

## ANTIHYPERTENSIVE THERAPY: THE CONCEPTS OF MANAGEMENT WITH HERBAL AND SYNTHETIC AGENTS FOR PULMONARY HYPERTENSION.

Susanta Kumar Rout<sup>1</sup>, Saptorshi Dutta<sup>2</sup>, Mukul Sengupta<sup>3</sup>, Srimanta Das<sup>4</sup>, Bikram Rout<sup>5</sup>

L.B. Rao Institute of Pharmaceutical Education & Research, Bethak Road, Khambhat, Anand, Gujarat, India.

\*Email: [susanta.rut81@gmail.com](mailto:susanta.rut81@gmail.com)

### ABSTRACT

Hypertension (Pulmonary hypertension) is a common clinical problem encountered in day-to-day practice. Major advances have taken place in recent years with respect to the understanding of hypertensive diseases. Drug therapy forms the backbone of management and appropriate drug selection is based upon the underlying causes. New therapeutic approaches in hypertension are urgently needed. The options available are widening with availability of newer therapeutic agents and thus it becomes necessary to be updated with the recent developments. Standard therapy today uses the basic of employing non-pharmacological modalities. Major advances have taken place in recent years with respect to our understanding of hypertensive diseases. Standard therapy today uses the basic of employing non-pharmacological modalities. Thereafter a stepped-care program with pharmacological entities has been advocated using diuretic, anti-adrenergic, and vasodilating agents with some natural medicaments. Clinical studies directed towards the new classes of pharmacotherapeutic agents as well as natural medicaments for hypertension. Moreover, knowledge of newer compounds that possess unique mechanisms of action should stimulate new thinking about this enigmatic disease of blood pressure regulation that we term 'essential hypertension' as well as more specific control of arterial pressure in this ubiquitous disease.

**Keywords:** Pulmonary hypertension, management, diuretics, antihypertensive drugs, pharmacotherapeutic.

### INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death worldwide. Hypertension is the most common cardiovascular disease and a major public health problem in both developed and developing countries.<sup>1</sup> A large number of population surveys from different parts of the globe have consistently demonstrated hypertension to be a ubiquitous disease encompassing all ethnic groups and geographic regions.<sup>2,3</sup> The disease affects both sexes and more and more patients are turning up at younger ages. Hypertension is the leading member of the group of so called "non-communicable diseases" (NCD) and a leading contributory cause of death worldwide.<sup>4</sup> It is believed that hypertension contributes about 57 per cent towards all deaths from strokes and 24 per cent towards all deaths from coronary artery disease.<sup>5</sup> The contribution towards morbidity from these crippling diseases, as also chronic renal failure, would be staggering indeed. Pulmonary hypertension, affects only the arteries in the lungs and the right side of the heart. Pulmonary hypertension begins when tiny arteries in the lungs, called pulmonary arteries and capillaries, become narrowed, blocked or destroyed. This makes it harder for blood to flow through your lungs, which raises pressure within the pulmonary arteries. As the pressure builds, the heart's lower right chamber (right ventricle) must work harder to pump blood through the lungs, eventually causing the heart muscle to weaken and sometimes fail completely. Pulmonary hypertension is a serious illness that becomes progressively worse and is sometimes fatal. Although it isn't curable, treatments are available that can help lessen symptoms and improve the quality of life. The Task Force of the National Heart, Lung and Blood institute issued the first standardized, algorithmic approach to treating hypertension in 1973. Pulmonary hypertension can develop suddenly but usually develops over months and years, depending on the

underlying aetiology. It follows that as pulmonary artery pressure rises gradually, the right ventricle has more time to adapt and compensate and symptoms may be slow to emerge. Often, the symptoms are not specific and an alternative diagnosis may be entertained before pulmonary hypertension is recognized.<sup>5</sup> A biochemical test that indicate the presence of subclinical disease would allow early intervention and possibly a better chance of altering the course of the disease. The concept of "the lower the blood pressure the better without causing symptoms" was the rule until the J-curve hypothesis emerged and generated a long debate. Major advances have taken place in recent years with respect to our understanding of hypertensive diseases, the mechanisms of action of other therapeutic agents, and the introduction of new classes of drugs. Standard therapy today uses the basic of employing non-pharmacological modalities. Now the current evidence supports the old concept, despite the repeated recommendations that ACE inhibitors, CCBs, thiazide-diuretics are preferred as the initial agent in hypertension treatment, many clinicians ignore the guidelines for treatment of hypertension and sometimes most it was observed due to use some traditional drugs, hypertension is controlled. This practice has added a significant cost to hypertension treatment worldwide. The current options for the drug therapy of pulmonary hypertension are increasing and the newer drugs show promising effects in the management of pulmonary hypertension. This review is high light the management of hypertension with special reference to pulmonary hypertension with, "Update on the Management of Hypertension.

