PHARMACOLOGICAL MANAGEMENT OF HYPERTENSIVE CLIENTS AT HYPERTENSION/DIABETES CLINIC OF KNUST HOSPITAL

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DEDICATION

This thesis is dedicated to all my family, especially my first daughter, Akosua Nhyira Osaebea Obirikorang, who has been my constant source of inspiration. They have given me the drive and discipline to tackle any task with enthusiasm and determination.

DECLARATION

The research described in this thesis was carried out at the Hypertensive (HPT)/Diabetes (DM) Clinic of the Kwame Nkrumah University of Science and Technology (KNUST) Hospital, Kumasi. This work has not been submitted for any other degree.

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ABSTRACT

The main aim of the study is to identify, describe and assess the pharmacological management of hypertensive clients at the Hypertension and Diabetes (HPT/DM) Clinic of the Kwame Nkrumah University of Science and Technology (KNUST) Hospital, Kumasi. HPT is a major public health issue because of its high prevalence and serious complications. Appropriate and timely management using pharmacological and non-pharmacological therapy is essential to minimize complications and death resulting from HPT.

A cross sectional retrospective study involving 100 clients was employed in this study. Data was collected through the administration of semi structured questionnaires from 1st July to 31st October, 2011. Case notes of the clients were also reviewed to obtain additional information and also to confirm and validate the clients' responses.

The classes of Antihypertensive Agents (AHA) commonly used at the HPT/DM Clinic of the KNUST Hospital are calcium channel blockers (CCB), diuretics (DIU), angiotensin converting enzyme inhibitors (ACEI), angiotensin II receptor blockers (ARB), and beta blockers (BB). Centrally acting agents (CAA) and vasodilators (VAS) are used sparingly. Clients' pharmacological management was frequently initiated with monotherapy (57.6%), of which CCB accounted for 77.2% of the prescriptions followed by DIU (10.5%). Dual- and three-drug therapies are also used in initiating management. Among the CCB, Nifedipine (71.4% / 57.303) is the most prescribed and bendrofluazide (94.1% / 83.78) is the most prescribed among the DIU. Aspirin 44 (46.8%) was the most prescribed non-AHA.

The target or goal blood pressure (BP) for HPT clients from World Health Organization/International Society of Hypertension (WHO/ISH) and European Society of Hypertension/European Society of Cardiology (ESH/ESC) guidelines is <130/85 mmHg and that of the Ghana Standard Treatment Guidelines (GSTG) of the Ministry of Health (MOH) of Ghana is < 140/ 90 mmHg. Based on these criteria BP control rates are 42% and 62% respectively.

In conclusion, the AHA in use at the HPT/DM Clinic of the KNUST Hospital and prescription pattern are in accordance with that of the international and national guidelines.

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ABBREVIATIONS

AB – Alpha Blockers

ACE - Angiotensin-Converting Enzyme

ACEI - Angiotensin-Converting Enzyme Inhibitors

AHA – Antihypertensive Agents

ARB - Angiotensin II Receptor Blockers

BB - Beta- Blockers

BP – Blood Pressure

CAA – Centrally-Acting Agents

CCB - Calcium Channel Blockers

DBP – Diastolic Blood Pressure

DIU – Diuretics

DM – Diabetes Mellitus

ESH - European Society of Hypertension

ESC - European Society of Cardiology

GSTG – Ghana Standard Treatment Guidelines

HPT – Hypertension

ISH - International Society of Hypertension

JNC – Joint National Committee

K^+ - Potassium

KATH – Komfo Anokye Teaching Hospital

KNUST – Kwame Nkrumah University of Science and Technology

LDIU – Loop Diuretics

MOH – Ministry of Health

SBP – Systolic Blood Pressure

TDIU – Thiazide Diuretics

VAS - Vasodilators

WHO - World Health Organization

Chapter 1

INTRODUCTION

1.1 GENERAL INTRODUCTION

Hypertension (HPT) is a major issue in public health because of its high prevalence and serious complications. Approximately 1 billion people worldwide have high blood pressure, and this number is expected to increase to 1.56 billion people by the year 2025 (He and Whelton, 1997). Cooper *et al* (1997) estimated the prevalence of hypertension in West Africa to be 16%, 26% in The Caribbean and 33% in the United States.

A recent cross sectional study of HPT in Ghana supported the evidence that HPT is a major health problem and is associated with relatively low level regarding awareness of drug management and BP control. The prevalence rate of HPT in Ghana has seen a significant rise, increasing in rural areas from 4.5% to 28.7% (Pobee *et al.*, 1977; Cappuccio *et al.*, 2004).

HPT is one of the main causes of coronary vascular disease and renal diseases, and is responsible for 12.8% of global deaths and 12.1% of deaths in low and middle income countries(WHO, 2009).Success in managing high BP is often assessed in terms of the proportion of clients reaching a goal BP of 130/85mmHg. Drugs and changes in one's lifestyle are the main ways of controlling and maintaining a well controlled BP (Ezzati *et al.*, 2002; WHO Guidelines Sub-Committee, 2003).

Classes of Antihypertensive agents (AHA) commonly in use include; diuretics (DIU), angiotensin-converting enzyme inhibitors (ACEI), calcium channel blockers

(CCB), angiotensin II receptor blockers (ARB), beta- blockers (BB), alpha blockers (AB) and centrally-acting agents (CAA) (WHO Guidelines Sub-Committee, 1999; Ministry of Health, 2010).

This study, therefore, is to assess the pharmacological management of HPT clients in the KNUST Hospital to help in making proposals that will streamline management protocols in the hospital to conform to national and international standards. Since there is no previous study of the management of HPT in the hospital, this research can serve as baseline for future assessments. The resulting deficiencies and shortcomings identified would be included in recommendations that will go a long way to improve the care and management of HPT clients in the hospital. This will eventually improve the quality of life of HPT clients and prevent and/ or reduce complications, morbidities and mortalities. The findings will also form an important part in the formulation of regional and national drug policies on any HPT control programme.

1.2 PROBLEM STATEMENT

HPT is one of the most important preventable causes of premature death worldwide; however, it is a major risk factor for death from cardiovascular causes such as heart attacks, heart failure, and stroke, and also for kidney failure and blood vessel diseases (Isles *et al.*, 1989; MacMahon *et al.*, 1990). It is estimated to cause 4.5 percent of current global disease burden according to the 2003 WHO/ISH statement on the management of HPT (Collins *et al.*, 1990). Also, it has been reported that BP is under control in less than 20% of clients with HPT in many countries (Murray and Lopez, 1996). Even though, the AHA employed in the

management of HPT in Africa are current, the burden of HPT management is still enormous (World Health Organisation, 2005).

In a systematic review of the epidemic of HPT in Ghana, between 1970 and 2009 there was an increase in awareness, management and control of HPT (Bosu, 2010). This is illustrated in Table 1.2 below.

Table 1.1 Awareness, Management and Control of Hypertension

Study reference	Total no. Hypertensives	Among total number of hypertensives:			Aware %	Management %	Control %
		Aware[a]	Management[b]	Control[c]			
Pobee et al 1979 [22-24,74]	540	130	39	20	24.1	7.2	3.7
Hesse 1998 [30]	38	14	5	0	36.8	13.2	0.0
Amoah 2003 [33]	1337	458	243	49	34.3	18.2	3.7
Addo et al 2006 [27]	93	30	15	5	32.3	16.1	5.4
Cappucio et al 2004 [36,75]	291	64	33	8	22.0	11.3	2.7
Agyeman et al 2006 [28,42]	421	143	118	26	34.0	28.0	6.2
Addo et al 2008 [31]	307	166	96	39	54.1	31.3	12.7

([a] Hypertensives who reported having ever been informed by a health professional of a diagnosis of hypertension were considered to be aware of their condition. [b] Hypertensives who reported taking recognized antihypertensive medication were considered to be on management. [c] Hypertensives on medication whose blood pressure measured during the study was less than140/90 mm Hg were considered to have controlled blood pressure controlled. Note that the percentages in columns 6-8 use the total number of hypertensives as a common denominator.)

Since the HPT/DM Clinic started working in 2008, clinic attendance, ward admissions and HPT related deaths have all been increasing at the KNUST Hospital as evidenced below in Table 2.1;

Table 1.2 Hospital records on HPT/DM Clinic attendance, admissions and deaths

	2008	**2009**	**2010**
Total Clinic attendance	1023	2005	2306
HPT admissions	245	302	478
Deaths	56	67	75

Are people now becoming aware of this equally preventable and manageable lifestyle disease and reporting? Are the right drugs being prescribed for these clients? Are prescribers following laid down international and national protocols for the management of HPT?

Information on pharmacological management of HPT in Ghana is scanty. Therefore, this study will throw more light on the pharmacological management of HPT and the pattern of AHA usage in the HPT/DM Clinic of the KNUST Hospital and serve as baseline for future studies.

1.3 PURPOSE OF STUDY

To identify, describe and assess the pharmacological management of HPT clients at the HPT/DM Clinic of the KNUST Hospital, Kumasi.

1.4 SPECIFIC OBJECTIVES

To identify the AHA in use at the HPT/DM Clinic of the KNUST Hospital.

To describe prescription pattern of AHA in HPT/DM Clinic.

To assess the short term outcome of AHA usage

To compare prescribing pattern at the KNUST Hospital with international and national guidelines.

Identify points for future intervention to improve outcomes.

Chapter 2

LITERATURE REVIEW

2.1 DEFINITION

HPT is a condition in which the BP of an individual is persistently higher, based on the average of two or more properly measured BP readings. The 2003 World Health Organization (WHO) and International Society of Hypertension (ISH) statement of the management of HPT and the 2007 European Society of Hypertension (ESH) and the European Society of Cardiology (ESC) defined and classified HPT as shown below in Table 2.1 (WHO Guidelines Sub-Committee, 2003; Mancia *et al.*, 2007);

Table 2.1 Definition and Classification of Blood Pressure Levels

CATEGORY	SYSTOLIC (mmHg)	DIASTOLIC (mmHg)
Optimal	<120	<80
Normal	<130	<85
High – Normal	130-139	85-89
Grade 1 Hypertension ("mild")	140-159	90-99
Subgroup: Borderline	140-149	90-94
Grade 2 Hypertension ("moderate")	160-179	100-109
Grade 3 Hypertension ("severe")	>180	>110
Isolated Systolic Hypertension	> 140	<90
Subgroup: Borderline	140-149	<90

The 1999 WHO/ISH statement of the management of HPT; definition and classification of HPT for adults ages 18 and older.

The Seventh USA Joint National Committee Guidelines (JNC 7) on HPT published in 2003 (Chobanian *et al.*, 2003a) unified the normal and high normal BP categories into a single entity termed ''prehypertension''. This was based on the evidence from the Framingham study (Vasan *et al.*, 2001; Vasan *et al.*, 2002), that in such individuals the chance of developing HPT is higher than in those with a BP <120/80mmHg (termed ''normal'' BP) at all ages.

The Ghana Standard Treatment Guidelines (GSTG) of the Ministry of Health (MOH), defines HPT as a condition in which the BP of an adult is persistently higher than 140/90mmHg in a non-diabetic, or above 130/80mmHg in a diabetic, based on the average of two or more properly measured BP readings(Ministry of Health, 2010).

HPT is classified as either primary (essential) or secondary (Ministry of Health, 2010).

2.1.1 Primary/Essential HPT

This is the most prevalent HPT type, affecting 90–95% of HPT clients (Carretero and Oparil, 2000). Although no direct cause has been identified, there are many factors such as sedentary lifestyle, smoking, stress, visceral obesity, hypokalemia (Rodriguez-Cruz and Ettinger, 2010), obesity (Wofford and Hall, 2004), of which more than 85% of cases occur in those with a body mass index greater than 25, salt (sodium) sensitivity (Lackland and Egan, 2007), alcohol intake (Djousse and Mukamal, 2009), and vitamin D deficiency that increase the risk of developing HPT (Lee *et al.*, 2008; Tuohimaa, 2009). Risk also increases with aging (Kosugi *et al.*, 2009), some inherited genetic mutations (Dickson and Sigmund, 2006), and having a family history of HPT (Luma and Spiotta, 2006). An elevated level of renin, a

hormone secreted by the kidney, is another risk factor (Segura and Ruilope, 2007), as is sympathetic nervous system over activity (Rahmouni *et al.*, 2005). Insulin resistance, (which is a component of syndrome X or the metabolic syndrome), is also thought to contribute to HPT (Sorof and Daniels, 2002; Segura and Ruilope, 2007). Recent studies have implicated low birth weight as a risk factor for adult essential HPT (Uchiyama, 2008).

2.1.2 Secondary HPT

Secondary HPT by definition results from an identifiable cause. This type is important to recognize since it is treated differently to essential HPT, by treating the underlying cause of the elevated HPT (Dodt *et al.*, 2009). HPT results in the compromise or imbalance of the pathophysiological mechanisms, such as the hormone-regulating endocrine system, that regulate blood plasma volume and heart function. Some are common, well-recognized secondary causes such as renovascular HPT and Cushing's syndrome, which is a condition where the adrenal glands overproduce the hormone cortisol (Dodt *et al.*, 2009; Ministry of Health, 2010). HPT is also caused by other conditions that cause hormone changes, such as hyperthyroidism, hypothyroidism, and certain tumors of the adrenal medulla (e.g., pheochromocytoma). Other common causes of secondary HPT include kidney disease, obesity, metabolic disorder, pre-eclampsia during pregnancy, the congenital defect known as coarctation of the aorta, and certain prescription and illegal drugs (Bullock, 2000; Porth, 2002; Dodt *et al.*, 2009; Ministry of Health, 2010).

2.2 MANAGEMENT OF HPT

2.2.1 Benefits of Lowering BP

In Clinical trials, antihypertensive therapy has been associated with reductions in stroke incidence averaging 35–40 percent; myocardial infarction, 20–25 percent; and heart failure, more than 50 percent (Neal *et al.*, 2000). It is estimated that in clients with stage 1 HPT (SBP 140–159 mmHg and/or DBP 90–99 mmHg) and additional cardiovascular risk factors, achieving a sustained 12 mmHg reduction in SBP over 10 years will prevent 1 death for every 11 clients treated. In the presence of CVD or target organ damage, only 9 clients would require such BP reduction to prevent a death (Ogden *et al.*, 2000).

The ultimate public health goal of HPT management is the reduction of complications such as cardiovascular, cerebrovascular and renal morbidities, and mortality. The goal BP as recommended by WHO/ISH, ESH/ESC, JNC-7 HPT report of US and GSTG of MOH, is that both systolic and diastolic BPs, be lowered intensively to at least below 140/90 mmHg and to lower values if tolerated, in all HPT clients, and to below 130/80 mmHg in diabetics (WHO Guidelines Sub-Committee, 2003; Mancia *et al.*, 2007; Ministry of Health, 2010).

HPT is managed with two main strategies;

1. Non-pharmacological or Lifestyle Modifications

2. Pharmacological or drug management.

2.2.2 Non-pharmacological or Lifestyle Modifications

Adoption of healthy lifestyles by all persons is critical for the prevention of high BP and is an indispensable part of the management of those with HPT. Lifestyle

modifications reduce BP, enhance antihypertensive drug efficacy, and decrease cardiovascular risk. For example, a 1,600 mg sodium DASH eating plan has effects similar to single drug therapy (Sacks *et al.*, 2001). Combinations of two or more lifestyle modifications can achieve even better results.

A variety of studies and Clinical trials have been conducted that shows that lifestyle modifications play important roles in the management of HPT. These include the following;

1. Weight reduction in those individuals who are overweight or obese (Leiter *et al.*, 1999),

2. Dietary sodium reduction (Cutler *et al.*, 1997; Whelton *et al.*, 1998; Sacks *et al.*, 2001),

3. Physical activity (Hagberg *et al.*, 2000),

4. Adoption of the Dietary Approaches to Stop Hypertension (DASH) eating plan which is rich in potassium and calcium (Group, 1997b; Group, 1997a; He *et al.*, 2000),

5. Moderation of alcohol consumption (Xin *et al.*, 2001)

A study by Sacks *et al* (2001), states that the overall antihypertensive effect of effective lifestyle interventions varies with the client's adherence to therapy. They further state that when adherence is optimal, systolic BP has been found to reduce by more than 10mmHg. However, in less-controlled clinical practice, more modest effects have been seen (Ebrahim and Smith, 1998). The table 2.2 below shows the lifestyle modification, recommendation and approximate SBP reduction.

