivolol is often characterized as a beta\textsubscript{1}-selective beta-blocker without ISA, the nitric oxide release induced by nebivolol leading to vasodilatation results from agonism at beta\textsubscript{3}-receptors, which is an ISA*³

---

Beta₁-selectivity of different beta-blockers: bisoprolol is a highly selective beta₁-blocker

Cruickshank JM. The Modern Role of Beta-blockers in Cardiovascular Medicine. Shelton, CT: People's Medical Publishing House-USA; 2011, Fig. 1-5


Bisoprolol: Beta_2/beta_1 selectivity ratio at human beta-receptors *in vitro*

Bisoprolol has a 19.6-fold higher affinity for the beta_1 receptor than for the beta_2 receptor.

Cruickshank JM. Essential Hypertension. Shelton, CT: People's Medical Publishing House-USA;2013, Fig. 8-28

Use of Beta Blockers

• BB have been used in the treatment of CV conditions for decades.
Recent meta-analyses: BB as appropriate therapy given outcomes data from other AHT drug classes.

However, BB are a heterogeneous class of agents with diverse pharmacologic and physiologic properties.

Data from studies involving non-vasodilating, traditional BB such as atenolol.

Findings with traditional BB cannot be extrapolated to other members of the class: more beta-1 selective.
Use of Beta Blockers

• Recent meta-analyses: unfavourable data from studies involving traditional BB such as atenolol.

• Findings with traditional BB cannot be extrapolated to other members of the class: more beta-1 selective
• Sympathetic overdrive in cardiovascular disease
Sympathetic overdrive is associated with increased heart rate and multiple cardiovascular risk factors.
Obesity is associated with increased sympathetic nerve activity

Lean

Peripherally obese

Centrally obese

Cruickshank JM. The Modern Role of Beta-blockers in Cardiovascular Medicine. Shelton, CT: People’s Medical Publishing House-USA; 2011; Fig. 3-4

Sympathetic overdrive plays a key role in the pathophysiology of cardiovascular disease

↑ Sympathetic nervous activity

 Neural release of norepinephrine

β1 receptor stimulation

Mechanical/vascular damage

- Pulsatile stress on vascular system
- Augment atherosclerosis
- Plaque rupture
- Risk of cardiac ischemia

β1 receptor stimulation

- Renin release
- Angiotensin
- Blood pressure
- Left ventricular hypertrophy
- Heart failure

↑ Heart rate
↓ Heart rate variability
↑ Contractility

Elevated heart rate increases the risk of mortality in young men

Increased mortality risk with increased heart rates among French men according to age (<55 years)

Elevated resting heart rate increases the risk of sudden death in middle-aged men

Prospective study of 7079 men aged 42-53 years followed for an average of 23 years

Sympathetic activity is elevated in patients with diabetes and hypertension

Essential hypertension (EHT)    Type 2 diabetes mellitus (DM)    Normotensives (NT)

Cruickshank JM. The Modern Role of Beta-blockers in Cardiovascular Medicine. Shelton, CT: People's Medical Publishing House-USA;2011; Fig. 3-6
Black Nigerian hypertensives demonstrate elevated levels of plasma noradrenaline when compared with normal controls. This is consistent with the hypothesis of hyper adrenergic state in hypertension.

Ethn Dis. 2011 Spring; 21(2):158-162
Pharmacotherapy options for elevated heart rate: only the beta-blockers reduce sympathetic overdrive

**Elevated heart rate**

- **Non-dihydropyridine CCBs** (verapamil, diltiazem)
  - Action is not related to SO but to reducing nerve conduction velocity and prolonging repolarization

- **Beta blockers (without ISA)**, e.g. bisoprolol
  - HR control via actions on SO

- **$I_f$ channel inhibitor (ivabradine)**
  - Specific action on the $I_f$ channel that controls the pacemaker activity in sinoatrial node

---

Calcium channel blockers (CCBs)  Sympathetic overdrive (SO)  Intrinsic sympathomimetic activity (ISA)  Coronary artery disease (CAD)

---

The $I_f$ channel inhibitor, ivabradine, is recommended as a second-line drug in CAD, only if beta-blockers are not tolerated or additional HR reduction is needed after the maximum dose of beta-blocker

---

Beta-blockers protect the heart at every stage of the cardiovascular continuum

- Coronary thrombosis
- Myocardial infarction
- Neurohormonal activation
- Arrhythmias and loss of muscle
- Remodelling
- Ventricular enlargement
- CHF
- Death
- Risk factors
  - Hyperlipidemia
  - Hypertension
  - Diabetes
  - Smoking
- Sudden death