### BACKGROUND

The upper or first number in a blood pressure reading is the systolic pressure and the lower or second number is

called the diastolic pressure. According to National Heart, Lung, and Blood Institute Guidelines:

Normal blood pressure is below 120/80 mmHg.

- Pre hypertension is systolic pressure that's between 120 to 139 or diastolic pressure between 80 and 89.
- Stage 1 hypertension is systolic pressure between 140 to 159 or diastolic pressure between 90 and 99.
- Stage 2 hypertension is systolic pressure higher than 160 or diastolic pressure of 100 or higher.

It became apparent early in the history of chronic dialysis therapy that patient survival was much shorter than in a general population sample of similar age. Hypertension is a major risk factor for stroke, coronary heart disease, cardiac failure and renal failure. Prevention and treatment of hypertension have been shown to reduce morbidity and mortality substantially.<sup>6</sup> Natural treatment of essential hypertension can bring blood pressure values into the normal range; however, if lifestyle changes are not maintained, hypertension will probably return. Secondary hypertension has an organic cause (i.e., kidney disease, pregnancy) and must be evaluated and monitored by a physician since the underlying cause must also be addressed.

## INCIDENCE

Cardiovascular disease was the attributed cause of death in an unexpectedly large proportion of patients. In 1974, Lindner et al published the Seattle experience, in which 60% of deaths in their dialysis patients were due to cardiovascular diseases.<sup>7</sup> Approximately half of all deaths in dialysis patients are reported to be due to cardiovascular diseases. It is likely that cardiovascular disease leads to uraemia and that uraemia leads to cardiovascular disease, a classic "vicious circle". Mortality from cardiovascular disease is an order of magnitude higher in dialysis patients. Transplant patients appear to have rates that are intermediate, though still excessive.<sup>8</sup> The incidence rates of coronary artery disease and cardiac failure are considerably higher in dialysis patients than in the age-matched general population. One in three adults in the United States has high blood pressure. But nearly one-third of those people don't know they have high blood pressure, because it's a silent disease. People can have high blood pressure for years without experiencing symptoms or knowing they have it. Affects one in five Canadians. It is the number one risk factor for stroke and a major risk factor for heart disease, so it is very important that it is properly controlled. Yet 42% of Canadians with high blood pressure don't even know they have it because there are no symptoms. More women than men had died of cardiovascular diseases every year since 1984. Untreated high blood pressure can cause kidney damage, and raises the risk of heart attack, stroke, and other cardiovascular diseases. The cause of 3 out of 5 cases of heart failure in women is high blood pressure. Coronary heart disease is the number one killer of American women, claiming more than 500,000 women's lives each year. Early detection and treatment of high blood pressure could prevent many of these deaths.

High blood pressure (HBP) is an important modifiable risk factor for cardiovascular and renal disease in Western and Asian populations.<sup>8</sup> It is an extremely common finding in the community and a risk factor for myocardial infarction, stroke, congestive heart failure, end-stage renal disease, and peripheral vascular diseases.

## SYMPTOMS

High blood pressure usually doesn't cause any symptoms in the early stages. Symptoms associated with high blood pressure can include:

- Shortness of breath (dyspnoea), either while exercising or at rest
- Fatigue
- Dizziness or fainting spells (syncope)
- Chest pressure or pain
- Swelling (oedema) in your ankles, legs and eventually in your abdomen (ascites)
- Bluish colour to your lips and skin (cyanosis)
- Racing pulse or heart palpitations
- Headache
- Nosebleeds

Pulmonary hypertension is a heterogeneous condition and even patients within a particular pathology subcategory vary in their natural history and response to treatment. The prospect of individualizing therapy in pulmonary hypertension is as topical as it is in many other conditions, and equally as elusive. One possible avenue worth exploring is the use of circulating cells, such as monocytes or endothelial progenitor cells, as sources of transcriptomic information that might phenotype patients at the molecular level.<sup>9,10</sup> This remains in the realm of ongoing research at the moment but might offer opportunities similar to the molecular classification used in tailoring chemotherapy in oncology.