Table 2.2 Lifestyle modifications to manage hypertension

Modification	Recommendation	Approximate SBP Reduction (Range)
Weight reduction	Maintain normal body weight (body mass index 18.5–24.9 kg/m2).	5–20 mmHg/10 kg weight loss (36,37)
Adopt DASH eating plan	Consume a diet rich in fruits, vegetables, and low fat dairy products with a reduced content of saturated and total fat	8–14 mmHg (39, 44)
Dietary sodium reduction	Reduce dietary sodium intake to no more than 100 mmol per day (2.4 g sodium or 6 g sodium chloride).	2–8 mmHg (39, 44,45)
Physical activity	Engage in regular aerobic physical activity such as brisk walking (at least 30 min per day, most days of the week).	4–9 mmHg (46, 47)
Moderation of alcohol consumption	Limit consumption to no more than 2 drinks (1 oz or 30 mL ethanol; e.g., 24 oz beer, 10 oz wine, or 3 oz 80-proof whiskey) per day in most men and to no more than 1 drink per day in women and lighter weight persons.	2–4 mmHg (42)

(DASH, Dietary Approaches to Stop Hypertension. * For overall cardiovascular risk reduction, stop smoking. † The effects of implementing these modifications are dose and time dependent, and could be greater for some individuals)

2.2.3 Pharmacological Management

Classes of AHA commonly in use include;

1. Diuretics (Thiazides and related agents, Loop and Potassium-sparing diuretics),
2. Angiotensin-Converting Enzyme Inhibitors,
3. Angiotensin II receptor blockers,
4. Calcium channel blockers,
5. Vasodilators,
6. Beta blockers,
7. Alpha blockers
8. Centrally-acting agents

2.2.3.1 Diuretics

Therapeutic action

DIU increases urine output by the kidney. This is accomplished by altering how the kidney handles sodium. If the kidney excretes more sodium, then water excretion will also increase (Kuncl and Nelson, 1997). Most diuretics produce diuresis by inhibiting the reabsorption of sodium at different segments of the renal tubular system. Sometimes a combination of two diuretics is given because this can be significantly more effective than either compound alone (synergistic effect). The reason for this is that one nephron segment can compensate for altered sodium

reabsorption at another nephron segment; therefore, blocking multiple nephron sites significantly enhances efficacy (Holcomb, 1997).

Loop diuretics (LDIU) inhibit the sodium-potassium-chloride cotransporter in the thick ascending limb. This transporter normally reabsorbs about 25% of the sodium load; therefore, inhibition of this pump can lead to a significant increase in the distal tubular concentration of sodium, reduced hypertonicity of the surrounding interstitium, and less water reabsorption in the collecting duct. This altered handling of sodium and water leads to both diuresis (increased water loss) and natriuresis (increased sodium loss). By acting on the thick ascending limb, which handles a significant fraction of sodium reabsorption, LDIU are very powerful DIU (Anderson *et al.*, 1999). These drugs also induce renal synthesis of prostaglandins, which contributes to their renal action including the increase in renal blood flow and redistribution of renal cortical blood flow (Morrison, 1997).

Loop diuretics are relied on for severe HPT and congestive heart failure. Example is furosemide or lasix (Skidmore-Roth, 2001).

Thiazide diuretics (TDIU), which are the most commonly used DIU, inhibit the sodium-chloride transporter in the distal tubule. Because this transporter normally only reabsorbs about 5% of filtered sodium, these DIU are less efficacious than LDIU in producing diuresis and natriuresis (Holcomb, 1997). Nevertheless, they are sufficiently powerful to satisfy most therapeutic needs requiring a DIU. They are considered most appropriate for mild - moderate HPT with otherwise normal heart and kidney function. Their mechanism depends on renal prostaglandin production. Examples are hydrochlorothiazide, chlorothiazide (Gilman *et al.*, 2002).

Because loop and thiazide DIU increase sodium delivery to the distal segment of the distal tubule, this increases potassium loss (potentially causing hypokalemia) because the increase in distal tubular sodium concentration stimulates the aldosterone-sensitive sodium pump to increase sodium reabsorption in exchange for potassium and hydrogen ion, which are lost to the urine. The increased hydrogen ion loss can lead to metabolic alkalosis. Part of the loss of potassium and hydrogen ion by loop and thiazide DIU results from activation of the renin-angiotensin-aldosterone system that occurs because of reduced blood volume and arterial pressure. Increased aldosterone stimulates sodium reabsorption and increases potassium and hydrogen ion excretion into the urine (Morrison, 1997; Karch, 2003; Galbraith *et al.*, 2007).

There is a third class of diuretic that is referred to as *potassium (K^+)-sparing DIU* (examples: spironolactone, amioloride). Unlike loop and thiazide DIU, some of these drugs do not act directly on sodium transport. Some drugs in this class antagonize the actions of aldosterone *(aldosterone receptor antagonists)* at the distal segment of the distal tubule. This causes more sodium (and water) to pass into the collecting duct and be excreted in the urine. They are called K^+-sparing DIU because they do not produce hypokalemia like the loop and thiazide DIU. The reason for this is that by inhibiting aldosterone-sensitive sodium reabsorption, less K^+ and hydrogen ion are exchanged for sodium by this transporter and therefore less K^+ and hydrogen are lost to the urine (Holcomb, 1997; Morrison, 1997). Other K^+-sparing DIU directly inhibits sodium channels associated with the aldosterone-sensitive sodium pump, and therefore have similar effects on K^+ and hydrogen ion as the aldosterone antagonists. Their mechanism depends on renal prostaglandin production. Because this class of DIU has relatively weak effects on overall sodium

balance, they are often used in conjunction with thiazide or loop DIU to help prevent hypokalemia (Karch, 2003).

Therapeutic Uses

Most clients with HPT, of which 90-95% have primary HPT, are effectively treated with DIU. Antihypertensive therapy with DIU is particularly effective when coupled with reduced dietary sodium intake. The efficacy of these drugs is derived from their ability to reduce blood volume, cardiac output, and with long-term therapy, systemic vascular resistance. The vast majority of HPT clients are treated with loop or thiazide DIU. K^+-sparing, aldosterone-blocking DIU (e.g., spironolactone) are used in secondary HPT caused by hyperaldosteronism, and sometimes as an adjunct to thiazide management in primary HPT to prevent hypokalemia (Morrison, 1997; Karch, 2003).

Contraindications

LDIU should be avoided in severe hypokalaemia, severe hyponatraemia, anuria, comatose and precomatose states associated with liver cirrhosis, and in renal failure due to nephrotoxic or hepatotoxic drugs (Holcomb, 1997).

K^+ supplements must not be given with potassium-sparing DIU. Administration of a K^+-sparing DIU to a client receiving an ACEI or an ARB can also cause severe hyperkalaemia (Morrison, 1997).

Thiazides and related DIU should be avoided in refractory hypokalaemia, hyponatraemia and hypercalcaemia, symptomatic hyperuricaemia, and Addison's disease (Kuncl and Nelson, 1997).

Side effects

Some clients may experience mild gastro-intestinal disturbances, pancreatitis, hepatic encephalopathy, postural hypotension, hyperglycaemia (less common than with thiazides), and acute urinary retention. There may be electrolyte disturbances (including hyponatraemia, hypokalaemia, hypocalcaemia etc), visual disturbances, tinnitus and deafness (usually with high parenteral doses and rapid administration, and in renal impairment), and hypersensitivity reactions (including rash, photosensitivity, and pruritus)(Morrison, 1997).

2.2.3.2. Angiotensin Converting Enzyme Inhibitors (ACEI)

Therapeutic actions

Angiotensin II is a very potent chemical that causes the muscles surrounding blood vessels to contract, thereby narrowing the vessels. The narrowing of the vessels increases the pressure within the vessels causing high BP. Angiotensin II is formed from angiotensin I in the blood by the enzyme angiotensin converting enzyme (ACE). ACEI are medications that slow or inhibit the activity of the ACE, which decreases the production of angiotensin II. As a result, the blood vessels enlarge or dilate thereby reducing BP. This lower BP makes it easier for the heart to pump blood and can improve the function of a failing heart. In addition, the progression of kidney disease due to high BP or diabetes is slowed (Karch, 2003).

Therapeutic Uses

ACEI are used for controlling BP, treating heart failure, preventing strokes, and preventing kidney damage in people with HPT or diabetes. They also improve survival after heart attacks. In studies, individuals with HPT, heart failure, or prior heart attacks who were treated with an ACEI lived longer than clients who did not

take an ACEI. Because they prevent early death resulting from HPT, heart failure or heart attacks, ACEI are one of the most important groups of drugs (Karch, 2003).

An ACEI may be the most appropriate baseline drug for HPT in younger Caucasian clients; Afro-Caribbean clients, those aged over 55 years, and those with primary aldosteronism respond less well. ACEI are particularly indicated for HPT in clients with type 1 diabetes with nephropathy. They may reduce BP very rapidly in some clients particularly in those receiving DIU therapy; the first dose should preferably be given at bedtime (Galbraith *et al.*, 2007).

Some individuals with HPT do not respond sufficiently to ACEI alone. In these cases, other drugs are used in combination with ACEI (Galbraith *et al.*, 2007).

Examples of ACEI are; Enalapril, Lisinopril, Perindopril, Ramipril (Lilley and Aucker, 2001).

Side effects

Most individuals tolerate ACEI well; however some side effects can be experienced. The most common side effects (Karch, 2003; Galbraith *et al.*, 2007) are; cough, elevated blood K^+ levels, low BP, dizziness, headache, drowsiness, weakness, abnormal taste (metallic or salty taste), and rash.

It may take up to a month for coughing to subside, and if one ACEI causes cough it is likely that the others will too. The most serious, but rare, side effects of ACEI are kidney failure, allergic reactions, a decrease in white blood cells, and swelling of tissues (Galbraith *et al.*, 2007)

Contraindication

ACEI usually are not prescribed for pregnant clients because they may cause birth defects. Individuals with bilateral renal artery stenosis (narrowing) may experience worsening of kidney function, and people who have had a severe reaction to ACEI probably should avoid them (Lilley and Aucker, 2001).

2.2.3.3. Angiotensin II Receptor Blockers (ARB)

Therapeutic action

Angiotensin II is a very potent chemical that causes muscles surrounding blood vessels to contract, thereby narrowing blood vessels. This narrowing increases the pressure within the vessels and can cause high BP. ARB are medications that block the action of angiotensin II by preventing angiotensin II from binding to angiotensin II receptors on blood vessels. As a result, blood vessels dilate and BP is reduced and makes it easier for the heart to pump blood and can improve heart failure. In addition, the progression of kidney disease due to high BP or diabetes is slowed. ARB have effects that are similar to angiotensin converting enzyme (ACEI), but ACEI act by preventing the formation of angiotensin II rather than by blocking the binding of angiotensin II to muscles on blood vessels (Lilley and Aucker, 2001; Karch, 2003).

Therapeutic uses

ARB is used for controlling high BP, treating heart failure, and preventing kidney failure in people with diabetes or high BP. They may also prevent diabetes and reduce the risk of stroke in clients with high BP and an enlarged heart. ARB may

also prevent the recurrence of atrial fibrillation. Since these medications have effects that are similar to those of ACEI, they often are used when ACEI are not tolerated by clients (for example, due to excessive coughing) (Galbraith *et al.*, 2007).

Differences among the different types of ARB

ARB is similar in actions and side effects. They differ in how they are eliminated from the body and the extent to which they are distributed throughout the body. Some ARB need to be converted to an active form in the body before they can lower BP. In addition, some ARB is better at lowering BP. In some studies, irbesartan and candesartan reduced BP better than losartan (Karch, 2003).

Examples of ARB are Candesartan, Irbesartan, Valsartan, and Losartan (Mosby's, 2000).

Side effects

ARB is well tolerated by most individuals. The most common side effects are cough, hyperkalaemia, low BP, dizziness, headache, drowsiness, diarrhea, abnormal taste sensation (metallic or salty taste), and rash. Compared to ACEI, cough occurs less often with ARB. The most serious, but rare, side effects are kidney failure, liver failure, allergic reactions, a decrease in white blood cells, and swelling of tissues (Karch, 2003; Galbraith *et al.*, 2007). ARB usually is not prescribed for pregnant clients because they may cause birth defects. Individuals who have narrowing of both kidney arteries or have had a severe reaction to ARB should avoid them. Like other antihypertensives, ARB have been associated with sexual dysfunction (Lilley and Aucker, 2001).

2.2.3.4. Calcium Channels Blockers (CCB)

Therapeutic action

Currently approved CCB bind to L-type calcium channels located on the vascular smooth muscle, cardiac myocytes, and cardiac nodal tissue (sinoatrial and atrioventricular nodes). These channels are responsible for regulating the influx of calcium into muscle cells, which in turn stimulates smooth muscle contraction and cardiac myocyte contraction (Karch, 2003). In cardiac nodal tissue, L-type calcium channels play an important role in pacemaker currents and in phase 0 of the action potentials. Therefore, by blocking calcium entry into the cell, CCB cause vascular smooth muscle relaxation (vasodilation), decreased myocardial force generation, decreased heart rate, and decreased conduction velocity within the heart, particularly at the atrioventricular node (Gilman *et al.*, 2002).

Therapeutic uses

CCB are used to treat HPT, angina and arrhythmias. By causing vascular smooth muscle relaxation, CCB decrease systemic vascular resistance, which lowers arterial blood pressure. These drugs primarily affect arterial resistance vessels, with only minimal effects on venous capacitance vessels (Lilley and Aucker, 2001; Lehne, 2010).

Different Classes of Calcium-Channel Blockers

There are three classes of CCB. They differ not only in their basic chemical structure, but also in their relative selectivity toward cardiac versus vascular L-type calcium channels. The most smooth muscle selective class of CCB is the *dihydropyridines.* Because of their high vascular selectivity, these drugs are primarily used to reduce systemic vascular resistance and arterial pressure, and therefore are primarily used to treat HPT (Karch, 2003). They are not, however,

generally used to treat angina because their powerful systemic vasodilator and pressure lowering effects can lead to reflex cardiac stimulation, which can dramatically increase myocardial oxygen demand. Note that dihydropyridines are easy to recognize because the drug name ends in "pine". Examples of Dihydropyridines include: Amlodipine, Felodipine, Nicardipine, Nifedipine, and Nimodipine (Galbraith *et al*., 2007).

Non-dihydropyridines, of which there are only two currently used clinically, comprise the other class of CCB. *Verapamil (phenylalkylamine class)*, is relatively selective for the myocardium, and is less effective as a systemic vasodilator drug (Galbraith *et al*., 2007).

Diltiazem (benzothiazepine class) is intermediate between verapamil and dihydropyridines in its selectivity for vascular calcium channels. By having both cardiac depressant and vasodilator actions, diltiazem is able to reduce arterial pressure without producing the same degree of reflex cardiac stimulation caused by dihydropyridines (Galbraith *et al*., 2007).

Side Effects and Contraindications

Dihydropyridine CCB can cause flushing, headache, excessive hypotension, edema and reflex tachycardia. Long-acting dihydropyridines have been shown to be safer AHA, in part, because of reduced reflex responses. The cardiac selective, non-dihydropyridine CCB can cause excessive bradycardia, impaired electrical conduction (e.g., atrioventricular nodal block), and depressed contractility. Therefore, clients having preexistent bradycardia, conduction defects, or heart failure caused by systolic dysfunction should not be given CCB, especially the cardiac selective, non-dihydropyridines (Galbraith *et al*., 2007). CCB, especially non-dihydropyridines, should not be administered to clients being treated with a

BB because they also depress cardiac electrical and mechanical activity and therefore the addition of a CCB augments the effects of beta-blockade (Lilley and Aucker, 2001; Skidmore-Roth, 2001).

2.2.3.5. Vasodilators

Therapeutic Use and Rationale

Vasodilator drugs relax the smooth muscle in blood vessels, which causes the vessels to dilate. Dilation of arterial vessels leads to a reduction in systemic vascular resistance, which leads to a fall in arterial BP. Dilation of venous vessels decreases venous BP (Lilley and Aucker, 2001; Gilman *et al.*, 2002).

Vasodilators are used to treat BP, heart failure and angina; however, some vasodilators are better suited than others for these indications. Vasodilators that act primarily on arterial vessels (arterial dilators) are used for HPT and heart failure, but not for angina because of reflex cardiac stimulation. Venous dilators are very effective for angina, and sometimes used for heart failure, but are not used as primary therapy for HPT (Gilman *et al.*, 2002). Most vasodilator drugs are mixed (or balanced) vasodilators in that they dilate both arteries and veins; however, there are some very useful drugs that are highly selective for arterial or venous vasculature. Some vasodilators, because of their mechanism of action, also have other important actions that can in some cases enhance their therapeutic utility as vasodilators or provide some additional therapeutic benefit. For example, some calcium channel blockers not only dilate blood vessels, but also depress cardiac mechanical and electrical function, which can enhance their antihypertensive actions and confer additional therapeutic benefit such as blocking arrhythmias (Lilley and Aucker, 2001; Karch, 2003).