Left ventricular hypertrophy (LVH)
Coronary artery disease (CAD)
Chronic heart failure (CHF)

Beta Blockers in the treatment of hypertension
Key Mechanistic Factors in Primary Hypertension

• Increased activity of renin-angiotensin-aldosterone

• Hyperfunction of sympathetic system

• Vasoactive substances - endothelial dysfunction

• Insulin resistance → obesity

• Arteriolar hypertrophy

• Renal defect to excrete sodium
Different classes of drugs have different sites of action
Why beta\(_1\)-selectivity is important in the treatment of hypertension associated with sympathetic overdrive

Primary distribution of beta-receptors and effects of stimulation\(^1,2\)

<table>
<thead>
<tr>
<th></th>
<th>Beta(_1) receptors</th>
<th>Beta(_2) receptors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Myocardium</strong></td>
<td>↑ Contractility and heart rate</td>
<td></td>
</tr>
<tr>
<td></td>
<td>↑ Myocardial necrosis/apoptosis</td>
<td></td>
</tr>
<tr>
<td><strong>Bronchial smooth muscle</strong></td>
<td></td>
<td>↑ Bronchodilation</td>
</tr>
<tr>
<td></td>
<td>↓ Myocardial necrosis/apoptosis</td>
<td>↓ Myocardial necrosis/apoptosis</td>
</tr>
<tr>
<td><strong>Blood vessel smooth muscle</strong></td>
<td></td>
<td>↑ Vasodilation</td>
</tr>
<tr>
<td><strong>Kidney</strong></td>
<td></td>
<td>↑ Renin release</td>
</tr>
</tbody>
</table>

Highly selective beta\(_1\)-blockers inhibit sympathetic activity in the heart and kidney, preserve beta\(_2\)-mediated vasodilation, and reduce the risk of adverse effects mediated by blockade of beta\(_2\) receptors in the lungs and peripheral tissues

Beta₁-blockade may be particularly beneficial in hypertensive patients with central obesity/diabetes/insulin resistance

DM2/Obese

Type 2 diabetes mellitus (DM2)

† Insulin resistance

† Insulin/Leptin

† Norepinephrine release

Benefits are mediated by blockade of beta₁-receptors

- Ventricular arrhythmias
- Beta₁-stimulation-induced cardiac and coronary damage († atheroma)
- † BP + non-dipping at night

† PRA

Plasma renin activity (PRA)

† Angiotensin II

† Intra-glomerular pressure + nephropathy

Blood pressure (BP)
Beta-blockers can reduce mortality in the overweight/obese, high-risk hypertensive patient with type 2 diabetes

20-year follow up of the United Kingdom Prospective Diabetes Study (UKPDS)

Cruickshank JM. The Modern Role of Beta-blockers in Cardiovascular Medicine. Shelton, CT: People's Medical Publishing House-USA;2011; Fig. 3-15


More effective 24-hour BP control with bisoprolol versus atenolol after once-daily dosing

Randomized, double-blind parallel-group study of 659 patients with mild-to-moderate hypertension (21-84 years) with 24-hour ABPM measured after 8 weeks’ treatment (bisoprolol 10 mg o.d., n=336, atenolol 50 mg o.d., n=323)

Bisoprolol was significantly more effective in reducing SBP (p<0.05) and DBP (p<0.01) during the final 4 hours of dosing interval

On 24-hour BP monitoring, bisoprolol demonstrated a 33% greater reduction in whole-day average DBP (11.6 vs 8.7 mmHg, p<0.01)
Bisoprolol is superior to other antihypertensive therapies in middle-aged hypertensive men (ADLIB study)

Under randomized, double-blind, cross-over conditions in young/middle-aged (28-55 years) diastolic hypertensive patients, bisoprolol was the most effective antihypertensive agent compared with the alpha-blocker, doxazosin, the calcium blocker, amlodipine, the ACE inhibitor, lisinopril, and the diuretic, bendrofluazide, dosed for 6 weeks each.