## Tests and diagnosis:

Pulmonary hypertension is hard to diagnose early because it's not often detected in a routine physical exam. Even when the disease is more advanced, its signs and symptoms often mimic those of other heart and lung conditions.<sup>11,12,13</sup> An echocardiogram is usually used to diagnose pulmonary hypertension. Tests to diagnose pulmonary hypertension include:

- **Echocardiogram:** Pulmonary hypertension is suspected based on the results of this test. This non-invasive test uses harmless sound waves that allow the doctor to see the heart without making an incision. During the procedure, a small, plastic instrument called a transducer is placed on the patient's chest. It collects reflected sound waves (echoes) from the heart and transmits them to a machine that uses the sound wave patterns to compose images of the beating heart on a monitor. These images show how well the heart is functioning, and recorded pictures allow to measure the size and thickness of the heart muscle. Sometimes doctor will recommend an exercise

echocardiogram to help determine how well the heart works under stress. In that case, the patient will have an echocardiogram before exercising on a stationary bike or treadmill and another test immediately afterward.

- **Transoesophageal echocardiogram:** If it's difficult to get a clear picture of the heart and lungs with a standard echocardiogram, doctor may recommend a transoesophageal echocardiogram. In this procedure, a flexible tube containing a transducer is guided down the throat and into the oesophagus. From this vantage point, the transducer can obtain detailed images of the heart.

- **Pulmonary function test:** This non invasive test measures how much air the lungs can hold, and the airflow in and out of the lungs. During the test, Patient will blow into a simple instrument called a spirometer.

- **Perfusion lung scan:** This test uses small amounts of radioactive substances (radioisotopes) to study blood flow (perfusion) in the lungs. The radioisotopes are injected into a vein in the arm. Immediately afterward, a special camera (gamma camera) takes pictures of blood flow in the lungs' blood vessels. A lung scan is then used to determine whether blood clots are causing symptoms of pulmonary hypertension. It's usually performed with another test known as a ventilation scan. In this test, patient inhale a small amount of radioactive substance while a gamma camera records the movement of air into the lungs. The two-test combination is known as a ventilation-perfusion (V/Q) scan, and in its entirety usually takes less than an hour with side effects or complications rarely occurring.

- **Right heart catheterization:** Performed on an outpatient basis using local anaesthesia, this test is often the most reliable way of diagnosing pulmonary hypertension. During the procedure, a cardiologist places a thin, flexible tube (catheter) into a vein in the neck or groin. The catheter is then threaded into the right ventricle and pulmonary artery. Right heart catheterization allows doctor to directly measure the pressure in the main pulmonary arteries and right ventricle. It's also used to evaluate the effect different drugs may have on the heart in order to find the most effective treatment.

- **Computerized tomography (CT):** A CT scan allows the doctor to see the organs in two-dimensional "slices." In this test, Patient will lie in a machine that takes images of the lungs so that the doctors can see a cross-section of them.

- **Magnetic resonance imaging (MRI):** This test uses no X-rays. Instead, a computer creates tissue "slices" from data generated by a powerful magnetic field and radio waves. It can't, however, measure artery pressure — a procedure that's necessary if the patients are taking medications to control IPH. But it can get good images of the pulmonary vessels.

- **Genetic tests:** If a family member has had pulmonary hypertension, the doctor may screen for genetic mutations that are linked with pulmonary hypertension to confirm a diagnosis. If the test positive, doctor may recommend that other family members be screened for the same genetic mutation.

- **Open-lung biopsy:** In rare situations doctor may recommend an open-lung biopsy. An open-lung biopsy is a type of surgery in which a small sample of tissue is removed from the lungs to check for pulmonary hypertension.

While shortness of breath is one of the first symptoms of pulmonary hypertension, this symptom is also common with many other diseases, such as asthma. But, if the patients are constantly short of breath, rather than only occasionally as is usually the case with asthma.

### Pulmonary hypertension classifications

Once patients have received a diagnosis of pulmonary hypertension, doctor may classify the disease using guidelines developed by the New York Heart Association.<sup>14,15</sup>

- **Class I.** Although patients have been diagnosed with pulmonary hypertension, patients have no symptoms.

- **Class II.** Patients don't have symptoms at rest, but patient experience fatigue, shortness of breath or chest pain with normal activity.

- **Class III.** Patient's feel comfortable at rest but have symptoms with slight exertion.

- **Class IV.** Patients have symptoms even at rest.

### Etiology:

High blood pressure can happen to anyone at any age. It is often difficult to pinpoint a cause for high blood pressure, since several factors and conditions often play a role in its development.