Arterial dilators

Arterial dilator drugs are commonly used to treat systemic and pulmonary HPT, heart failure and angina. They reduce arterial pressure by decreasing systemic vascular resistance. This benefits clients in heart failure by reducing the afterload on the left ventricle, which enhances stroke volume and cardiac output and leads to secondary decreases in ventricular preload and venous pressures. Most drugs that dilate arteries also dilate veins; however, hydralazine, a direct acting vasodilator, is highly selective for arterial resistance vessels (Gilman *et al.*, 2002).

Venous dilators

Drugs that dilate venous capacitance vessels serve two primary functions in treating cardiovascular disorders:

Venous dilators reduce venous pressure, which reduces preload on the heart thereby decreasing cardiac output. This is useful in angina because it decreases the oxygen demand of the heart and thereby increases the oxygen supply/demand ratio. Oxygen demand is reduced because decreasing preload leads to a reduction in ventricular wall stress by decreasing the size of the heart (Karch, 2003).

Reducing venous pressure decreases proximal capillary hydrostatic pressure, which reduces capillary fluid filtration and edema formation. Therefore, venous dilators are sometimes used in the management of heart failure along with other drugs because they help to reduce pulmonary and/or systemic edema that results from the heart failure (Karch, 2003).

Although most vasodilator drugs dilate veins as well as arteries, some drugs, such as organic nitrate dilators are relatively selective for veins.

Mixed or "balanced" dilators

As indicated above, most vasodilators act on both arteries and veins, and therefore are termed mixed or balanced dilators. Notable exceptions are hydralazine (arterial dilator) and organic nitrate dilators (venous dilators).

Mixed vasodilators, in general decrease systemic vascular resistance and arterial pressure with relatively little change in right atrial (or central venous) pressure (i.e., little change in cardiac preload), and they have a relatively little effect on cardiac output (Galbraith *et al.*, 2007).

Side-Effects

There are three potential drawbacks in the use of vasodilators;

Systemic vasodilation and arterial pressure reduction can lead to a baroreceptor-mediated reflex stimulation of the heart. This increases oxygen demand, which is undesirable if the patient also has coronary artery disease.

Vasodilators can impair normal baroreceptor-mediated reflex vasoconstriction when a person stands up, which can lead to orthostatic hypotension and syncope upon standing.

Vasodilators can lead to renal retention of sodium and water, which increases blood volume and cardiac output and thereby compensates for the reduced systemic vascular resistance (Karch, 2003; Galbraith *et al.*, 2007).

2.2.3.6. Beta-blockers (BB)

Therapeutic action

BB, also known as beta-agonist blocking agents, beta-agonist antagonists, or beta antagonists, are a type of drug that block the action of the sympathetic nervous system of the heart, resulting in a relief of stress on the heart. BB blocks beta-agonist substances, for example adrenaline (epinephrine) in the involuntary nervous system (autonomic nervous system). BB slow down the heart beat, reduce the force of the heart muscle's contractions, and decrease blood vessel contraction in the heart, brain, and the rest of the body. Some examples of BB are: Acetabutolol, Atenolol, Bisoprolol, Carvedilol, Metoprolol, Nadolol, Pindolol, Propranolol, Sotalol, and Timolol (Mosby's, 2000; Nordqvist *et al.*, 2009).

Therapeutic uses

BB blocks the release of noradrenalin in parts of the body. Noradrenalin is released by the nerves when they are stimulated - it is a chemical that conveys messages to other parts of the body, including muscles, blood vessels and the heart. They are used for the following;

Heart problems - for a patient with heart problems beta-blockers can reduce the workload for the heart; so that it does not have to work so hard to supply all parts of the body with oxygen-rich blood. For people with angina, heart failure, or after a heart attack, reducing the heart's workload is crucial. BB can also block the stimulation of the heart form electrical impulses - they can control irregular

heartbeats - thus lowering the activity of the heart and slowing down the heart rate (Nordqvist *et al.*, 2009).

HPT - BB lower blood pressure by slowing down the heart rate, as well as reducing the force of the heart. Blood still gets to all parts of the body, but at reduced pressure (Lilley and Aucker, 2001; Nordqvist *et al.*, 2009).

Glaucoma - pressure within the eyeball is reduced with BB eye drops. The medication lowers the production of fluid inside the eye ball (Nordqvist *et al.*, 2009).

Contraindications

Clients with a history of asthma, bronchospasm, and clients with second or third degree heart block, severe peripheral arterial disease (including Raynaud's syndrome) and worsening, unstable heart failure should not take BB. However, clients with diabetes (especially those with regular episodes of low blood sugar), myasthenia gravis, bradycardia, and hypotension, HPT that results from pheochromocytoma, metabolic acidosis, and Prinzmetal angina should take BB with caution. In some cases during pregnancy and breastfeeding, certain types of BB may be used (Nordqvist *et al.*, 2009).

Side effects

The most common side effects are; cold feet and hands, diarrhea, fatigue, nausea, and very slow heartbeat. The following less common side effects are also possible; sleeping difficulties and disturbances, bad dreams or nightmares, erectile dysfunction. During driving, some clients may experience dizziness or fatigue; in such cases they should not drive. However, this is rare (Nordqvist *et al.*, 2009).

2.2.3.7. Alpha Blockers (AB)

Therapeutic action

These drugs block the effect of sympathetic nerves on blood vessels by binding to alpha-adrenoceptors located on the vascular smooth muscle. Most of these drugs act as competitive antagonists to the binding of norepinephrine that is released by sympathetic nerves synapsing on smooth muscle. Therefore, sometimes these drugs are referred to as sympatholytics because they antagonize sympathetic activity (Gilman *et al.*, 2002).

Alpha blockers dilates both arteries and veins because both vessel types are innervated by sympathetic agonist nerves; however, the vasodilator effect is more pronounced in the arterial resistance vessels. Because most blood vessels have some degree of sympathetic tone under basal conditions, these drugs are effective dilators. They are even more effective under conditions of elevated sympathetic activity (e.g., during stress) or during pathologic increases in circulating catecholamines caused by pheochromocytoma (Lilley and Aucker, 2001; Galbraith *et al.*, 2007).

Therapeutic Uses

Alpha blockers, especially α1-adrenoceptor antagonists, are useful in the management of primary HPT, although their use is not as widespread as other AHA. The non-selective antagonists are usually reserved for use in HPT emergencies caused by a pheochromocytoma. This HPT condition, which is most commonly caused by an adrenal gland tumor that secretes large amounts of catecholamines, can be managed by non-selective AB (in conjunction with beta-blockade to blunt the reflex tachycardia) until the tumor can be surgically removed (Lilley and Aucker, 2001).

Specific Drugs

Newer AB used in treating HPT are relatively selective α_1-adrenoceptor antagonists (e.g., prazosin, terazosin, doxazosin, trimazosin), whereas some older drugs are non-selective antagonists (e.g., phentolamine, phenoxybenzamine) (Mosby's, 2000; Lilley and Aucker, 2001).

Side Effects and Contraindications

The most common side effects include dizziness, orthostatic hypotension (due to loss of reflex vasoconstriction upon standing), nasal congestion (due to dilation of nasal mucosal arterioles), headache, and reflex tachycardia (especially with non-selective AB). Fluid retention is also a problem that can be rectified by use of DIU in conjunction with the AB. AB have not been shown to be beneficial in heart failure or angina, and should not be used in these conditions (Lilley and Aucker, 2001).

2.2.3.8 Centrally-Acting Agents (CAA)

Therapeutic action

CAA blocks sympathetic activity by binding to and activating alpha$_2$ (α_2)-adrenoceptors. This reduces sympathetic outflow to the heart thereby decreasing cardiac output by decreasing heart rate and contractility. Reduced sympathetic output to the vasculature decreases sympathetic vascular tone, which causes vasodilation and reduced systemic vascular resistance, which decreases arterial pressure (Mosby's, 2000; Lilley and Aucker, 2001).

Therapeutic Uses

Centrally acting agents are used in the treatment of HPT. However, they are not considered first-line therapy in large part because of side effects that are associated with their actions within the brain. They are usually administered in combination with a DIU to prevent fluid accumulation, which increases blood volume and compromises the BP lowering effect of the drugs. Fluid accumulation can also lead to oedema. CAA are effective in HPT clients with renal disease because they do not compromise renal function (Lilley and Aucker, 2001).

Specific Drugs

Several different centrally acting α_2-adrenoceptor agonists are available for clinical use: clonidine, guanabenz, guanfacine, α-methyldopa (Mosby's, 2000; Skidmore-Roth, 2001).

Side Effects and Contraindications

Side effects include sedation, dry mouth and nasal mucosa, bradycardia, orthostatic hypotension, and impotence. Constipation, nausea and gastric upset are also associated with the sympatholytic effects of these drugs. Fluid retention and oedema is also a problem with chronic therapy; therefore, concurrent therapy with a DIU is necessary. Sudden discontinuation of clonidine can lead to rebound HPT, which results from excessive sympathetic activity (Lilley and Aucker, 2001).

2.2.4 When to initiate antihypertensive therapy

Initiation of antihypertensive management is based on two criteria (WHO Guidelines Sub-Committee, 2003):

- Total level of cardiovascular risk
- Level of systolic and diastolic BP

Table 2.3 **Initiation of antihypertensive management.**

Blood pressure (mmHg)					
Other risk factors and disease history	Normal: SBP 120–129 or DBP 80–84	High normal: SBP 130–139 or DBP 85–89	Grade 1: SBP 140–159 or DBP 90–99	Grade 2: SBP 160–179 or DBP 100–109	Grade 3: SBP > 180 or DBP > 110
No other risk factors	No BP intervention	No BP intervention	Lifestyle changes for several months, then drug management if preferred by the patient and resources available	Lifestyle changes for several months, then drug management	Immediate drug management and lifestyle changes
1-2 risk factors	Lifestyle changes	Lifestyle changes	Lifestyle changes for several months, then drug management	Lifestyle changes for several months, then drug management	Immediate drug management and lifestyle changes
3 or more risk factors or TOD or diabetes	Lifestyle changes	Drug management and lifestyle changes	Drug management and lifestyle changes	Drug management and lifestyle changes	Immediate drug management and lifestyle changes

ACC	Drug management and lifestyle changes	Immediate drug management and lifestyle changes	Immediate drug management and lifestyle changes	Immediate drug management and lifestyle changes	Immediate drug management and lifestyle changes

ACC, associated Clinical conditions; DBP, diastolic blood pressure; SBP, systolic blood pressure; TOD, target organ damage.

All clients in whom repeated BP measurements show grade 2 or 3 HPT are definite candidates for antihypertensive management because, as detailed in the 2003 ESH/ESC and the 2003 WHO/ISH HPT Guidelines, a large number of placebo controlled trials have conclusively demonstrated that in clients with these BP values BP reduction lowers the incidence of cardiovascular morbid and fatal events, independently of their level of total risk. Evidence for the benefit of treating grade 1 HPT is admittedly more scant, as specific trials have not addressed the issue. However, the recent findings of the FEVER study on the protective effect of lowering SBP to < 140 rather than slightly > 140mmHg even in HPT clients at moderate risk lends support to the recommendation to consider antihypertensive interventions when SBP is ≥140mmHg (WHO Guidelines Sub-Committee, 2003; Mancia *et al.*, 2009).

In all grade 1 to 3 HPT, lifestyle instructions should be given as soon as HPT is diagnosed or suspected, while promptness in the initiation of pharmacological therapy depends on the level of total cardiovascular risk. Drug management should be initiated promptly in grade 3 HPT, as well as in grade 1 and 2 when total cardiovascular risk is high or very high. In grade 1 or 2 HPT with moderate total cardiovascular risk drug management may be delayed for several weeks and in grade 1 HPT without any other risk factor (low added risk) for several months. However, even in these clients, lack of BP control after a suitable period of non-

pharmacological interventions should lead to the institution of drug management in addition to lifestyle changes. When baseline BP is in the high normal range (130–139/85–89mmHg), the decision on drug intervention heavily depends on the level of risk (WHO Guidelines Sub-Committee, 2003; Galbraith *et al.*, 2007; Mancia *et al.*, 2009).

2.2.5 Choice of antihypertensive drugs

The large number of randomized trials of antihypertensive therapy, both those comparing active management versus placebo and those comparing management regimens based on different compounds, confirm the conclusion of the 2003 ESH/ESC and 2003 WHO/ISH HPT Guidelines that; the main benefits of antihypertensive management are due to lowering of BP, and are largely independent of the drugs employed. TDIU, BB, CCB, ACEI and ARB can adequately lower BP and significantly and importantly reduce cardiovascular outcomes (WHO Guidelines Sub-Committee, 2003; Mancia *et al.*, 2007).

Therefore all these drugs are suitable for the initiation and maintenance of antihypertensive management either as monotherapy or in some combinations with each other. Each of the recommended classes may have specific properties, advantages and limitations, which are helpful making the most appropriate choice in individual clients (WHO Guidelines Sub-Committee, 2003; Mancia *et al.*, 2007).

Most guidelines now advocate the use of a more individualized approach in which the client's age, race, concomitant diseases, risk of adverse effects and therapies, lifestyle, and even, possibly, the socioeconomical status are considered. For example, it is known that blacks generally maintain a low rennin state, and therefore tend to perform poorly on ACEI and ARB as AHA or a DIU may exacerbate gout or hyperglycemia. Also in choosing the baseline first line therapy,

issues such as side effects, quality of life, cost and efficacy of drugs in certain subgroups of HPT subjects are considered (Tu *et al.*, 2005).

The recommended management strategy is to try one medication and increase the dose until the goal BP is achieved. If goal BP is not achieved and the side effects are intolerable or the maximum dose is reached another agent can be added or substituted. An example of adding another agent is that of a DIU and an ACEI resulting in greatly enhanced hypotensive potency. However, if two AHA having similar modes of action are chosen, response will be inadequate because the client will be on two drugs that have the effect of one. Where two drugs are unable to control the BP adequately, a third agent can be added to the existing regimen (Tu *et al.*, 2005). It has been observed that when these agents are used alone, effectiveness is limited to about 30% (National Institute of Health, 2004). Monotherapy controls BP effectively for those clients who are in stage one of HPT. Most clients in stage 2 (and stage 3, if applicable) will need a combination of two or more antihypertensive drugs. Combinations of AHA can yield an efficacy rate of not less than 60% (Black *et al.*, 2003).

2.2.6 Implementation of Guidelines

Despite overwhelming evidence that HPT is a major cardiovascular risk factor and that BP lowering strategies substantially reduce the risk, studies performed in various continents (Kearney *et al.*, 2004), consistently show that a noticeable proportion of HPT individuals are unaware of their condition or, if aware, do not undergo management (Burt *et al.*, 1995; Fagard *et al.*, 2002), and goal BP levels are seldom achieved, regardless of whether management is prescribed and clients are followed by specialists or practitioners (Amar *et al.*, 2003; Mancia *et al.*, 2005).

This explains why high BP remains a leading cause of death and cardiovascular morbidity worldwide. It also emphasizes the strong need to extend to a larger fraction of the population the procedures that allow HPT to be detected, and effectively treated (Burt *et al.*, 1995).

2.2.7 Prescribing Patterns

According to the WHO the first choice of therapy on the basis of comparative trial data, availability and cost for the majority of clients without a compelling indication for another drug class should be a low dose of a DIU. In most places, DIU are the cheapest and therefore most cost-effective option (WHO Guidelines Sub-Committee, 2003). However, the ESC-ESH 2007 guidelines and 2009 reappraisal, as well as the 2003 WHO recommendations, suggest the use of any of the AHA approved (CCB, ARB, ACEI, BB and DIUs) for baseline management of arterial HPT (WHO Guidelines Sub-Committee, 2003; Mancia *et al.*, 2007; Mancia *et al.*, 2009).

The JNC 7 recommends that clients with SBP between 120-139 mmHg and DBP between 80-89 mmHg should be considered prehypertensive and requires health-promoting lifestyle modifications to prevent cardiovascular disease (CVD). Thiazide-type DIU should be the baseline drug therapy for most clients, either alone or in combination with other drug classes, but certain high-risk conditions are compelling indications for other drug classes (Chobanian *et al.*, 2003b).

European and international guidelines strongly recommend the use of combination therapy. The 2007 ESH-ESC guidelines recommend the combination of two drugs to be considered as baseline management whenever HPT clients have a high baseline BP or are classified as being at high or very high cardiovascular

risk. The WHO and JNC 7 share this recommendation as well, and specify the need of a second agent in stage 2 HPT or for clients whose BP is more than 20 mm Hg above the SBP goal or more than 10 mm Hg above the DBP goal and in clients with compelling indications (Chobanian *et al.*, 2003b; WHO Guidelines Sub-Committee, 2003; Mancia *et al.*, 2007). Even though all guidelines strongly recommend combination therapy, only the ESC-ESH guidelines offer detailed data on the evidence supporting the synergistic efficacy of drug combination.

Figure 2.1 shows the combinations recommended for dual therapy of HPT according to the ESC-ESH 2007 guidelines (Mancia *et al.*, 2007).