Amlodipine: 5 mg/day
Doxazosin: 1-4 mg/day
Bendrofluazide: 2.5 mg/day
Lisinopril: 2.5-10 mg/day
Bisoprolol: 5 mg/day

Cruickshank JM. The Modern Role of Beta-blockers in Cardiovascular Medicine. Shelton, CT: People’s Medical Publishing House-USA;2011, Fig. 3-32b
Bisoprolol is superior to losartan in middle-aged hypertensive patients

In middle-aged hypertensive patients (mean age 52 years; n=72), bisoprolol is superior to losartan in controlling blood pressure over 1 year, with no evidence of renoprotection for losartan.

Cruickshank JM. The Modern Role of Beta-blockers in Cardiovascular Medicine. Shelton, CT: People's Medical Publishing House-USA; 2011, Fig. 3-34

Bisoprolol is safe and effective in stage I essential hypertensive patients in India.

The average dose required was 5 mg/day.

Target BP was achieved in 96.44% patients over 3 months' period.

BMJ Open 2012;2:e000683
V. Treatment of Adults with Systolic/Diastolic Hypertension without Other Compelling Indications

TARGET <140/90 mmHg

INITIAL TREATMENT AND MONOTHERAPY

Lifestyle modification therapy

- Thiazide
- ACEI
- ARB
- Long-acting CCB
- Beta-blocker*

A combination of 2 first line drugs may be considered as initial therapy if the blood pressure is >20 mmHg systolic or >10 mmHg diastolic above target

• BBs are not indicated as first line therapy for age 60 and above

ACEI, ARB and direct renin inhibitors are contraindicated in pregnancy and caution is required in prescribing to women of child bearing potential
Consider beta-blockers in younger people with evidence of increased sympathetic drive

The NICE evidence review identified four studies that reported beta-blockers and ACE inhibitors as being more effective at lowering blood pressure in younger people than calcium channel blockers or thiazide-type-diuretics.

The guidelines recommend that beta-blockers should be considered for initial therapy of hypertension in younger people, particularly:

• when there is evidence of increased sympathetic drive
• in those with an intolerance or contraindication to ACE inhibitors and angiotensin II receptor antagonists
• in women of childbearing potential.

NICE guidelines specifically recommend beta-blockers as initial therapy for hypertension in younger people
European guidelines recommend beta-blockers for the initiation and maintenance of antihypertensive treatment

1. BP measurements **SHOULD ALWAYS** be associated with measurement of heart rate, because resting heart rate values independently predict CV morbid or fatal events in hypertension

2. Diuretics, **beta-blockers**, calcium antagonists, angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers are all suitable for the initiation and maintenance of antihypertensive treatment, either as monotherapy or in some combinations

• RCTs and meta-analyses demonstrate that when compared with placebo, BB significantly reduce the risk of CVA, HF and major CV events in hypertensive patients.

• When compared with other BP-lowering drugs, BB are usually equivalent in preventing major CV events, except for less effective prevention of CVA, which has been a consistent finding.

• BB have been shown to be particularly useful for the treatment of hypertension in specific situations such as symptomatic angina, for HR control, post- MI, HFrEF, and as an alternative to ACEIs or ARBs in younger hypertensive women planning pregnancy or of child-bearing potential.
Beta Blockers in the treatment of heart failure
**DIET: Approach to the Patient With Heart Failure**

- **D**iagnose
  - Etiology
  - Severity (LV dysfunction)
- **I**nitiate
  - Diuretic/ACE inhibitor
  - β-blocker
  - Spirololactone
  - Digoxin
- **E**ducate
  - Diet
  - Exercise
  - Lifestyle
  - CV Risk
- **T**itrated
  - Optimize ACE inhibitor
  - Optimize β-blocker
Patient with symptomatic\textsuperscript{a} HFrEF\textsuperscript{b}

Therapy with ACE-I\textsuperscript{c} and beta-blocker
(Up-titrate to maximum tolerated evidence-based doses)

Still symptomatic and LVEF ≤35%

Yes

Add MR antagonist\textsuperscript{a, e}
(up-titrate to maximum tolerated evidence-based dose)

Yes

Still symptomatic and LVEF ≤35%

No

If LVEF ≤35% despite OMT or a history of symptomatic VT/VF, implant ICD

Diuretics to relieve symptoms and signs of congestion

Able to tolerate ACEI (or ARB)\textsuperscript{d}

ARNI to replace ACE-I

Sinus rhythm, QRS duration ≥130 msec

Evaluate need for CRT\textsuperscript{d}

Sinus rhythm,\textsuperscript{h} HR ≥70 bpm

Ivabradine

These above treatments may be combined if indicated

Resistant symptoms

Yes

Consider digoxin or H-ISDN or LVAD, or heart transplantation

No

No further action required

Consider reducing diuretic dose
Mechanism of Action of Beta Blockers in Heart Failure