Race and even geographic location appear statistically significant in some cases. African-American women who live in the Southeast United States are more likely to have high blood pressure than those who live elsewhere. Overall, African-Americans are more likely to develop high blood pressure at an earlier age and more severely than whites.<sup>16</sup>

However, this certainly does not mean that the white population should consider high blood pressure an African-American disease. In fact, 11 states (Alabama, Arkansas, Georgia, Indiana, Kentucky, Louisiana, Mississippi, North Carolina, South Carolina, Tennessee, and Virginia) in the Southeast are known as the "Stroke Belt States" because of the high rate of strokes experienced by males and females of all races.

Other factors that contribute to high blood pressure include smoking, lack of physical activity, overweight, high sodium intake, high cholesterol excessive intake of alcoholic beverages, and heredity. Diabetes patients also are at greater risk for high blood pressure and other cardiovascular diseases.

Women who use oral contraceptives should have their blood pressure closely monitored, although the risk from oral contraceptives is much lower than it was previously because the amount of estrogen and progesterin in today's pills is significantly less. Women with high blood pressure who smoke and use oral contraceptives face a 10 to 15 times greater risk of stroke.

After menopause a woman's risk of high blood pressure and other cardiovascular diseases increases greatly; the risk increases significantly faster for women after hysterectomy perhaps because the uterus produces chemicals that help regulate blood pressure.

"Hypertension" is the medical term for high blood pressure. High blood pressure that has no known cause is called primary, or essential, hypertension. This type of high blood pressure is the most common and responds well to lifestyle changes, such as losing weight, dietary changes, exercise, and stress reduction. It is usually a combination of factors, such as:

- Weight: Greater the body mass, the more pressure there is on the artery walls. That's because more blood is produced to supply oxygen and nutrients to tissues in the body.
- Activity level: Lack of physical activity tends to increase heart rate, which forces the heart to work harder with each contraction.
- Tobacco use: Chemicals in cigarettes and tobacco can damage artery walls.
- Sodium intake: Excessive sodium in the diet can result in fluid retention and high blood pressure, especially in people sensitive to sodium.
- Potassium intake: Low potassium can result in elevated sodium in cells, because the two balance one another.
- Stress: Stress can raise blood pressure.
- Alcohol consumption: Excessive alcohol intake can, over time, increase the risk of heart disease.
- Age: The risk of high blood pressure increases as patient get older.
- Family history. High blood pressure often runs in families.

High blood pressure can also be caused by an underlying condition, such as kidney disease, hormonal disorders, thyroid disease, adrenal gland disease, and the use of certain drugs, such as oral contraceptives, or herbs such as liquorice. This type of high blood pressure is called secondary hypertension.

#### **Pathophysiology**

Essentially, BP is the outcome of cardiac output and peripheral vascular resistance ( $BP = \text{cardiac output} \times \text{peripheral vascular resistance}$ ). Therefore, maintenance of a normal BP is dependent on the balance between the cardiac output and peripheral vascular resistance.

#### *Essential Hypertension:-*

The pathogenesis of essential hypertension is multi factorial and highly complex.<sup>17</sup> Many factors (and risk factors) have been implicated in the genesis of essential hypertension, which include the following:

- Increased sympathetic nervous system activity.
- Increased production of sodium-retaining hormones and vasoconstrictors.

- Deficiencies of vasodilators such as prostacyclin and nitric oxide.
- Inappropriate or increased renin secretion, resulting in increased production of angiotensin-II and aldosterone.
- Genetic predisposition.

#### *Secondary Hypertension*

The common identifiable causes of hypertension are the following:

- Chronic kidney disease
- Renovascular disease
- Cushing's syndrome (hypersecretion of the hormone cortisol)
- Pheochromocytoma (adrenal tumor)
- Drugs such as nonsteroidal antiinflammatory drugs (NSAIDs) and oral contraceptives

#### **Management**

This review gives some information about synthetic and natural (herbal) medicines that affect the cardiovascular system with special reference to Pulmonary hypertension both in terms of efficacy and safety as gleaned from the scientific literature that is available. The agents both synthetic and herbs are categorized under the primary diseases they treat.<sup>18,19</sup> However, most herbal medicines have multiple cardiovascular effects that frequently overlap. Treating high blood pressure can save the life. Lowering blood pressure reduces the chance of heart attack by 27 percent, stroke by 38 percent, and heart failure by 55 percent.<sup>20</sup>

According to the American Heart Association, nearly one in three adults in the United States has high blood pressure. But nearly one-third of those people don't know they have high blood pressure, because it's a silent disease. People can have high blood pressure for years without experiencing symptoms or knowing they have it.