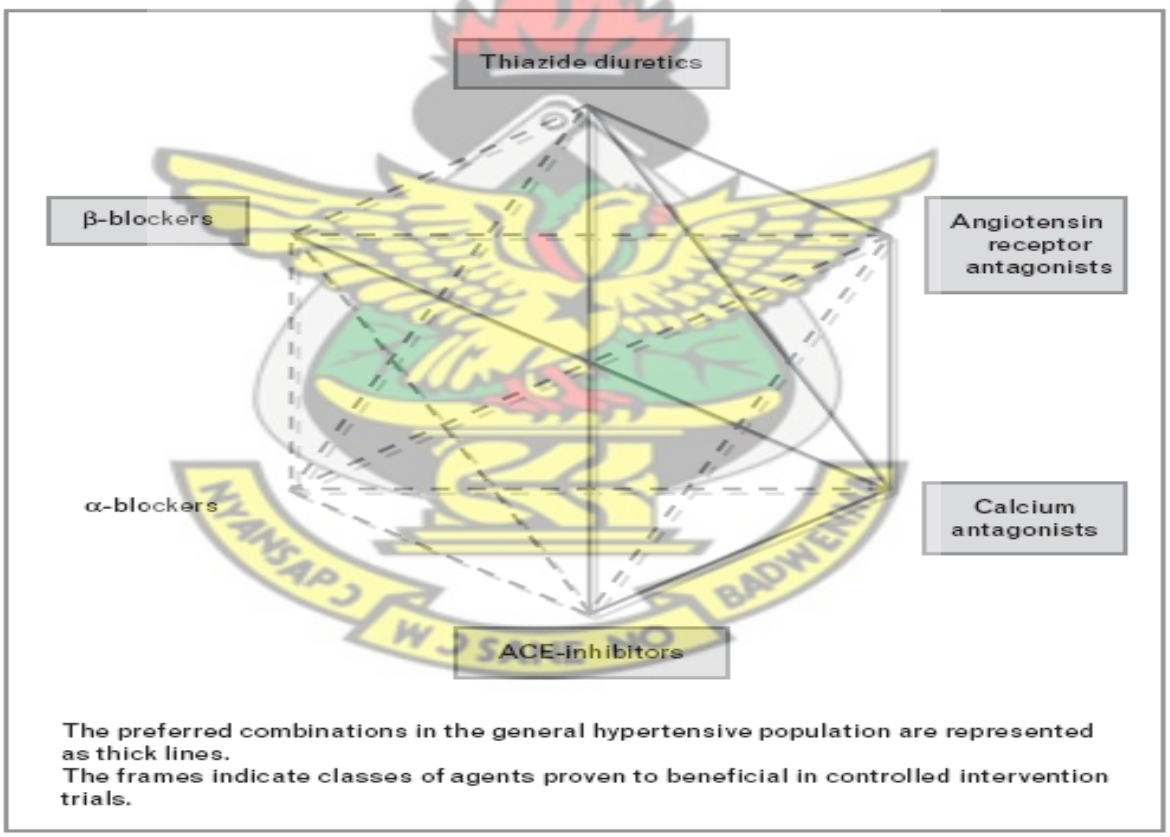

Figure 2.1 Evidence-based recommended combination of drug classes for management of HPT.

Several studies have been done in various countries that either follows international standard guidelines or goes against it, however, all these studies are influenced in one way or another by the international guidelines.

Yusuff and Balogun (2005), concluded in their study "Pattern of drug utilization among hypertensives in a Nigerian teaching hospital" that DIU and CAA were the most frequently prescribed AHA in a tertiary care setting in Nigeria. This is in agreement with international guidelines for the management of HPT.

Similarly, Etuk, Isezuo *et al* (2008), found that DIU were the most frequently prescribed drug either as a single agent or as combination therapy and that most of the clients in that study were on combination therapy.

Liu and Wang (2008), in their study however found that prescription patterns varied by age, gender and clinical facilities, with monotherapies being found to be dominant in the first year, which declines over time. CCB and BB were the most frequently prescribed AHA, either alone or in combinations. Although least expensive, the prescription rates of DIU were low, at 8.3% for monotherapies and 19.9% overall. The prescription rate for ARB was elevated considerably over time. ARB was found to be prescribed mainly by medical centers or regional hospitals.

In the study of drug prescribing patterns for HPT in Al Shifa hospital, India, it was found that most clients were being treated with two or more drugs. BB were the most frequently prescribed AHA, CCB and DIU were prescribed sparingly (Lis *et al.*, 2010).

In a recent study done in south India by Pai, Shenoy *et al* (2011), they concluded that CCB are the leading group of AHA prescribed followed by DIU.

Similarly, Cheng (2011b), showed that most out patients with HPT received monotherapy although national and international guidelines indicated that monotherapy achieves the BP target in only a limited number of HPT clients. We also found that the most frequently used class of HPT was CCB then ARB. Despite the various benefits of DIU, they remain underutilized (Cheng, 2011a).

Chapter 3

MATERIALS AND METHODS

3.1 STUDY SETTING

The University Health Services started as a dressing station in 1952 when the entire University population was barely 1000, and has grown into a full-fledged 100-bed hospital.

The hospital currently caters for a catchment area of over 200,000 inhabitants. This is made of: Students – 30,000, Staff and dependants about 30,000; and about 150,000 people from over 30 surrounding communities, such as Ayigya, Bomso, Ayeduase, Kotei, Boadi etc. It is the medical arm of the Kwame Nkrumah University of Science and Technology.

The KNUST Hospital was primarily set up to cater for the health needs of the staff, their dependents and student of the university. Services has however been extended to the general public. KNUST hospital is known to be an important health care service provider to about 30 communities surrounding the hospital, which is increasing rapidly in population. In other words, the hospital is in the status of a District Hospital. Services provided by the hospital include; general medical care as well as specialist services such as obstetrics and gynaecology, surgery, dental and a clinic for clients with a HPT and DM.

3.1.1 Profile of the HPT/DM Clinic

In line with the determination of the hospital to provide effective and accessible health care services to its clients, the KNUST Hospital established the HPT/DM Clinic which commenced its activities on the 30th of May 2008. The main aim of the clinic is for the efficient management of HPT and DM cases in order to improve their quality of life and reduce and prevent complications in these clients. The

clinics are held on Mondays, Wednesdays and Fridays and have an average clientele of about 480 in a month.

Health education programmes that focus on the two conditions are given for 10-15 minutes at the start of each clinic session. Emphasis is placed on their health, diet, exercise and lifestyle modification strategies. Blood glucose levels (fasting and random) are measured with a glucometer for all attendants on their first visit. Repeat blood glucose levels checks are done on each review visit for diabetics and that of the HPT clients are repeated half-yearly. Heights and weights of clients are measured on the first visit and weight on every visit. Body Mass Index, (BMI) are calculated for all attendants on each visit. BP are also checked on the first visit and repeated on every review visit.

Hypertensive and diabetic emergencies are admitted to the ward for further management. New cases come directly to the HPT/DM Clinic with referrals from other units in the hospital and the wards on discharge. The choice of medications is tailored to the client's needs. Classes of drugs commonly in use at the Clinic are; DIU (Thiazides and thiazide-like agents) e.g. bendrofluazide; ACEI e.g. Lisinopril; CCB e.g. amlodipine; ARB e.g. losartan; BB e.g. Atenolol; and CAA e.g. methyldopa.

Other laboratory and ancillary investigations, (i.e. renal function tests, lipid profile, chest x-rays and eye examinations), are done as a means of monitoring the effect of disease and therapeutic outcomes. Clients who develop complications are referred to the Eye Clinic in the hospital and to the Physiotherapy Centre at Komfo Anokye Teaching Hospital, (KATH), for further management. Clients are given appointments for review based on their level of BP control and compliance to the

medications. Thus clients' reviews could be a couple of weeks or several months. However, a minimum of four reviews in a year is the target of the Clinic.

Clients are encouraged to visit the Clinic outside their review dates if they have problems with medications, questions about their conditions or notice unusual symptoms.

The clinic is managed by 2 doctors – a physician specialist and a senior medical officer, a senior nursing officer with a degree in nursing, a nursing officer with a diploma, a public health nurse with a State Registered Nurse Certificate, a laboratory technologist with a degree in medical laboratory and a nurse assistant trained on the job. All staff of the clinic underwent specialized training before the start of the clinic, and also in-service workshops are organized at least twice a year. As at the end of 2011, the clinic had over 2000 clients.

3.2 STUDY DESIGN

3.2.1 Study type

This study was a cross-sectional study undertaken at the HPT/DM Clinic of the KNUST Hospital, Kumasi. A retrospective search was carried out on the clients' notes to assess the pharmacological management of HPT clients.

3.2.2 Sampling and Questionnaire Administration

3.2.2.1Sampling

A convenience sampling method was used for data collection. Semi structured questionnaires were administered randomly on Clinic days to clients who consented to take part in the project. 400 clients were intended to be randomly

sampled for the study, however for some unforeseen limitations, 100 clients were sampled randomly for the study. A pilot study using 10 clients was done at the HPT/DM Clinic of the KATH.

Inclusion Criteria: hypertensive clients ≥ 18years but ≤ 75 years; who have been visiting the clinic actively in the last 24 months; currently or had previously been treated with at least one antihypertensive medication.

Exclusion Criteria: clients with pre-hypertension which do not require drug therapy; HPT clients with DM and hypertensives with other severe co-morbidities such as heart failure or renal disease; clients attending the clinic on the day of data collection who are very sick and may need hospital admission; defaultants, and clients who refused to take part in the study.

3.2.2.2 Questionaire Administration

Informed consent was obtained from all clients. The objectives of the survey and survey procedures were explained to them. In addition, prospective client were made aware that participation is entirely voluntary and that they have the right to refuse to participate or to withdraw from the survey at anytime and that their decision will not in any way affect the care that they receive in the hospital.

Data was collected through the administration of semi structured questionnaires from 1st July to 31st October, 2011. Case notes of the clients were also reviewed to obtain additional information and also to confirm and validate the clients' responses.

The BP of the clients was monitored using a calibrated Accoson dekamet 0125 mercury sphygmomanometer BP monitoring apparatus and a Littman's stethoscope. Clients were made aware of their BP readings.

3.2.3 Study Variables

Data obtained included classes of antihypertensive agents, time management was initiated, duration, BP (measured in millimeters of mercury, mmHg), age, weight (kilograms, kg) and height (meters, m). The weight and height were used to calculate the body mass index (BMI, kg/m^2) of subjects.

3.3 STATISTICAL ANALYSIS

Continuous data were expressed as mean ± SD with descriptive statistics and categorical data expressed as proportions. Unpaired *t*-test was used to compare means and the Chi-square test statistic was used to compare proportions. In all comparisons, a p-value <0.05 was considered to be statistically significant. All statistical analyses were performed using GraphPad prism® version 5.01 for windows.

3.4 ETHICAL CONSIDERATION

Research participants were protected to the maximum degree possible as semi-structured questionnaire were administered and each respondent was interviewed separately in a room. Privacy was also maintained by the use of code numbers.

Consent and permission were sought from the hospital administration of KNUST Hospital.

Informed consent was also taken from the research participants.

3.4 LIMITATIONS OF THE STUDY

The confines of this study were mainly due to;

- The sample size was small due to financial and time constraints. In order to be able to generalize the research findings, respondents were chosen conveniently on different days
- Most of the initial BP measurements were not done at the clinic, however all BP measurements taken at the time of data collection were done by the researcher.
- Difficulty in obtaining ethical clearance from the hospital delayed the time scheduled for data collection.

Chapter 4

RESULTS

The general characteristics of the study population as stratified by gender are shown in Table 4.1 below. The mean age of the study population was 53.3 ± 11.0 years. There was no statistical differences between the mean ages for males (54.0 ± 10.1 years) and females (53.1 ± 11.7 years) p = 0.694. However, 30.0% of the study population was within the age brackets of 50 – 59 years, followed by the age groups of 40 – 49, 60 – 69, 30 – 39, 70 – 75 and ≥18 - 30 years. No significant difference was observed in weight between males (73.5 ± 10.5 kg) and females (71.0 ± 13.4 kg) (p = 0.325). A comparison of BMI between the sexes showed females having a significantly higher BMI (27.6 ± 5.0 kg/m^2) than males (25.8 ± 3.7 kg/m^2) (p = 0.043). A further classification of BMI showed 37.5% of the females being obese compared to 11.4% of the males and the difference in proportion was statistically significant (p = 0.003). Seventy-three percent (73.0%) of the study population were married, 11.0% were single, 9.0% divorced and 7.0% widowed. On religious background, 81.0% were Christians and 19.0% were Moslems (p = 0.017). On educational status, 40.0% of the study population have had tertiary education with the number of males (56.8%) being more than the females (26.8%) (p = 0.002). They were followed closely by those with secondary education (37.0%), no formal education (19.0%) and primary education (4.0%). Out of the 19.0% who had no formal education, 28.6% were females and 6.8% were males (p = 0.006). All clients were accredited members of the NHIS.

Table 4.1 General characteristics of the studied population stratified by gender

Variables	Male (N = 44)	Female (N = 56)	All Clients	*p values*
Age (years)	54.0 ± 10.1	53.1 ± 11.7	53.5 ± 11.0	0.694
Age Groups				
≥18 – 29	1(2.3)	0(0.0)	1(1.0)	0.257
30 – 39	2(4.5)	8(14.3)	10(10.0)	0.107
40 – 49	11(25.0)	17(30.4)	28(28.0)	0.554
50 – 59	17(38.6)	13(23.2)	30(30.0)	0.095
60 – 69	11(25.0)	14(25.0)	25(25.0)	1.000
70 – 75	2(4.5)	4(7.1)	6(6.0)	0.587
Weight (kg)	73.5 ± 10.5	71.0 ± 13.4	72.1 ± 12.2	0.325
Height (m)	1.7 ± 0.1	1.6 ± 0.1	1.6 ± 0.1	< 0.0001
BMI (kg m^{-2})	25.8 ± 3.7	27.6 ± 5.0	26.8 ± 26.8	0.043
BMI Class				
Underweight	0(0.0)	1(1.8)	1(1.0)	0.373
Normal	22(50.0)	19(33.9)	41(41.0)	0.105
Overweight	17(38.6)	15(26.8)	32(32.0)	0.207
Obese	5(11.4)	21(37.5)	26(26.0)	0.003
Marital Status				
Single	6(13.6)	5(8.9)	11(11.0)	0.455
Married	33(75.0)	40(71.4)	73(73.0)	0.690
Divorced	4(9.1)	5(8.9)	9(9.0)	0.978
Widowed	1(2.3)	6(10.7)	7(7.0)	0.101
Religion				
Christian	31(70.5)	50(89.3)	81(81.0)	0.017
Islam	13(29.5)	6(10.7)	19(19.0)	
Educational Status				
No formal education	3(6.8)	16(28.6)	19(19.0)	0.006
Primary	2(4.5)	2(3.6)	4(4.0)	0.805
Secondary	14(31.8)	23(41.1)	37(37.0)	0.341
Tertiary	25(56.8)	15(26.8)	40(40.0)	0.002

Data are presented as means ± SD and proportions. P values define the level of significance when males were compared to females; unpaired t-test (for continuous variables) and Chi-square test (for ordinal variables)

Out of a total of 100 study participants, 1 (1.0%) had no record of baseline antihypertensive therapy leaving a total of 99 for further analysis. Out of the remaining 99, 57 (57.6%) were on a baseline antihypertensive monotherapy, 36 (36.4%) were on a baseline antihypertensive dual therapy and 6 (6.1%) were on a baseline antihypertensive three-drug combination. Of the clients on monotherapy, 77.2% (44/57) were on CCB, 10.5% (6/57) were on DIU, 7.0% (4/57) were on BB, with ACEI, ARB and CAA contributing 1.8% (1/57) respectively (Figure 4.1).