• Reduction of the hyper phosphorylation of calcium release channels of sarcoplasmic reticulum thereby normalising their function
• Bradycardia: thereby increasing coronary blood flow and decreasing myocardial oxygen demand
• Protection of cardiac cells from catecholamine myocyte toxicity
• Suppression of ventricular arrhythmias
• Anti-apoptosis
• Inhibit the RAAS therefore augmenting the actions of ACEIs and ARBs
CIBIS II: Cardiac Insufficiency Bisoprolol Study II

Purpose
To determine whether bisoprolol, a $\beta_1$-selective adrenoreceptor blocker, reduces all-cause mortality in chronic heart failure

Reference
CIBIS II: Cardiac Insufficiency Bisoprolol Study II  
- RESULTS -

- Study halted early because all-cause mortality significantly less in bisoprolol group than placebo group
- Also significant reduction in:
  - Sudden deaths
  - All cardiovascular deaths
  - All-cause hospitalization, as well as hospitalization due to worsening heart failure
- Treatment effects independent of severity or cause of heart failure
- Drug well tolerated as defined by permanent early treatment withdrawals (15% in both groups, P=0.98)
All-cause mortality

CIBIS II: Cardiac Insufficiency Bisoprolol Study II - RESULTS continued-

P < 0.0001

In patients with class III or IV heart failure, bisoprolol in addition to standard therapy reduced:

- All-cause mortality
- Sudden death and cardiovascular death
- All-cause hospitalization and hospitalization due to worsening heart failure
CIBIS III Trial

1010 patients ≥ 65 years with mild to moderate CHF (NYHA class II or III) and LV ejection fraction ≤ 35% in 3 months prior to randomization, clinically stable CHF for 7 days

Randomized
32% female, mean age 72 years, mean follow-up 1.22 years
13% received aldosterone-receptor blocker and 84% diuretic

Monotherapy with beta-blocker
bisoprolol (first 6 mos)
10mg O.D.
n=505

Monotherapy with ACE-inhibitor
enalapril (first 6 mos)
10mg B.I.D.
n=505

Combination beta-blocker and ACE-inhibitor therapy (6-24 mos)

- Primary Endpoint: Time-to-the-first-event of combined all-cause mortality and all-cause hospitalization throughout study.
- Secondary Endpoint: Combined primary endpoint at end of monotherapy phase; individual components of primary endpoint at study end and at end of monotherapy phase.
CIBIS III

Trial Design: CIBIS III was a randomized, open-label trial of initial 6-month monotherapy with the beta-blocker bisoprolol (target dose 10 mg QD) (n=505) or initial 6-month monotherapy with the ACE inhibitor enalapril (target dose 10 mg BID) (n=505), followed by combination beta-blocker and ACE-I therapy during the 6- to 24-month period in patients with newly diagnosed mild to moderate heart failure. Primary endpoint was all-cause mortality or all-cause hospitalization, evaluating non-inferiority in the per-protocol population.

Results

- Death or rehospitalization upper 95% CI 1.21, missing pre-specified criteria for noninferiority of HR 1.17 (Figure), but was met in intent-to-treat analysis (HR 0.94, 95% CI 0.77-1.16, p=0.019 for noninferiority)
- By intent-to-treat, no difference in individual components of mortality (n=65 for bisoprolol-first strategy vs n=73 for enalapril-first strategy, HR 0.88, p=0.44) or hospitalization (n=151 and n=157, respectively, HR 0.97, p=0.86)
- Adverse event rate similar between two strategies

Conclusions

- Among patients with newly diagnosed mild to moderate heart failure, a strategy of initial treatment with the beta-blocker bisoprolol did not meet criteria for noninferiority in per-protocol population for death or hospitalization compared with a strategy of initial treatment with the ACE inhibitor enalapril
- However, intent-to-treat analysis did demonstrate noninferiority

Presented at ESC 2005
Beta Blockers in the treatment of CAD
Beta Blockade Effects on Ischemic Heart

- ↓↓Heart rate
- ↓Afterload
- ↑Wall stress
- ↑Heart size
- ↓Contractility
- ↓O₂ wastage