The treatments are often complex and require extensive follow-up care. Doctor may also need to change the treatment because it's no longer effective. The best approach for hypertension will depend on a number of factors, including the age, the type and class of pulmonary hypertension, and overall health.

Several types of medications are available to treat high blood pressure. Medical treatment is often used in conjunction with lifestyle therapies.<sup>21</sup> Some of the most commonly used medications to treat high blood pressure include:

Diuretics

Beta-blockers

ACE (angiotensin converting enzyme) inhibitors

Calcium channel blockers

Alpha-beta blockers



These drugs may be used alone or in combination, depending on what the physician determines is best for the situation. If physician orders medication, it is important that patient take the medication exactly as prescribed and don't stop without physician's order. Suddenly stopping blood pressure medication can cause blood pressure to rise rapidly.

Treatments for pulmonary hypertension include the following:

- **Blood vessel dilators:** These medications, also known as vasodilators, open narrowed blood vessels. One of the most commonly prescribed vasodilators for pulmonary hypertension is epoprostenol (Flolan). The drawback to epoprostenol is that its effects last only for few minutes. This drug is continuously injected through an intravenous (IV) catheter via a small pump that patient wear in a pack on the belt or shoulder. This means that patients will learn to prepare their own medication mixture, operate the pump and care for the IV catheter. Patient will need comprehensive follow-up care. Potential side effects of epoprostenol include jaw pain, nausea, diarrhoea, leg cramps, as well as pain and infection at the IV site.

A newer form of the drug, iloprost (Ventavis), avoids many of these problems. Iloprost can be inhaled every three hours through a nebulizer, a machine that vaporizes the medication, making it far more convenient and less painful to use.<sup>22</sup> And because it's inhaled, it goes directly to the lungs. Side effects associated with iloprost include chest pain — often accompanied by headache and nausea — and breathlessness.

- **Endothelin receptor antagonists:** These medications reverse the effect of endothelin, a substance in the walls of blood vessels that causes them to narrow. One of these medications, Bosentan (Tracleer), may improve patient's stamina and symptoms. The drug isn't for pregnant women. If patient take this, patient will need monthly liver monitoring because the drug can damage liver.
- **Sildenafil:** Revatio, a medication that contains sildenafil, the same active ingredient as the impotence drug Viagra, is sometimes used to treat pulmonary hypertension. It works by opening the blood vessels in the lungs. Side effects include dizziness and vision problems.
- **High-dose calcium channel blockers:** These drugs help relax the muscles in the walls of patients blood vessels. They include medications such as amlodipine (Norvasc), diltiazem (Cardizem, Tiazac) and nifedipine (Adalat, Procardia). Although calcium channel blockers can be effective, only a small number of people with pulmonary hypertension respond to them.<sup>23</sup>
- **Ambrisentan:** Ambrisentan (Letairis) is another medication that stops the narrowing of the blood vessels. Because of the risk of liver damage, and to minimize the risks to unborn children, patient can only be prescribed ambrisentan through the Letairis Education and Access Program (LEAP). Before taking the drug, tell doctor about any liver conditions patients have.

- **Anticoagulants:** Doctor is likely to prescribe the anticoagulant warfarin (Coumadin) to help prevent the formation of blood clots within the small pulmonary arteries. Because anticoagulants prevent normal blood coagulation, they increase the risk of bleeding complications. Take warfarin exactly as prescribed, because warfarin can cause severe side effects if taken incorrectly.<sup>24</sup> If patients taking warfarin, doctor will ask patients to have periodic blood tests to check how well the drug is working. Many other drugs, herbal supplements and foods can interact with warfarin, so be sure with doctor knows all of the medications patient taking.

- **Diuretics:** Commonly known as water pills, these medications help eliminate excess fluid from the body. This reduces the amount of work heart has to do. They also may be used to limit fluid buildup in the lungs.

- **Oxygen:** Doctor may suggest that sometimes breathe pure oxygen, a treatment known as oxygen therapy, to help treat pulmonary hypertension, especially if patient live at a high altitude or have sleep apnea. Some people with pulmonary hypertension eventually require constant oxygen therapy.

- **Transplantation:** In some cases, a lung or heart-lung transplant may be an option, especially for younger people who have idiopathic pulmonary hypertension. Major risks of any type of transplantation include rejection of the transplanted organ and serious infection, and must take immunosuppressant drugs for life to help reduce the chance of rejection.