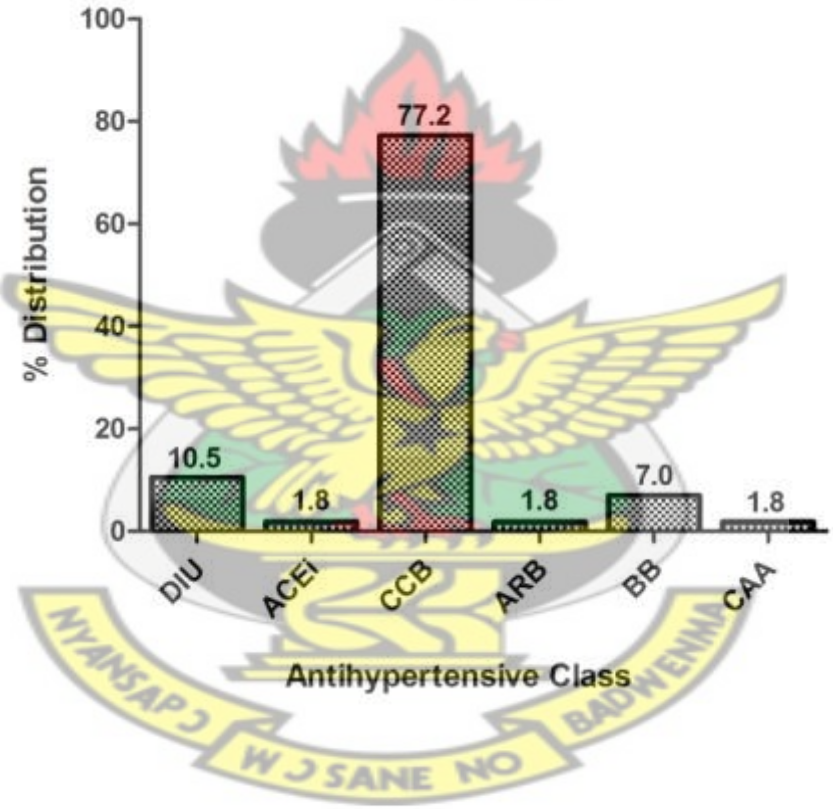

Figure 4.1 **Baseline pattern of prescription of antihypertensives as mono-therapeutic agents**

For study participants on dual therapy, 25.0% (9/36) were on a combination of CCB + BB, 22.2% (8/36) each on ACEI + CCB and CCB + CAA respectively, 16.7% (6/36) on DIU + CCB, 8.3% (3/36) on CCB + ARB and 2.8% (1/36) each were on CAA + BB and DIU + BB respectively (Figure 4.2A). For study participants on three-drug

combination therapy of antihypertensives, 2 each were on a combination therapy of DIU + ACEI + CCB and DIU + CCB + CAA respectively and 1 each on a combination therapy of ACEI + CCB + CAA and ACEI + CCB + BB respectively (figure 4.2B).

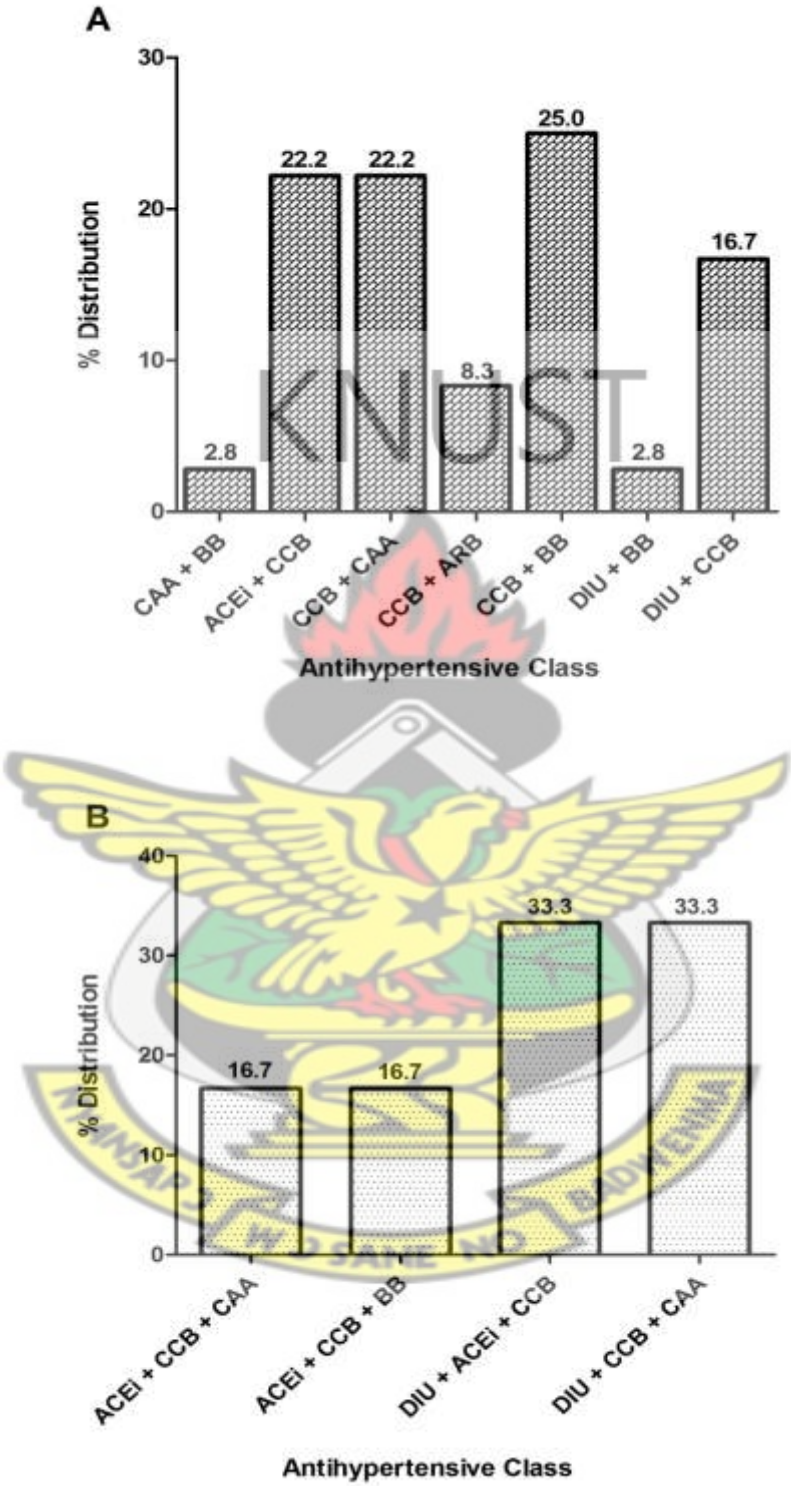

Figure 4.2 Baseline patterns of prescription of antihypertensives as 2-drug (A) and three-drug combinations(B)

A comparison of administered baseline antihypertensives prescribed as monotherapies in male and female study participants is shown in Figure 4.3. CCB were more likely to be prescribed as a monotherapy in females (31/35; 88.6%) compared to males (13/22; 59.1) (p = 0.009). However, males (5/22; 22.7%) were more likely to receive DIUs as monotherapy compared to females (1/35; 2.9%) (p = 0.017). A comparison of the other classes of antihypertensives being administered as mono-therapeutic agents among males and females showed no statistical significance (p > 0.05). (figure 4.3)

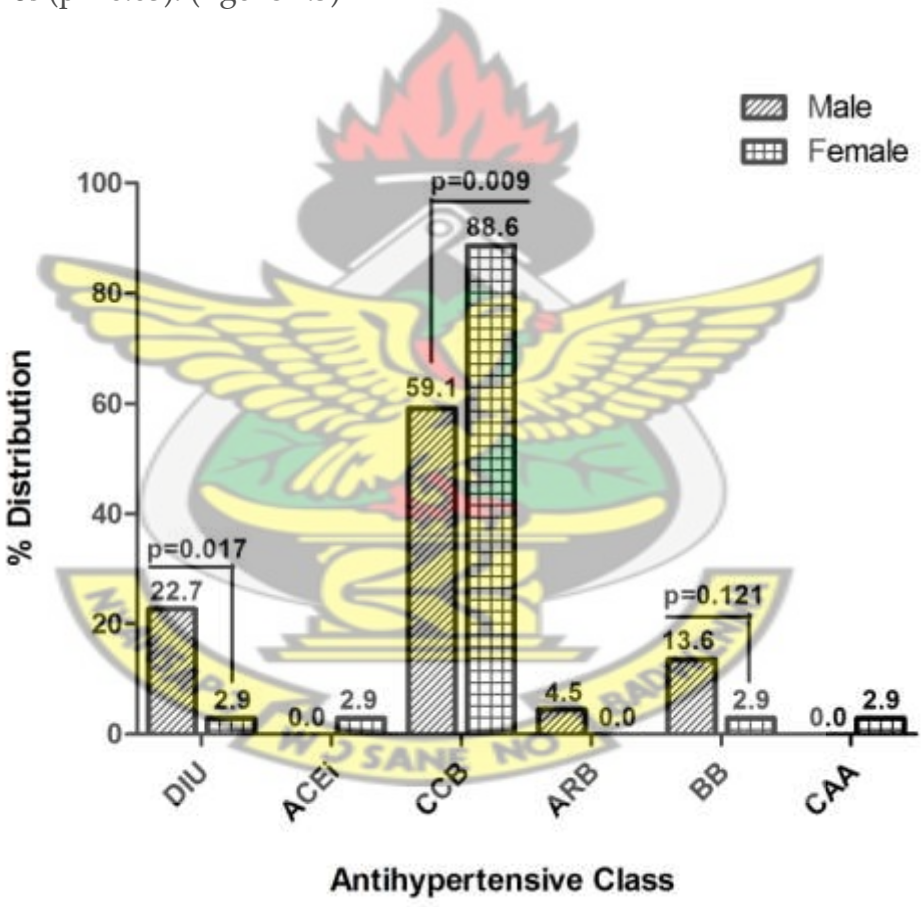

Figure 4.3 Baseline antihypertensives prescribed as monotherapy in the study population stratified by gender

For antihypertensives administered as dual therapy among the study participants, with the exception of dual therapy of ACEI + CCB which were more likely to be prescribed in males (7/18; 38.9%) compared to females (1/18; 5.6%) (p = 0.016), all the other dual antihypertensive class combinations among males and females showed no statistical significance difference (p > 0.05) (Figure 4.4).

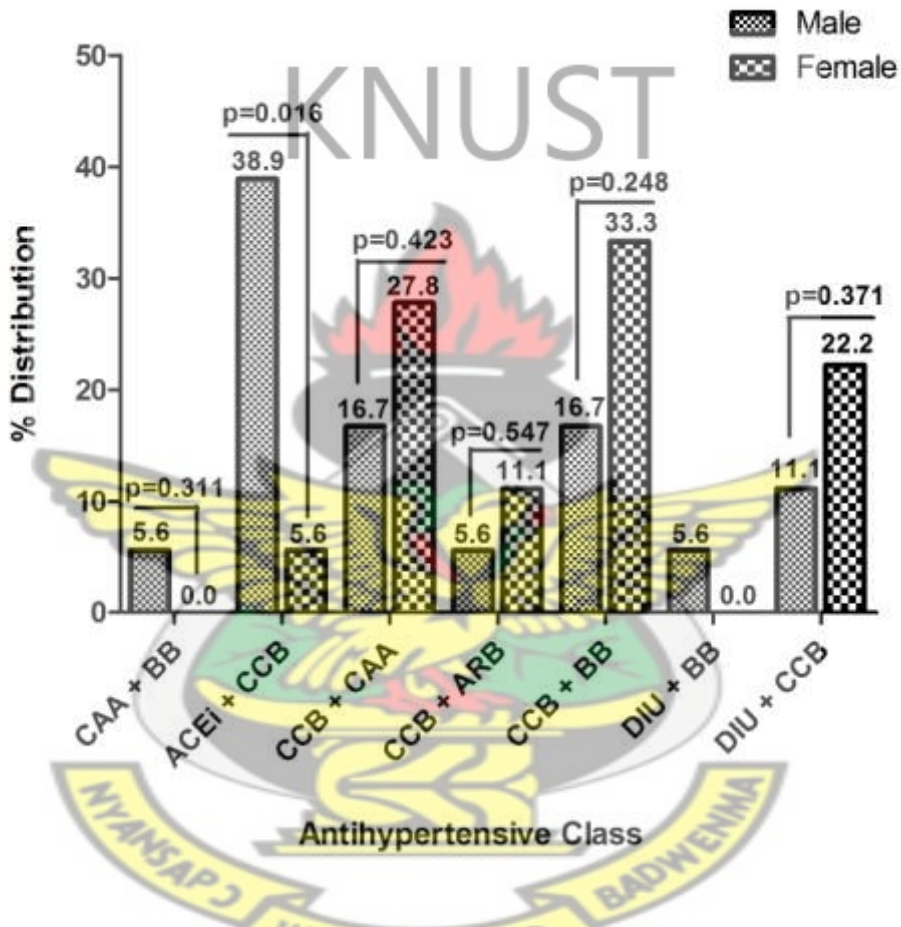

Figure 4.4 Baseline antihypertensives prescribed as 2-drug combinations in the study population stratified by gender

Among the CCB, Nifedipine was the most prescribed both in the baseline 60 (71.4%) and after study AHA 51 (57.3%). Prescription of Amlodipine increased from 23 (27.4%) in the baseline prescription to 51 (57.3%) in the after study prescription. Felodipine was prescribed once in the baseline and after study

prescriptions, 1 (1.2%) and 1 (1.1%) respectively. Atenolol was the most prescribed among the BB with 13 (81.3%) baseline prescriptions. In the after study prescription there was an increase to 35 (97.2%). baseline Propranolol prescription was 3 (18.8%) but was not used in the after study prescriptions. Bisoprolol was not prescribed in the baseline prescriptions but was prescribed once (2.8%) in the after study prescriptions of the AHA. Prescription of ACEI increased considerably from a baseline prescription of 13 to 46 in the after study prescriptions. Among the ACEI, Lisinopril was the most prescribed with a baseline prescription of 13 (100%) to 31 (67. 4%) in the after study prescription of AHA. Though Ramipril was not in the baseline prescriptions, in the after study prescriptions it accounted for 15 (32.6%). ARB prescriptions also increased from a baseline prescription of 4 to 32 in the after study prescriptions. Losartan was the only ARB that was prescribed in the baseline AHA prescriptions. Of the 32 ARB in the after study, Losartan accounted for 27 (84.4%) and Candesartan 5 (15.6%). Methyldopa is the only CAA in use at the hospital. Its prescription increased from 13 in the baseline prescription to 18 in the after study prescriptions. DIU prescription increased from 17 in the baseline prescription to 37 in the after study prescriptions. Furosemide accounted for 1(5.9%) and Bendrofluazide 16(94.1%) in the baseline AHA prescriptions. In the after study DIU prescriptions, Furosemide accounted for 3(8.1%), Bendrofluazide 31(83.8%) and Hydrochlorothiazide 3 (8.1%). VAS was not prescribed as a baseline AHA; however in the after study prescriptions, hydralazine was the only VAS in use, accounting for 5(100%) prescriptions. This is illustrated in table 4.2 below.

Table 4.2 Class and specific antihypertensive agents

Class of Antihypertensive Agents (AHA)	Specific AHA (baseline) n(%)	Specific AHA (after study) n(%)
Calcium channel blockers (CCB)		
Amlodipine	23 (27.4%)	37 (41.6%)
Nifedipine	60 (71.4%)	51 (57.3%)
Felodipine	1 (1.2%)	1 (1.1%)
Beta blockers (BB)		
Atenolol	13 (81.3%)	35 (97.2%)
Propranolol	3 (18.8%)	0 (0%)
Bisoprolol	0 (0%)	1 (2.8%)
Angiotensin converting enzyme inhibitors (ACEI)		
Lisinopril	13 (100%)	31 (67.4%)
Ramipril	0 (0%)	15 (32.6%)
Angiotensin II receptor blockers (ARB)		
Losartan	4 (100%)	27 (84.4%)
Candesartan	0 (0%)	5 (15. 6%)
Centrally-Acting Agents (CAA)		
Methyldopa	13 (100%)	18 (100%)
Diuretics (DIU)		
Furosemide	1 (5.9%)	3 (8.1%)
Hydrochlorothiazide	0 (0%)	3 (8.1%)
Bendrofluazide	16 (94.1%)	31 (83.8%)
Vasodilators (VAS)		

Hydrallazine	0 (0%)	5 (100%)

The mean duration for being on antihypertensive therapy among the study participants was 4.0 ± 3.2 years with a minimum of 0.5 years, a median of 3 years and maximum antihypertensive therapy duration of 20 years. The baseline mean systolic blood pressure (SBP) among the study participants was 175.5 ± 24.3 mm Hg with a minimum of 140 mm Hg, a median of 170 mm Hg and maximum SBP of 270 mm Hg. The baseline mean diastolic blood pressure (DBP) was 105.0 ± 19.4 mm Hg with a minimum DBP of 80 mm Hg, a median of 100 mm Hg and maximum DBP of 200 mm Hg. A look at the after study mean SBP among the study participants over the duration for which they have been on antihypertensives showed a mean SBP of 135.7 ± 18.7 mm Hg with a minimum of 90 mm Hg, a maximum of 130 mm Hg and maximum SBP of 210 mm Hg. The after study mean DBP among the study participants was 84.0 ± 10.1 mm Hg with a minimum DBP of 60 mm Hg, a median DBP of 80 mm Hg and maximum DBP of 120 mm Hg. An estimation of mean percentage changes in SBP of the after study and baseline measurements showed an overall mean percentage change of -22.9 ± 12.5 %. The overall mean percentage change in after study DBP from the baseline value was -18.7 ± 14.6 %. There was no statistical significant difference in the SBP and DBP changes between males and females (p=0.533; p=0.475). This illustrated in table 4.3. Out of the 100 clients who participated in this study, 62 (62%) had their BP under control (< 140/90 mmHg) based on the GSTG of MOH criteria and 42 (42%) based on WHO/ISH statement on HPT and ESH/ESC guidelines criteria (< 130/85 mmHg).