Subendocardial ischemia

O₂ demand vs O₂ supply

Increased diastolic perfusion
Less exercise vasoconstriction
More spasm?↓

Collaterals

DEMAND ↓↓↓
SUPPLY ↓↑

O₂ deficit↓↓
anaerobic metabolism
Mechanism of Beta Blocker Benefits in Coronary Artery Disease

• Reduction in myocardial oxygen requirements via a decrease in HR, BP and ventricular contractility
• Slowing of HR: prolongs coronary diastolic filling period
• Increase in threshold for ventricular fibrillation
• Reduction in infarct size
• Reduction in the risk of cardiac rupture
• Reduction in the rate of re-infarction
• Regression in the size of atheromatous plaque
**β-blocker Recommendations**

**I  IIa  IIb  III**

Start and continue indefinitely in all post MI, ACS, LV dysfunction with or without HF symptoms, unless contraindicated.

**I  IIa  IIb  III**

Consider chronic therapy for all other patients with coronary or other vascular disease or diabetes unless contraindicated.

*Precautions but still indicated include mild to moderate asthma or chronic obstructive pulmonary disease, insulin dependent diabetes mellitus, severe peripheral arterial disease, and a PR interval >0.24 seconds.

MI=Myocardial infarction, HF=Heart Failure
**β-blocker Evidence**

Summary of Secondary Prevention Trials of β-blocker Therapy

<table>
<thead>
<tr>
<th>Phase of Treatment</th>
<th>Total # Patients</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute treatment</td>
<td>28,970</td>
<td>0.87 (0.77-0.98)</td>
</tr>
<tr>
<td>Secondary prevention</td>
<td>24,298</td>
<td>0.77 (0.70-0.84)</td>
</tr>
<tr>
<td>Overall</td>
<td>53,268</td>
<td>0.81 (0.75-0.87)</td>
</tr>
</tbody>
</table>

Cl=Confidence interval, RR=Relative risk

Heart Rate and Use of Beta-Blockers in Stable Outpatients with Coronary Artery Disease

Ph. Gabriel Steg\textsuperscript{1,2,3}, Roberto Ferrari\textsuperscript{4}, Ian Ford\textsuperscript{5}, Nicola Greenlaw\textsuperscript{5}, Jean-Claude Tardif\textsuperscript{6}, Michal Tendera\textsuperscript{7}, Hélène Abergel\textsuperscript{1,2,3}, Kim M. Fox\textsuperscript{8}, for the CLARIFY Investigators

\textsuperscript{1} INSERM U698, Paris, France, \textsuperscript{2} Université Paris Diderot, Paris, France, \textsuperscript{3} AP-HP, Hôpital Bichat, Paris, France, \textsuperscript{4} Department of Cardiology and LIITA Centre, University of Ferrara, Salvatore Maugeri Foundation, IRCCS, Lumezzane, Italy, \textsuperscript{5} University of Glasgow, Glasgow, United Kingdom, \textsuperscript{6} Montreal Heart Institute, Université de Montreal, Montreal, Canada, \textsuperscript{7} Medical University of Silesia, Katowice, Poland, \textsuperscript{8} NHLI Imperial College, ICMS, Royal Brompton Hospital, London, United Kingdom

CLARIFY is an international, prospective, observational, longitudinal registry of outpatients with stable CAD, defined as prior MI or revascularization procedure, evidence of coronary stenosis of 50\% or chest pain associated with proven myocardial ischemia.

A total of 33,438 patients from \textbf{45 countries} in Europe, the Americas, Africa, Middle East, and Asia/Pacific were enrolled. Among 24,910 patients on BB, 41.1\% had HR >70 bpm.

HR>70 bpm was independently associated with higher prevalence and severity of angina, more frequent evidence of myocardial ischemia, and lack of use of HR-lowering agents.

PLoS ONE 7(5): e36284
Heart rate control is associated with reduced cardiovascular events in Asian patients with coronary artery disease treated with Bisoprolol (BISO-CAD): results from a multi-national, real-world experience

Phase IV, multi-national, single-arm, open-label, non-randomized, observational trial was conducted between October 2011 and July 2015 across 42 hospitals from China, South Korea and Vietnam.

Bisoprolol to be efficacious in lowering RHR and causing a significant decrease in the occurrence of the composite cardiac outcome, as well as safe in Asian patients with CAD.

Beta-blockers offer additional protection to BP reductions in preventing recurrent events in patients with a history of CHD.