#### Treatment based on home and herbal remedies:

Herbal medicine has made many contributions to commercial drug preparations manufactured today herbal medicine has been losing ground to new synthetic medicines touted by scientists and physicians to be more effective and reliable . Hypertension is reported to be the fourth contributor to premature death in developed countries and the seventh in developing countries<sup>1</sup>. Recent reports indicate that nearly 1 billion adults (more than a quarter of the world's population) had hypertension in 2000, and this is predicted to increase to 1.56 billion by 2025. High blood pressure is the most common and responds well to lifestyle changes, such as losing weight, dietary changes, exercise, and stress reduction. Natural treatment of essential hypertension can bring blood pressure values into the normal range; however, if lifestyle changes are not maintained, hypertension will probably return. Secondary hypertension has an organic cause (i.e., kidney disease, pregnancy) and must be evaluated and monitored by a physician since the underlying cause must also be addressed. It often takes some time to find the best treatment for pulmonary hypertension.<sup>25</sup> The treatments are often complex and require extensive follow-up care. The best approach for patient will depend on a number of factors, including age, the type and class of pulmonary hypertension, and overall health. When pulmonary hypertension is the result of another condition, doctor will treat the underlying cause whenever possible. Although medical treatment can't cure pulmonary hypertension, it can lessen symptoms. They should also:

## Herbal Medicine

**Lime blossom (*Tilia europea*):** For treating hypertension associated with arteriosclerosis and anxiety, take an infusion. Pour one cup of boiling water onto one teaspoonful of the dried flowers; leave to infuse ten minutes, filter, and drink.

**Hawthorn (*Crataegus, various species*):** Hawthorn has been used as a heart tonic for centuries.

Make a tea by adding one teaspoon of dried hawthorn herb to cup of boiling water. Drink up to two cups a day.

**Kudzu (*Pueraria lobata*):** Chinese studies suggest that kudzu helps normalize blood pressure. When a tea containing about eight teaspoons of kudzu root was given daily to 52 people for two to eight weeks, 17 people experienced marked decline in their blood pressure. Kudzu is a powerful antioxidant. It has 100 times the antioxidant activity of vitamin E. Hence it also helps prevent heart disease and cancer.

**Garlic (*Allium sativum*):** Garlic is a wonder drug for heart. It has beneficial effects in all cardiovascular system including blood pressure. In clinical studies, garlic has been shown to decrease the systolic pressure by 20-30 mm Hg and the diastolic by 10-20 mm Hg. When people with high blood pressure were given one clove of garlic a day for 12 weeks, their diastolic blood pressure and cholesterol levels were significantly reduced. Eating quantities as small as one clove of garlic a day was found to have beneficial effects in managing hypertension.<sup>25,26,27,28</sup>

The pharmaceutical mechanism of garlic's effect on blood pressure is believed to be related to its effect on the autonomic nervous system, lipid-lowering properties and perhaps its high content of sulphur-containing compounds. Patients with high blood pressure were found to have decreased levels of sulphur-containing amino acids in their plasma.

Use garlic in your cooking, salad, soup, pickles, etc. It is very versatile.

**Saffron (*Crocus sativus*):** Saffron contains a chemical called crocetin that lowers the blood pressure. You can use saffron in your cooking. (It is a very popular spice in Arabic cooking.) You can also make a tea with it. Many Indians add a pinch of saffron in the brewed tea to give a heavenly flavour. Unfortunately, it is very expensive.

**Valerian (*Valeriana officinalis*):** Valerian is good for hypertension. It contains a chemical called valerenic acid that inhibits an enzyme that breaks down GABA. GABA (Gamma-amino butyric acid) is known to control blood pressure. Its effect on blood pressure may also be from its sedative action.

**Mistletoe (*Viscum album*):** Mistletoe is believed to function as a regulator of blood pressure, exerting a healing effect in both hypertension and hypotension. In Europe, mistletoe has often been combined with hawthorn (*crataegus*) in treating hypertension.

▪ **Get plenty of rest:** Getting ample rest can reduce the fatigue that may accompany pulmonary hypertension.

▪ **Stay as active as possible:** Even the mildest forms of activity may be too exhausting for some people with pulmonary hypertension. For others, moderate exercise such as walking may be of great benefit, and using oxygen during exercise may be especially helpful. But first, talk to the doctor about specific exercise restrictions. In most cases, it's recommended that patients not lift more than 50 pounds (22.7 kilograms). Doctor can help the patient for plan an appropriate exercise program.