Table 4.3 Duration of antihypertensive use and reduction in BP

Variables	Male	Female	All Clients	p values
Mean time on antihypertensive (years)	4.1 ± 3.2	3.9 ± 3.2	4.0 ± 3.2	0.728
Minimum	0.5	0.5	0.5	
Median	4	3	3	
Maximum	18	20	20	
Baseline mean SBP (mm Hg)	171.9 ± 18.8	178.7 ± 27.9	175.5 ± 24.2	0.285
Minimum	140	150	140	
Median	170	170	170	
Maximum	210	270	270	
Baseline mean DBP (mm Hg)	104.1 ± 17.8	105.8 ± 20.9	105.0 ± 19.4	0.738
Minimum	90	80	80	
Median	100	100	100	
Maximum	180	200	200	
After study mean SBP (mm Hg)	132.0 ± 20.6	138.6 ± 16.6	135.7 ± 18.7	0.082
Minimum	100	90	90	
Median	130	140	130	
Maximum	210	180	210	
After study mean DBP (mm Hg)	82.7 ± 10.2	85.0 ± 9.9	84.0 ± 10.1	0.264
Minimum	60	60	60	
Median	80	80	80	
Maximum	120	120	120	
Mean percentage change in SBP	-24.0 ± 11.5	-21.9 ± 13.5	-22.9 ± 12.5	0.533
Minimum	-44.4	-52.6	-52.6	
Median	-25.0	-22.2	-24.3	
Maximum	5.0	13.3	13.3	
Mean percentage change in DBP	-20.2 ± 12.2	-17.4 ± 16.4	-18.7 ± 14.6	0.475
Minimum	-55.6	-60.0	-60.0	
Median	-20.0	-20.0	-20.0	
Maximum	0.0	20.0	20.0	

Data are presented as means ± SD with descriptive statistics. P value defines the level of significance when males were compared with females. Percentage change was defined as the difference between after study blood pressure and baseline blood pressure expressed over the baseline blood pressure and multiplied by 100%.

An assessment of after study antihypertensive therapy based on possible modifications of baseline therapy and comprising an add on of any class of antihypertensive; a complete change of the baseline therapy; maintaining the same class or classes of baseline therapy or a change in one/more components of the therapy among males and females are shown in Figures 4.6, 4.7 and 4.8.

From Figure 4.6A, 1 (100%) male study participant on ARB at baseline had CCB added on in the after study therapy. For males on BB, 66.7% (2/3) had DIUs added on to their baseline regimen whilst 33.3% (1/3) had a complete change of medication from BB to ACEI + CCB. For males on CCB, 23.1% (3/13) had ACEI added on to the baseline therapy whilst 7.7% (1/13) had ARB; DIU; DIU + ACEI; DIU + BB; ARB + BB + CAA or ACEI + CCB + ARB + BB respectively being added on to the baseline CCB. Another 7.7% (1/13) of the males had a complete change of CCB being made for ACEI + BB or ARB respectively. For the remaining 15.4% (2/13) males the baseline CCB was maintained. For males on DIU, 60.0% (3/5) had their baseline antihypertensive therapy added on with ACEI + CCB with 20.0% (1/5) having CCB + CAA + VAS or ACEI + CCB +ARB + BB added on to the baseline DIU (Figure 4.6A).

From Figure 4.6B, 1 (100.0%) female on a monotherapy of CAA had a complete change to CCB. A female (1; 100.0%) on a baseline ACEI had CCB + BB added on to the baseline therapy and likewise another female (1; 100.0%) on a baseline BB therapy had DIU added on to the baseline therapy. For 31 females on a baseline CCB therapy, 12.9% (4/31) had ACEI added onto the baseline drug with 3.2% (1/31) having either ACEI + ARB; ACEI + ARB + BB; ACEI + ARB + BB + CAA; ACEI + BB + CAA; CAA; DIU + ACEI + BB; DIU + CAA + VAS; DIU + BB being added on the baseline CCB drug respectively. Two (6.5%) had DIU + ACEI; DIU + ARB and DIU

being added on to the baseline CCB drug respectively whilst 9.7% (3/31) had ARB; ARB + BB and BB being added to their baseline CCB drug respectively. One representing 3.2% had a complete change from the CCB baseline therapy to either ACEI + BB; ACEI + BB + CAA or DIU + ACEI + ARB + CAA respectively. Only 1 (3.2%) of the female study participant had the baseline CCB being maintained. One female of baseline DIU had a complete change to CCB + BB therapy.

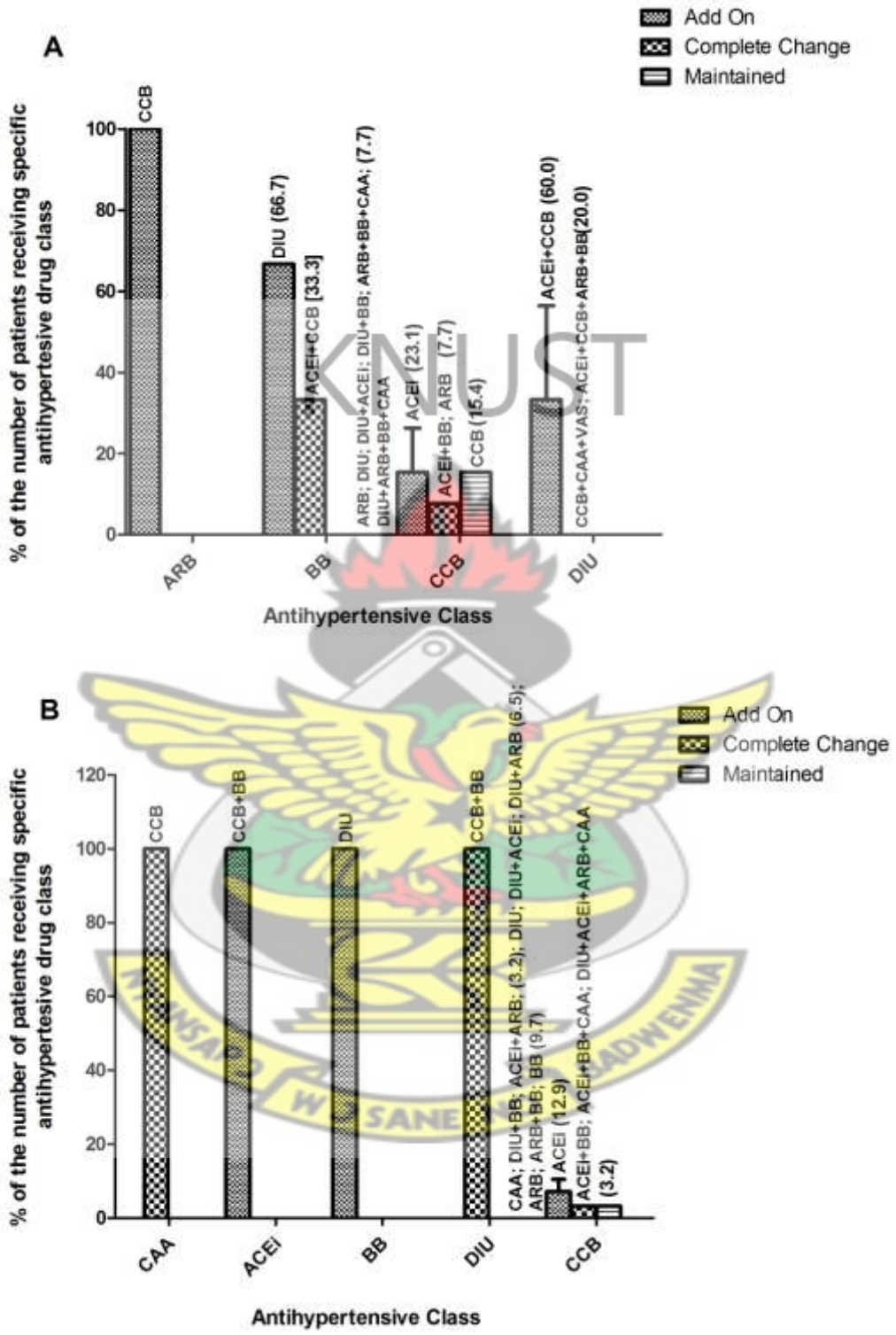

Figure 4.5 Patterns of after study prescription modifications in male (Figure 4.5A) and female (Figure 4.5B) clients on antihypertensive monotherapy

From Figure 4.6A, 1 (100.0%) male who was on a baseline dual therapy of CAA + BB had CCB added on to the therapy. Out of a total of 7 males who were on a baseline dual therapy of ACEI + CCB, 14.3% (1/7) had ARB + BB or BB respectively being added on to the baseline management. Another 14.3% had a complete change of baseline management from ACEI + CCB to DIU + ARB + BB with 57.1% (4/7) maintaining their baseline dual therapy management. For 3 males on baseline dual therapy of CCB + CAA, 14.3% (1/3) had ACEI or ARB respectively being added on to the baseline therapy and the other 14.3% having a change in component from CAA to ARB. One male on a baseline dual therapy of CCB + ARB was maintained. Of three males with a baseline dual therapy of CCB + BB, 66.7% (2/3) had ACEI being added onto the baseline therapy with 1 (33.3%) maintaining the same baseline therapy. One male on dual therapy of DIU + BB had CCB + ARB being added onto the baseline therapy. Two males on a baseline dual therapy of DIU + CCB had a change in DIU for ACEI.

For females on dual antihypertensive therapy, 6 were on baseline therapy comprising CCB + BB of which 16.7% (1/6) were maintained with a change in BB for CAA + DIU + ACEI and DIU in 16.7% (1/6). Another 50.0% (3/6) had their baseline BB changed for ARB + DIU. For the one female study participant who was on a dual therapy of ACEI + CCB, a combination of DIU + BB was added on. Two (2) females on a dual therapy of CCB + ARB had their baseline medication maintained. For the 5 females who were on a dual combination therapy of CCB + CAA, 60.0% (3/5) were maintained on the same dual baseline therapy with 20.0% (1/5) each having the CAA component replaced with ARB or DIU + VAS respectively. Four female study participants were on a baseline DIU + CCB therapy with 25.0% (1/4) having ACEI or ARB + CAA + VAS respectively being added on to

the baseline drug whilst the other 25% had the DIU component being replaced with ACEI or ARB + CAA + VAS (Figure 4.6B).

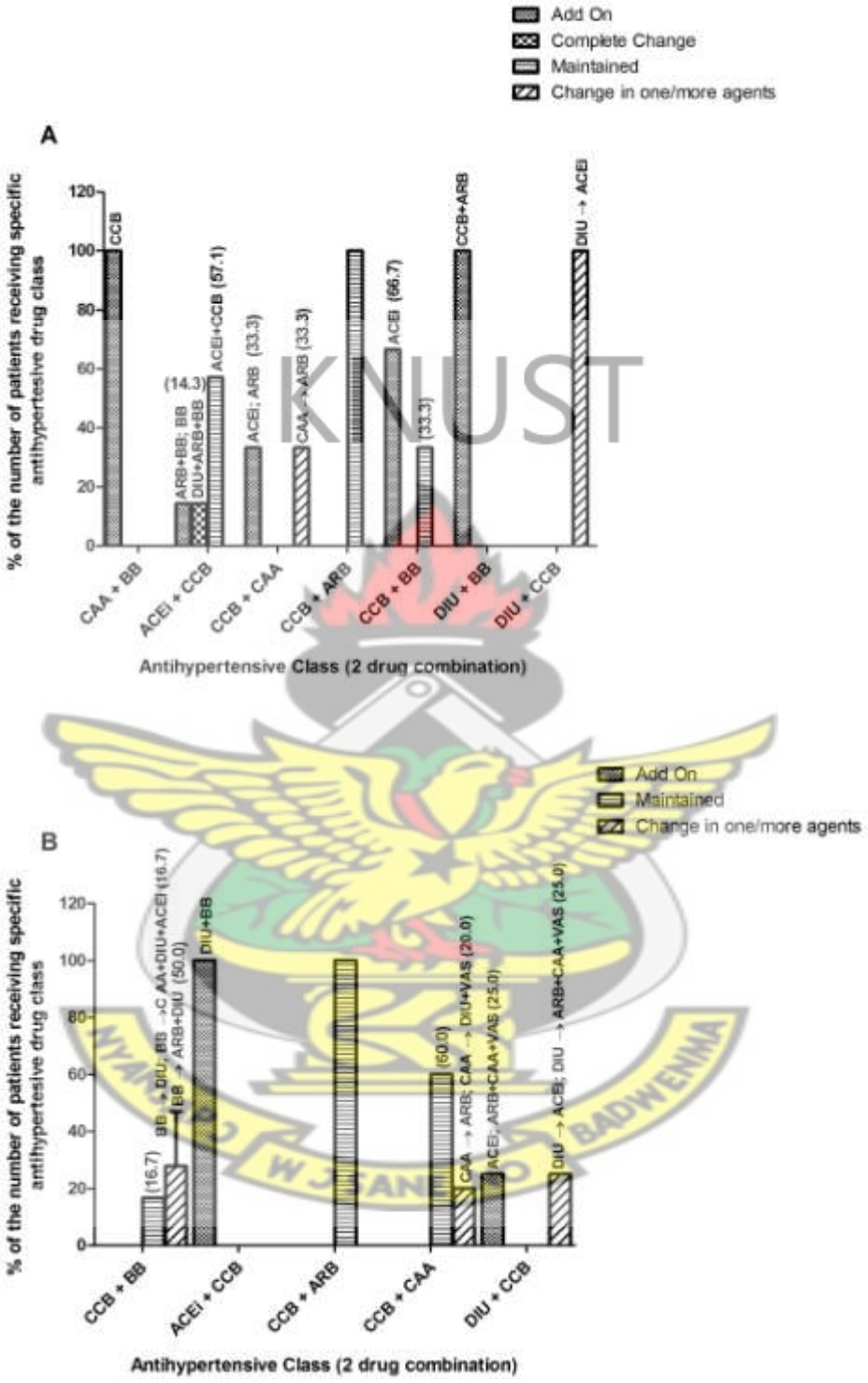

Figure 4.6 Patterns of after study prescription modifications in male (Figure 4.6A) and female (Figure 4.6B) clients on antihypertensive 2-drug combination

For one (1) male study participant who was on a three-drug baseline combination therapy of ACEI + CCB + BB, the same drug combination was maintained. Another male study participant who was on a three-drug therapy of DIU + ACEI + CCB was also maintained on the same drug therapy. For the remaining two (2) male clients on three-drug combination therapy of DIU + CCB + CAA, DIU + CAA was changed for ARB in one client and CAA for ARB in the other (Figure 4.7A).

In female study participants on three-drug baseline therapy one (1) was on a combination of ACEI + CCB + CAA for which DIU + ARB + BB was added on. The other was on a baseline therapy of DIU + ACEI + CCB and this was maintained throughout the management process (Figure 4.7B).