<table>
<thead>
<tr>
<th>Trials of beta-blockers</th>
<th>No of trials</th>
<th>No of events</th>
<th>Relative risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>People with history of CHD</td>
<td>37</td>
<td>2524</td>
<td>0.71 (0.66 to 0.78)</td>
</tr>
<tr>
<td>Entry after acute myocardial infarction</td>
<td>27</td>
<td>2155</td>
<td>0.69 (0.62 to 0.76)</td>
</tr>
<tr>
<td>Entry after long term coronary heart disease</td>
<td>11</td>
<td>369</td>
<td>0.87 (0.71 to 1.06)</td>
</tr>
<tr>
<td>People with no history of CHD</td>
<td>6</td>
<td>851</td>
<td>0.89 (0.78 to 1.02)</td>
</tr>
</tbody>
</table>

| Trials of drugs other than beta-blockers       |              |              |                                                |
| People with history of CHD                     | 37           | 5834         | 0.85 (0.79 to 0.91)                             |
| People with no history of CHD                  | 24           | 3217         | 0.84 (0.79 to 0.90)                             |

| All trials except ones of beta-blockers in people with history of CHD | 64 | 9417 | 0.85 (0.81 to 0.89) |

Blood pressure (BP)  Coronary heart disease (CHD)
Pattern of Prescription of Anti-Hypertensive Medications in a Tertiary Health Care Facility in Abuja, Nigeria

Introduction: Marked changes have been made in the pharmacotherapy of hypertension over the years. In sub-Saharan Africa, hypertension pharmacotherapy is often thought to include only thiazide diuretics, beta blockers and centrally acting medications and, it is unclear if and how often calcium channel blockers, angiotensin converting enzyme inhibitors and angiotensin receptor blockers are used.

Dike B. Ojji, MD; Samuel O. Ajayi, MD; Manmak H. Mamven, MD; Jacob Alfa, MD; Damasceno Albertino, MD, PhD

Key Words: Hypertension, Pharmacotherapy, Sub-Saharan Africa

We examined the anti-hypertensive prescription

**Introduction**

![Graph showing the pattern of anti-hypertensive prescriptions]

**Fig 1.** Pattern of anti-hypertensive prescriptions

1=CCBs; 2=THZ; 3=ACEIs; 4=BB; 5=ARBs; 6=CAM
CCB=Calcium Channel Blockers, THZ=Thiazide diuretics, ACEIs=Angiotensin Converting Enzyme Inhibitors, BB=Beta Blockers, ARBs=Angiotensin Receptor Blockers, CAM=Centrally Acting Medications
A total of 100 males (44.6%) and 124 females participated in the study.
The age ranged between 35-82 years.
Calcium channel blockers were the most frequently prescribed medication (39.3%) followed by diuretics (14.3%)
Combination therapy was seen in 35.7% of the patients.
B-blockers were the rarest drug as a single agent (1.8%)

ANTIHYPERTENSIVE THERAPY AMONG HYPERTENSIVE PATIENTS AS SEEN IN THE MIDDLE BELT OF NIGERIA

I. A. Katibi and J. K. Olarinoye

Department of Medicine, University of Ilorin Teaching Hospital, Ilorin, Nigeria
Reprint requests to: Dr. I. A. Katibi, Department of Medicine, University of Ilorin Teaching Hospital, P. O. Box 13880, Ilorin, Kwara State, Nigeria. E-mail: iakatibi@skannet.com
Thesus Registry: BB used in 28% as against 59% Euro HF Survey
Summary

• Beta blockers are heterogeneous in terms of its pharmacologic and hemodynamic properties

• BB have been used in the treatment of CV conditions for decades

• Although the appropriateness of BB therapy in the management of CVD has been queried given outcomes data from other AHT drug classes, these data were limited to more traditional BB like Atenolol

• There is now overwhelming evidence benefits of the use of beta1-selective agents like Bisoprolol in CVD management

• Beta\textsubscript{1}-blockade helps to prevent the adverse effects of sympathetic overdrive and could protect the heart at every stage of the cardiovascular continuum
Summary

• Bisoprolol is a treatment of choice in young hypertensive patients with additional risk factors for sympathetic overdrive: overweight or obese, DM and high levels of stress

• BB have been shown to be particularly useful for the treatment of hypertension in specific situations: symptomatic angina, for HR control, post-MI, HFREF, and alternative to ACEIs or ARBs in younger hypertensive women planning pregnancy or of child-bearing potential.
THANK YOU VERY MUCH