▪ **Don't smoke:** If patient smoke, the single most important thing patient can do for his/her heart and lung health is to stop. If patient can't stop smoking by him/her self, ask doctor to prescribe a treatment plan to help patient quit. Also, avoid second hand smoke if possible.<sup>30,31</sup>

▪ **Avoid becoming pregnant or using birth control pills:** If patient is a woman of childbearing age, avoid becoming pregnant. Pregnancy can be life-threatening for both patient and her baby. Also avoid using birth control pills, which can increase the risk of blood clots. Talk to doctor about alternative forms of birth control.

▪ **Avoid travelling to or living at high altitudes:** High altitudes can aggravate the symptoms of pulmonary hypertension. If patients live at a high altitude, doctor may advise the patient to move to a lower elevation.

▪ **Avoid situations that can excessively lower blood pressure:** These include sitting in a hot tub or sauna or taking long hot baths or showers. These activities lower the blood pressure and cause fainting or even death. Patient should also avoid activities that cause prolonged straining, such as lifting heavy objects or weights.<sup>32</sup>

▪ **Find ways to reduce stress:** These can range from yoga, meditation and biofeedback to warm baths, music or a good book. Try to allow at least 30 minutes a day for an activity so, patient find relaxing. Many people with pulmonary hypertension find that simply reducing stress can greatly improve the quality of their lives.<sup>29,30</sup>

▪ **Follow a nutritious diet and maintain a healthy weight:** Ask your doctor for guidelines regarding salt intake. For most people with pulmonary hypertension sodium (salt) restriction will be recommended to minimize swelling of your body's tissues (edema).<sup>129</sup> Most experts agree that patient should eat no more than 1,500 to 2,400 milligrams of salt a day. Keep in mind that processed foods often are very high in salt content, so it will be important to check labels carefully

## CONCLUSION

At present, no single biochemical biomarker stands out as a 'must have' measurement for the management of pulmonary hypertension. Biochemical biomarkers are highly attractive tools for the management of pulmonary disease. For cardiovascular diseases, herbal treatments have been used in patients with congestive heart failure, systolic hypertension, angina pectoris, atherosclerosis, cerebral insufficiency, venous insufficiency, and arrhythmia. However, many herbal remedies used today have not undergone careful scientific assessment, and some have the potential to cause serious toxic effects and

major drug-to-drug interactions.<sup>33,34,35</sup> With the high prevalence of herbal use in the United States and other countries today, clinicians must inquire about such health practices for cardiac disease particularly Pulmonary hypertension and be informed about the potential for benefit and harm. Continuing research is necessary to elucidate the pharmacological activities of the many herbal remedies now being used to treat cardiovascular diseases special reference to pulmonary hypertension. We are in an era where this is an area of active research and the prospects for discovery are exciting. Success is dependent upon the availability of large cohorts of well-phenotype patients that enable not only discovery but also replication of findings in large, prospective studies. This has been achieved in other cardiovascular diseases, but is more difficult in PAH due to the relatively small number of patients available. Discovery is just the start of the journey. It is a long road to the formal acceptance of a novel biomarker by the practicing community of physicians, let alone the regulatory authorities who would need to agree that drug approval and treatment decisions can be based on such a measure. It is always likely that no single biomarker will stand alone and that any marker will need to find its place in the integrated body of data on which management decisions need to be made.