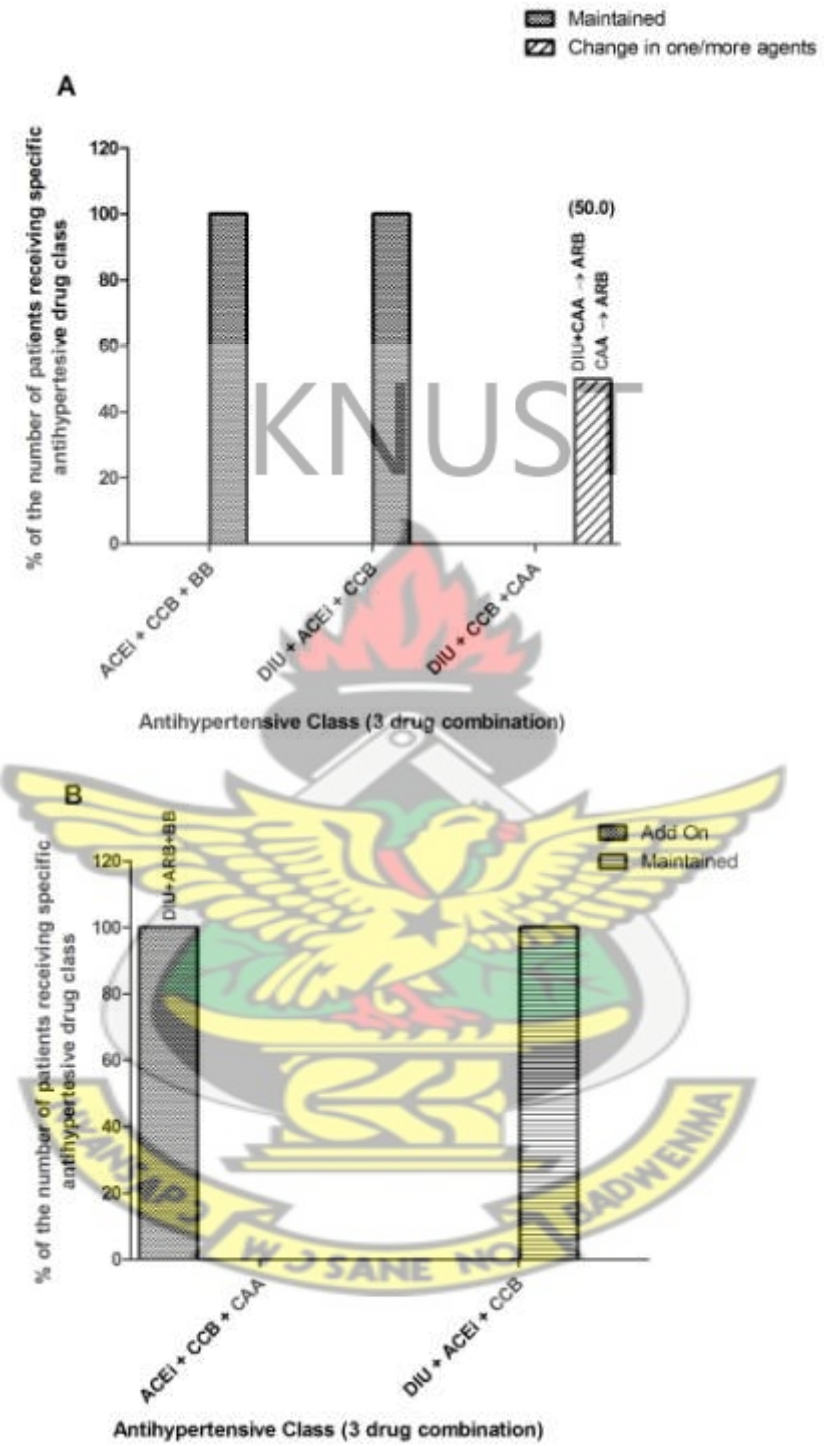

Figure 4.7 Patterns of after study prescription modifications in male (Figure 4.7A) and female (Figure 4.7B) clients on antihypertensive 3-drug combination

Clients' visit to the clinic averaged 3.1, with a minimum of 2.0 and a maximum of 5.0 times in a year. Clients who had changes in their medication over this duration were 83 (83%). There was an average of 2.4 times change in medications, a minimum of 1 and a maximum of 6 times. Clients gave the following reasons for the changes in their medications; side effects experienced 38(45.8%), not reaching a goal BP 33(39.8%), unavailability of medications 2(2.4%) and personal request 10(12.1%). Clients were registered with the National Health Insurance Scheme (NHIS) and used that to collect their medications either at the hospital pharmacy or nearby pharmacies which are NHIS accredited.

Clients were also put on other medications other than their AHA. Those who were on these other medications were 64 and 36 had no other medications. The other drugs that were prescribed for these clients includes; Non-steroidal anti-inflammatory drugs like Aspirin 44 (46.8%), Celecoxib 1(1.1%); lipid lowering drugs like Atorvastatin 14(14.9%) , Simvastatin 5(5.3%), Fluvastatin 3(3.2%), and Rosuvastatin 1(1.1%); Anti-uricaemic medication, Allopurinol 12(12.8%); Antidepressants like Amitriptyline 5(5.3%) and Imipramine 1(1.1%); Multivitamin preparation, Vitron 2(2.1%); Herbal product, Mannix 3(3.2%); Benzodiazepines like Lorazepam 1(1.1%) and Diazepam 1(1.1%); Antihistamine, Cinnarizine 1(1.1%). This shown in table 4.4;

Table 4.4 Other medications commonly prescribed.

Other drugs	Number (%)
Aspirin	44 (46.8)
Vitron	2 (2.1)
Atorvastatin	14 (14.9)
Simvastatin	5 (5.3)
Imipramine	1 (1.1)
Lorazepam	1 (1.1)
Allopurinol	12 (12.8)
Fluvastatin	3 (3.2)
Celecoxib	1 (1.1)
Rosuvastatin	1 (1.1)
Amitriptyline	5 (5.3)
Mannix	3 (3.2)
Cinnarizine	1 (1.1)
Diazepam	1 (1.1)
Total	94 (100)

Common side effects experienced by clients are shown Table 4.5 in were headache 73(27.3%), body weakness 63(23.6%), cough 49(18.4%), decreased sense of taste 17(6.4%), dizziness 16(6.0%). Other side effects were fatigue 15(5.6%), decreased sex drive 12(4.5%), loss of appetite 6(2.3%), flushing 5(1.9%). The less common side effects were erectile dysfunction 4(1.5%), sleeplessness 3(1.1%), constipation 2(0.8%), drowsiness 1(0.4%) and diarrhoea 1(0.4%). Clients complained of the number of pills that they took at a time as they were taking two or more pills. They also complained about the time they spend at the clinic and then spend almost as equal amount of time looking for their medications outside the hospital from other NHIS accredited pharmacies.

Table 4.5 Side Effects

Side effects	Number (%)
Headache	73 (27.3)
Drowsiness	1 (0.4)
Fatigue	15 (5.6)
Cough	49 (18.4)
Decreased sex drive	12 (4.5)
Diarrhoea	1 (0.4)
Constipation	2 (0.8)
Flushing	5 (1.8)
Dizziness	16 (6.0)
Body weakness	63 (23.6)
Decreased sense of taste	17 (6.4)
Loss of appetite	6 (2.3)
Sleeplessness	3 (1.1)
Erectile dysfunction	4 (1.5)
Total	267 (100)

Chapter 5

DISCUSSION

5.1 DEMOGRAPHIC CHARACTERISTICS OF RESPONDENTS

The mean age of the study population was 53.3 ± 11.0 years with no statistical difference between the mean ages for males (54.0 ± 10.1 years) and females (53.1 ± 11.7 years) (p = 0.694). A further stratification by age group showed 30% of the study population to be in age brackets of 50-59 years, followed by 28% in 40-49 years, and 25% in 60-69 years. There was no statistically significant difference in the weight between males (73.5 ± 10.5 kg) and females (71.0 ± 13.4 kg) (p = 0.325). However, a comparison of BMI between the sexes showed females having a significantly higher BMI (27.6 ± 5.0 kg/m^2) than males (25.8 ± 3.7 kg/m^2) (p = 0.043). A further classification of BMI showed 37.5% of the females being obese compared to 11.4% of the males and the difference in proportion was statistically significant (p = 0.003). Together 48.9% of the study participants as the time of data collection were obese. Obesity, and especially abdominal obesity, is a major risk factor for HPT. It was estimated in the Framingham study that each 10% weight gain is associated with a 6.5 mm Hg increase in SBP (Ashley and Kannel, 1974). A direct association between HPT and BMI has also been observed in cross-sectional and longitudinal population studies from early childhood to old age. A BMI of <25 is considered normal or healthy, whereas a BMI of 26 to 28 increases the risk of high BP by 180% (Carretero and Oparil, 2000;).

5.2 BASELINE ANTIHYPERTENSIVE AGENTS

Out of a total of 100 study participants, 1 (1.0%) had no record of baseline antihypertensive therapy leaving a total of 99 for further assessment. Out of the remaining 99, 57 (57.6%) were on a baseline antihypertensive monotherapy,

which is in accordance with the ESC-ESH 2007 guidelines and 2009 reappraisal, as well as the 2003 WHO recommendations, which suggest the use of anyone of the AHA approved (CCB, ARB, ACEI, BB, CAA and DIUs) to be used as monotherapy for baseline management of HPT (WHO Guidelines Sub-Committee, 2003; Mancia *et al*., 2007; Mancia *et al*., 2009).

CCB are highly effective AHA, well tolerated in general, especially in black clients (Saunders *et al.,* 1990; Materson *et al.,* 1993a). Clinical trial data also proved that lowering BP with CCB reduces the complications of HPT (Neal *et al*., 2000; Black *et al.,* 2003). The hypotensive response to these drugs is enhanced by a low-renin state (Resnick *et al.,* 1985) and a high dietary salt intake (Nicholson *et al.,* 1987), features which are generally common in the Black hypertensive population. Also, TDIUs are generally well tolerated and have good BP lowing effect in particular older clients. TDIUs are also more affordable than other AHA and are recommended as the baseline therapy for most clients with HPT by US JNC-7 guideline (Chobanian *et al.,* 2003b). BB are generally less effective in Black hypertensives as a result of the tendency towards a low-renin state and a lower cardiac output, with increased peripheral resistance, as a result higher doses of BB are therefore required to achieve target BP. Therefore, unless there are clear indications, for example in clients following a myocardial infarction, BB are generally not considered to be first-line monotherapy in Black clients. Also, ACEI are less effective when used as monotherapy in Black hypertensives, especially when used at low doses (Gibbs *et al*., 1999).

In this study however, CCB were the most prescribed AHA as monotherapy as 44 (77.2%) clients were using it, followed by DIU 6 (10.5%). The least prescribed AHA were ACEI, ARB and CAA with 1(1.8%) client respectively.

A comparison of prescription of baseline AHA as monotherapy between male and female study participants showed that CCB were more likely to be prescribed for females (31/35; 88.6%) than for males (13/22; 59.1%) ($p = 0.009$). However, in a large study of women aged 50 to 79 with high BP but no history of heart disease, management with a CCB alone had a higher risk of heart-related death than women treated with a DIU alone. Because of this finding, CCB are not the drug of choice for lowering BP in older women (Psaty *et al.*, 2004).

Males (5/22; 22.7%) were more likely to receive DIU as monotherapy compared to females (1/35; 2.9%) ($p = 0.017$). DIU is the best baseline drug for most men and women with high BP. TDIU are usually used first because they tend to have fewer side effects than other types of DIU (Chobanian *et al.*, 2003b). A comparison of the other classes of AHA between males and females showed no statistical significance ($p > 0.05$).

The study participants who were on baseline dual therapy were 36 (36.4%) which is also in accordance with the recommendation of the JNC-7, the 2007 ESH-ESC and 2003 WHO guidelines that the combination of two drugs should be considered as baseline management whenever hypertensive clients have a high baseline BP or are classified as being at high or very high cardiovascular risk (Chobanian et al., 2003b; WHO Guidelines Sub-Committee, 2003; Mancia et al., 2007). Also it is the recommendation of the 2007 ESH-ESC guidelines (Mancia et al., 2007) to consider two-drug management as an alternative to monotherapy as a first choice therapeutic approach. An obvious disadvantage of initiating management with two drugs is that of potentially exposing some clients to an unnecessary agent. The advantages, however, are that;

1) By using a combination both the first and the second drug can be given in the low dose range which is more likely to be free of side effects compared to full dose monotherapy;

2) The frustration of repetitively and vainly searching for effective monotherapies in clients with very high BP values or organ damage may be avoided;

3) Fixed low dose combinations are available, allowing the two agents to be administered in a single tablet, the management simplification optimizing compliance; and

4) Starting management with a two-drug combination may allow BP targets to be reached earlier than with monotherapy.

Dual drug therapy can be initiated either by prescription of two separate pills or by prescribing a single combination pill. Even though all guidelines strongly recommend combination therapy, only the ESC-ESH guidelines offer detailed data on the evidence supporting the synergistic efficacy of drug combination. The combinations recommended for dual therapy of HPT according to the ESC-ESH 2007 guidelines (Mancia *et al.*, 2007) as shown in the figure 5.1 are;

1. CCB and either of the following, TDIU, ARB, ACEI, or BB,

2. TDIU and either of the following, ARB, CCB, or ACEI,

3. BB and CCB,

4. ARB and CCB or TDIU,

5. ACEI and CCB or TDIU.

The frames are combinations which have been shown to be beneficial in controlled intervention trials.

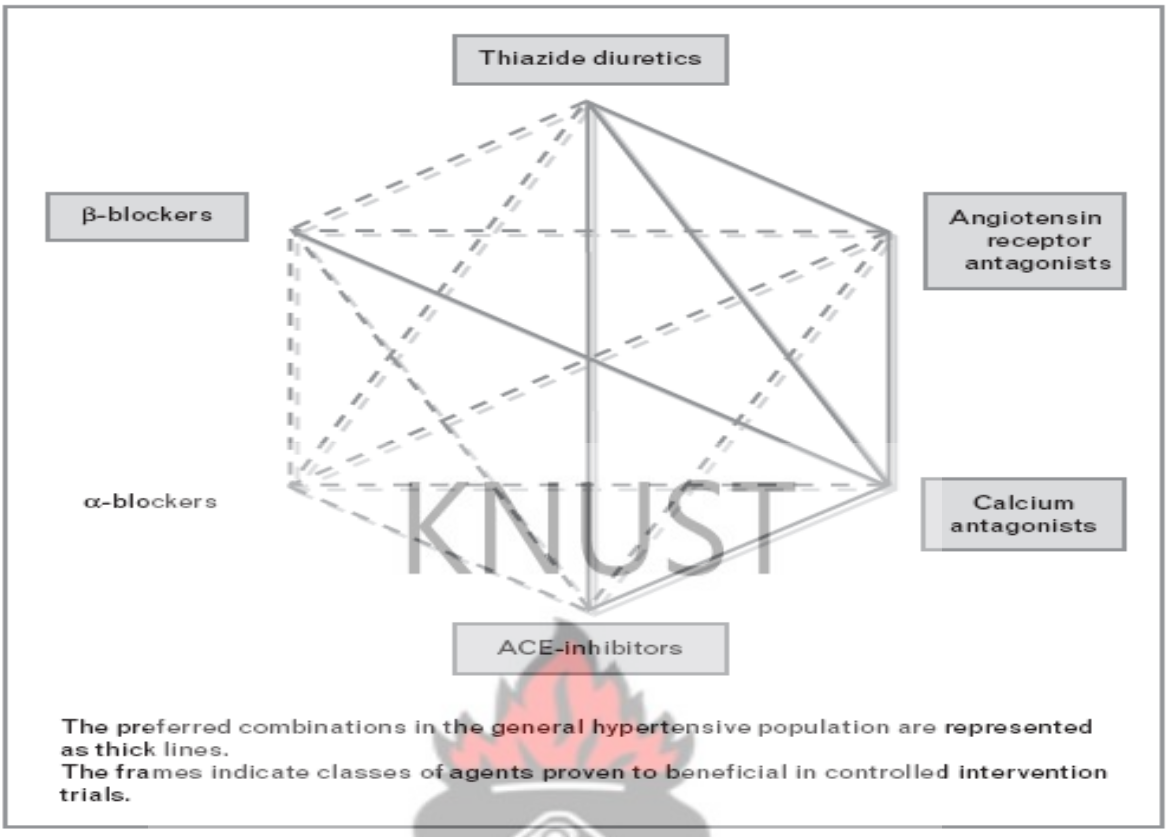

Figure 5.1 Evidence-based recommended combination of drug classes for management of HPT.

The prescribing pattern for clients on dual AHA therapy is in accordance with the ESC-ESH 2007 guidelines for the baseline management of HPT. For this study, CCB + BB were the most prescribed dual AHA therapy with 9 (25.0%) clients, 8 (22.2%) were on ACEI + CCB and CCB + CAA respectively, 6 (16.7%) on DIU + CCB, 3 (8.3%) on CCB + ARB and the least prescribed were CAA + BB and DIU + BB with 1 (2.8%) respectively. One client was on a single combination pill of CCB/BB. Comparing prescribing pattern of dual AHA therapy between males and females, ACEI + CCB were more likely to be prescribed in males (7/18; 38.9%) than in females (1/18; 5.6%) ($p = 0.016$). There was no statistical significance ($p > 0.05$) in the other dual AHA combinations among males and females.

Baseline AHA three-drug combination was prescribed for 6 (6.1%) clients. This pattern of prescription is not recommended by any of the international guidelines for baseline management of HPT. For study participants on three-drug combination therapy of AHA, 33.3% (2/6) were on a combination therapy of DIU + ACEI + CCB and DIU + CCB + CAA respectively and 16.7% (1/6) were on a combination therapy of ACEI + CCB + CAA and ACEI + CCB + BB respectively.

5.3 AFTER STUDY ANTIHYPERTENSIVE AGENTS

This is an assessment of after study antihypertensive therapy based on possible modifications of baseline therapy. Most clients who are hypertensive will require two or more antihypertensive medications to achieve their BP goals. Addition of a second drug from a different class should be initiated when use of a single drug in adequate doses fails to achieve the goal BP. When BP is more than 20/10 mmHg above goal, consideration should be given to initiating therapy with two drugs, either as separate prescriptions or in fixed-dose combinations (Chobanian *et al.*, 2003b). Also, because monotherapy is effective in achieving target goal BP in only about 50% of clients, management with two or more agents from different pharmacologic classes is often necessary to achieve adequate BP control (Materson *et al.*, 1993b).

From this study, clients on baseline monotherapy had either a complete change of their AHA medication or had other classes added on or had the baseline medication maintained. For the male clients, one had a complete change of medication from BB to ACEI + CCB and, two from CCB to ACEI + BB or ARB + ACEI. Those on CCB had at least one and/or at most four of the other classes of AHA (ACEI, DIU, ARB, BB, or CAA) added on and the rest maintained their CCB. Clients on BB had DIU added on and those on DIU had two or more of

the other AHA added on. Two (2) study participants were on a single combination pill of ACEI/DIU.

For the female clients, one had a complete change from CAA to CCB, another from DIU to CCB + BB and three from CCB to ACEI + BB; ACEI + BB + CAA or DIU + ACEI + ARB + CAA. Those on CCB had at least one and/or at most four of the other classes of AHA (ACEI, DIU, ARB, BB, or CAA) added on and the rest maintained their CCB. A female on a baseline ACEI had CCB + BB added on and another female on BB had DIU added on to the baseline therapy.

Clients on baseline dual therapy had at least one or more of the other classes of AHA added on or had a complete change to other AHA. For others there was no change in their medications. Male clients on a baseline dual therapy of CAA + BB had CCB added on to the therapy. Others on ACEI + CCB had ARB and/or BB added on to the baseline management. There was a complete change of baseline management from ACEI + CCB to DIU + ARB + BB, while the rest maintained their baseline dual therapy of ACEI + CCB. ACEI or ARB was added on to clients on baseline dual therapy of CCB + CAA. One male on a baseline dual therapy of CCB + ARB was maintained. Males on baseline dual therapy of CCB + BB had ACEI being added onto the baseline therapy and the rest maintained the same baseline therapy. One male on dual therapy of DIU + BB had CCB + ARB being added onto the baseline therapy. Two males on a baseline dual therapy of DIU + CCB had a change in DIU for ACEI.

For the female participants on baseline dual therapy, those on CCB + BB had it maintained and others had a change in the BB for CAA + DIU + ACEI or DIU. Others had their baseline BB changed for ARB + DIU, or a combination of DIU + BB was added on to ACEI + CCB. Two (2) females on a dual therapy of CCB + ARB had their baseline medication maintained. Females who were on a dual combination therapy of CCB + CAA, whilst some were maintained, others had

the CAA component replaced with ARB or DIU + VAS respectively. Clients on a baseline DIU + CCB therapy had ACEI or ARB + CAA + VAS added on whilst the others had the DIU component being replaced with ACEI or ARB + CAA + VAS.

Study participants who were on a three-drug baseline combination therapy maintained their baseline medication or had one or two AHA replaced with another. Three of the study participants maintained their baseline medication of ACEI + CCB + BB, or DIU + ACEI + CCB. Clients on DIU + CCB + CAA, had DIU + CAA replaced with ARB, whilst another had the CAA replaced with ARB. Another had DIU + ARB + BB added on to the baseline medication of ACEI + CCB + CAA.

5.4 EVALUATION OF AHA THERAPY

The baseline mean SBP among the study participants was 175.5 ± 24.3 mmHg with a minimum of 140 mmHg, and maximum SBP of 270 mmHg. The baseline mean DBP was 105.0 ± 19.4 mmHg with a minimum DBP of 80 mmHg, a median of 100 mmHg and maximum DBP of 200 mmHg.

A look at the after study mean SBP among the study participants over the duration for which they have been on antihypertensives showed a mean SBP of 135.7 ± 18.7 mmHg with a minimum of 90 mmHg and maximum SBP of 210 mmHg. The after study mean DBP among the study participants was 84.0 ± 10.1 mmHg with a minimum DBP of 60 mmHg and maximum DBP of 120 mmHg. An estimation of mean percentage changes in SBP and DBP of the after study and baseline measurements showed an overall mean percentage change of -22.9 ± 12.5 % and -18.7 ± 14.6 % respectively. The target or goal BP for HPT clients from WHO/ISH and ESH/ESC guidelines is <130/85 mmHg and that of the MOH of Ghana is < 140/ 90 mmHg (WHO Guidelines Sub-Committee, 2003;

Mancia *et al.*, 2009; Ministry of Health, 2010) . Based on these criteria BP control rates are 42% and 62% respectively.

A major problem is the very high rate of discontinuance or change in medications by hypertensive clients: 50% to 70% of new managements are changed or discontinued within the first 6 months in most practices. These high discontinuance or change rates probably reflect a combination of adverse drug effects, cost of drugs, poor efficacy, changes in provider, dissatisfaction with other aspects of care, and lack of understanding of the risks of target organ damage (Oparil and Calhoun, 1997).

From this study, 83 clients had changes in their medications with an average time of 2.39, a minimum of 1 and maximum of 6 times. Antihypertensive therapy is a lifelong therapy which requires the medication to be taken every day. Frequent changes in medications of clients over short periods do not facilitate achievement of goal BP in good time. From this study, the mean duration for being on AHA therapy was 4.0 ± 3.2 years with a minimum of 0.5 years and maximum duration of 20 years. A comparison between the mean durations for being on AHA in males and females showed no statistical significance ($p = 0.728$). Clients' medications were changed because of the following; side effects experienced 38(45.8%), not reaching a goal BP 33(39.7%), unavailability of medications 2(2.4%) and personal request 10(12.1%).

Keeping clients on medication and treating to a goal BP are difficult in most practices. In the United States, 46% of hypertensive clients have their BPs controlled (BP <140/90 mm Hg)(Prevention, 2011). However, the WHO/ISH guidelines recommend the setting of stringent BP targets for young, middle aged and diabetes clients, a target of "normal" BP (<130/85mmHg) rather than the more traditional target of <140/90mmHg or "high normal" levels which is advocated for older subjects (WHO Guidelines Sub-Committee, 2003). These

recommendations are based on the totality of the evidence, which includes the epidemiological evidence that there is no BP level below which a lower pressure is not associated with a lower cardiovascular risk (MacMahon et al., 1990).

In Ghana, awareness, management and control rates, though low has seen some increment as shown in the study "a systematic review of the epidemic of hypertension in Ghana, between 1970 and 2009". Management and control rates in 1970 was 7.2% and 3.7% and in 2009, it had increased to 31.3% and 12.7% (Bosu, 2010). In this study, 42% of the clients had their BPs controlled with BP values < 130/80 mmHg.

Clients who were on medications other than the AHA were 63. Most of the clients did not know that these medications were not AHA, but were given for management, preventive and possibly curative purposes for either possible complications that could arise from the HPT or for side effects of the AHA therapy. Non-steroidal anti-inflammatory drugs (NSAIDs) are generally known to cause varying increases in BP because of inhibitory effect on prostaglandin synthesis which in the renal system causes sodium and water retention, thereby increasing plasma volume and, vasodilatory prostacyclin which increases peripheral resistance(Page and Henry, 2000). However, Aspirin which accounted for 44 (46.8%) of these prescriptions has more benefits than harmful effects. Aspirin is effective as a pain killer, an anti-inflammatory agent, and has actions that provide protection against serious diseases like heart attack and stroke. While there is not yet a clear aspirin BP connection, the protective benefits are so large that routine, daily administration of aspirin is now recommended by the American Heart Association as a standard component of maintaining a healthy heart (Hennekens, 1997). Aspirin in the body inhibits the formation of chemicals called "prostaglandins" by blocking an essential enzyme needed for their

formation. Among the many properties of prostaglandins is their ability to promote blood cells to stick together. Thus, by blocking the formation of prostaglandins, aspirin decreases the likelihood of blood clots forming in your blood vessels. Since a large number of heart attacks and strokes are directly caused by small, spontaneously forming blood clots, the ability of aspirin to prevent the formation of these small clots means that heart attacks and strokes become less likely(Burch, 1978; Patrono, 1994). Aspirin was found in the HOT trial to reduce major cardiovascular events by 15% (p=0·03) and all myocardial infarction by 36% (p=0·002), with no effect on stroke (Hansson *et al.*, 1998). However, Aspirin increases risk of bleeding, stomach or intestine irritation and toxicity, while serious, these reactions are rare, very easily noticed and can be treated. Celecoxib 1(1.1%), a Cycloxygenase-2 inhibitor does not cause significant changes in BP (Curhan, 2002).

Hyperlipidaemia and HPT are common conditions that both contribute synergistically to cardiovascular risk. The management of cardiovascular risk now forms the principal function of both lipid and HPT Clinics (Wierzbicki, 2002). With statins, data are currently scarce, but small-scale studies showed a reduction in the hypertensive response to mental stress in hyperlipidaemic clients and a nonsignificant decrease in BP of 3 mmHg with lovastatin in 26 clients (Sung *et al.*, 1997). Other studies with Fluvastatin in 49 clients and 23 clients, respectively, showed significant reductions in BP (6/3 mmHg) after 6 weeks (Jarai, 1996; Abetel G, 1998). At the HPT/DM Clinic of the KNUST Hospital, the Lipid lowering drugs commonly prescribed included; Atorvastatin 14(14.9%) , Simvastatin 5(5.3%), Fluvastatin 3(3.2%), and Rosuvastatin 1(1.1%). Though, laboratory request forms are given to clients occasionally to monitor their cholesterol levels, there was not much documentation in their folders.

Most clients on the Anti-uricaemic medication, Allopurinol 12(12.8%) had no well documented uric acid levels in their folders to justify its prescription. However, clients' uric acid levels are monitored closely in the clinic as hyperuricaemia is associated with HPT, renal disease progression and cardiovascular disease (Goicoechea *et al.*, 2010).

Indications for the use of Vitron 2(2.1%), a multivitamin preparation and Tricyclic antidepressants- Amitryptillin 5(5.3%) and Imipramine 1(1.1%), were not documented in the clients' folders.

Mannix 3(3.2%) is an herbal product commonly prescribed for men with erectile dysfunction or decreased sexual drive. Only three clients had these problems documented in their folders and hence were being treated for it, though decreased sex drive accounted for 12(4.5%) and erectile dysfunction 4(1.5%), which are very common side effects of BB and DIUs.

Clients who reported that they have sleep problems were 3(1.1%), however, only two had it documented in their folders hence were being treated with Benzodiazepines like Lorazepam 1(1.1%) and Diazepam 1(1.1%). These medications are the common prescription to manage HPT clients with sleep problems which are common side effect of BB (Karch, 2003; Galbraith *et al.*, 2007).

Clients who experienced headache were 73(27.3%). Almost all clients had it documented in their folders. This is very common with most of the clients, especially for those taking CCB, CAA and VAS. Body weakness 63(23.6%) were also a very common complaint from clients and were well documented in their folders. It is a common complain among the elderly. Cough which is very common among clients taking ACEI, ARB and VAS accounted for 49(18.4%). However, the cough is more severe in those taking ACEI.

Decreased sense of taste accounted for 17(6.4%) and common in clients on ACEI. Dizziness was common among clients taking ARB, CCB, CAA, ACEI, and DIU and accounted for 16(6.0%), only one client had it recorded and was being treated with the Antihistamine, Cinnarizine 1(1.1%). Other side effects were fatigue 15(5.6%), common among clients on DIU, BB, CCB, and CAA; loss of appetite 6(2.3%) in clients on DIU, flushing 5(1.8%). The less common side effects were constipation 2(0.8%) common among clients on CCB and DIU; drowsiness 1(0.4%) common among clients on CAA; and diarrhoea 1(0.8%) which is common in clients on ARB, ACEI and CCB (Karch, 2003; Galbraith *et al.*, 2007).

Clients complained of the number of pills that they took at a time. They suggested that if possible single-pill combination medications should be produced by the pharmaceutical companies to reduce the pill burden and improve compliance as most of them were taking two or more drugs to manage their HPT. They also suggested that the hospital should manage to stock the pharmacy with their medications so that the total time that they spend during a visit is reduced and most importantly, they get almost the same brand of medications as most of the pharmacies do not always provide them with the same brands as they get from the hospital when they are in stock.

CONCLUSION

The classes of AHA commonly used at the HPT/DM Clinic of the KNUST Hospital are CCB, DIU, ACEI, ARB, and BB. CAA and VAS are used sparingly. Clients' pharmacological management of HPT is frequently initiated with monotherapy, of which CCB accounted for most of the prescriptions followed by DIU. Dual- and three-drug therapies are also used in initiating management. Among the CCB, Nifedipine is the most prescribed and bendrofluazide is the most prescribed among the DIU. Aspirin was the most prescribed non-AHA.

Two or more agents from different pharmacological classes were used to achieve and maintain a goal of BP of < 130/85mmHg from the WHO/ISH and ESH/ESC guidelines and < 140/ 90 mmHg from the MOH of Ghana. Most clients had their BP under control.

In conclusion, the AHA in use at the HPT/DM Clinic of the KNUST Hospital and the prescription pattern are in accordance with that of the international and national guidelines.

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APPENDIX

QUESTIONAIRE

Code number:

I am an MPhil student at the Department of Pharmacology, Kwame Nkrumah University of Science and Technology (KNUST), carrying out a research designed to assess the **pharmacological management of hypertensive clients at KNUST Hospital, Kumasi**. Your rights and choices are greatly respected; hence you could willingly participate or otherwise. Your choice however, would not in any way affect the quality of care you will receive. You are also assured of confidentiality and anonymity. Please tick in the box or where necessary provide answers. Thank you for taking part in this study.

Client's background information

Age ☐ **Sex**: M ☐ F ☐

Weight (kg) ☐ Height (cm) ☐

Marital Status: Single ☐ Married ☐ Divorced ☐
Widow/Widower ☐

Religion: Christian ☐ Islam ☐ Traditional ☐ Other (specify)……

Educational status: None ☐ JHS ☐ SHS ☐ MSLC ☐
POST-SEC ☐

Tertiary ☐ Others (specify) _____

Employment status: employed ☐ unemployed ☐

Insurance status: Insured ☐ Uninsured ☐

1.When was your "high BP" diagnosed?

Date (year) ☐ Don't know ☐

2. What was your blood pressure reading at diagnosis? Reading: ☐

Don't know ☐

3. How long did it take you to start antihypertensive management? ☐

Immediately

1-3mths ☐ 4-6mths ☐ 7mths-1year ☐ other (specify)

_____

4. How long has it been since you started antihypertensive management?

1-3mths ☐ 4-6mths ☐ 7mths-1year ☐ other (specify)

_____

5. How many antihypertensive medicines did you start with?

1 ☐ 2 ☐ 3 ☐ ≥4 (specify) _____. Don't remember ☐

6. Please provide details of your initial antihypertensive management. Include names of medication, dosage and how often taken.

Class of AHA	Name of specific drug
A. Diuretics (DIU)	
B. Angiotensin-Converting Enzyme Inhibitors (ACEI)	
C. Calcium channel blockers (CCB)	
D. Angiotensin II receptor blockers (ARB)	
E. Beta- blockers (BB)	
F. Centrally acting agents (CAA)	
G. Vasodilators (VAS)	
H. Alpha blockers (AB)	

7. Please provide details of your current antihypertensive management. Include names of medication, dosage and how often taken.

Class of AHA	Name of specific drug
Diuretics (DIU)	
Angiotensin-Converting Enzyme Inhibitors (ACEI)	
Calcium channel blockers (CCB)	
Angiotensin II receptor blockers (ARB)	
Beta- blockers (BB)	

Centrally acting agents (CAA)	
Vasodilators (VAS)	
Alpha blockers (AB)	

8. What is your BP presently? Reading _____ mmHg

9. Has your antihypertensive management changed since initial diagnosis?

Yes ☐ No ☐

10. How many times has your drugs been changed? Once ☐ Twice ☐

Thrice ☐ ≥ 4 ☐

11. Why were the medications changed?

Side effects ☐ not reaching a goal BP ☐ unavailability of drugs ☐

Personal request ☐

12. Please list all other medication(s), not previously mentioned in this questionnaire, that you are taking regularly or intermittently whether for this or any other condition/illness.

Name of specific drug

13. How often do you visit the Clinic in a year?

1 ☐ 2 ☐ 3 ☐ ≥4 (specify) _____

14. What side effects do you experience since taking the antihypertensive medications?

Headache ☐ Drowsiness ☐ Fatigue ☐ Cough ☐ Fluid Retention ☐ Nausea/vomiting ☐ Decreased sex drive ☐

Diarrhoea/constipation ☐ Flushing ☐ Dizziness ☐ Body weakness ☐

Decreased sense of taste ☐ loss of appetite ☐ erectile dysfunction ☐

Others (specify) ----------