## REFERENCES

- Benowitz NL. Antihypertensive agents. In: Katzung BG, editor. Basic & Clinical Pharmacology. 8th Ed. New York: McGraw-Hill Lange; 2001. p.155-80.
- Stergiou GS, Salgami EV. New European, American and International guidelines for hypertension management: Agreement and disagreement. *Expert Rev Cardiovasc Ther* 2004;2:359-68.
- Achard JM, Fournier A, Mazouz H, Caride VJ, Penar PL, Fernandez LA. Protection against ischemia: A physiological function of the renin-angiotensin system. *Biochem Pharmacol* 2001;62:261-71.
- Kearney PM, Whelton M, Reynolds K, Munter P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. *Lancet* 2005; 365 : 217-23.
- Lawes CMM, Vander Hoorn S, Rodgers A. International Society of Hypertension. Global burden of blood-pressure-related disease, 2001. *Lancet* 2008; 371: 1513-8.
- Sanderson JE, Mayosi B, Yusuf S, Reddy S, Hu S, Chen Z, et al. Global burden of cardiovascular disease. *Heart* 2007;93 : 1175-83.
- Yusuf S, Reddy S, Ounpuu S, Anand S. Global burden of cardiovascular diseases: Part II: Variations in cardiovascular disease by specific ethnic groups and geographic regions and prevention strategies. *Circulation* 2001; 104: 2855-64.
- Gupta R. Trends in hypertension epidemiology in India. *J Hum Hypertens* 2004; 18: 73-8.
- Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Med* 2006;2011-29. Available at: <http://medicine.plosjournals.org>, accessed on May 1, 2007.
- Ernst E. "Complementary/alternative medicine for hypertension: a mini-review." *Wien Med Wochenschr.* 155.17-18 (2005): 386-391.
- Chockalingam A, Campbell NR, Fodor JG. Worldwide epidemic of hypertension. *Can J Cardiol* 2006; 22: 553-5.
- Cheung BM, Ong KL, Man YB, Lam KS, Lau CP. Prevalence, awareness, treatment, and control of hypertension: United States National Health and Nutrition Examination Survey 2001-2002. *J Clin Hypertens* (Greenwich) 2006; 8: 93-8.
- Nissinen A, Bothig S, Granroth H, Lopez AD. Hypertension in developing countries. *World Health Stat Q* 1988; 41: 141-54.
- Walker AF, Marakis G, Simpson E, Hope JL, Robinson PA, Hassanein M, Simpson HC. "Hypotensive effects of hawthorn for patients with diabetes taking prescription drugs: a randomised controlled trial." *Br J Gen Pract.* 56. 527 (2006): 437-443.
- Primates P, Poulter NR. Improvement in hypertension management in England: results from the Health Survey for England 2003. *J Hypertens* 2006; 24 : 1187-92.
- Reddy KS. Hypertension control in developing countries. Genetic issues. *J Hum Hypertens* 1996; 10: S33-8.
- Eisenberg DM, Kessler RC, Foster C, et al. Unconventional medicine in the United States. *N Engl J Med.* 1993;328:246-252.
- Ernst E: Harmless herbs? a review of the recent literature. *Am J Med.* 1998;104:170-178.
- Sutter MC, Wang YX. Recent cardiovascular drugs from Chinese medicinal plants. *Cardiovasc Res.* 1993;27:1891-1901.
- Dickinson HO, Mason JM, Nicolson DJ, Campbell F, Beyer FR, Cook JV, Williams B, Ford GA. Lifestyle interventions to reduce raised blood pressure: a systematic review of randomized controlled trials. *J Hypertens.* 24.2 (2006): 215-233.
- Dickinson HO, Nicolson DJ, Campbell F, Beyer FR, Mason J. "Potassium supplementation for the management of primary hypertension in adults." *Cochrane Database Syst Rev.* 19.3 (2006): CD004641.
- Dickinson HO, Nicolson DJ, Cook JV, Campbell F, Beyer FR, Ford GA, Mason J. Calcium supplementation for the management of primary hypertension in adults. *Cochrane Database Syst Rev.* 19.2 (2006): D004639.

24. Dickinson HO, Nicolson DJ, Campbell F, Cook JV, Beyer FR, Ford GA, Mason J. "Magnesium supplementation for the management of essential hypertension in adults." *Cochrane Database Syst Rev.* 19.3 (2006): CD004640.
25. Silagy CA, Neil HA. A meta-analysis of the effect of garlic on blood pressure. *J Hypertens.*1994;12:463-468.
26. Geleijnse JM, Giltay EJ, Grobbee DE, et al. "Blood pressure response to fish oil supplementation: metaregression analysis of randomized trials." *J Hypertens.* 20 (2002): 1493-1499.
27. He FJ, MacGregor GA. "Effect of longer-term modest salt reduction on blood pressure." *Cochrane Database Syst Rev.* 3 (2004): CD004937.
28. Hodgson JM, Watts GF, Playford DA, Burke V, Croft KD. "Coenzyme Q10 improves blood pressure and glycaemic control: a controlled trial in subjects with type 2 diabetes." *Eur J Clin Nutr.* 56.11 (2002): 1137-1142.
29. Jurgens G, Graudal NA. "Effects of low sodium diet versus high sodium diet on blood pressure, renin, aldosterone, catecholamines, cholesterols, and triglyceride." *Cochrane Database Syst Rev.* 1(2004): CD004022.
30. Linden W, Moseley JV. "The efficacy of behavioral treatments for hypertension." *Appl Psychophysiol Biofeedback.* 31.1 (2006): 51-63.
31. Mangoni AA, Sherwood RA, Swift CG, Jackson SH. "Folic acid enhances endothelial function and reduces blood pressure in smokers: a randomized controlled trial." *J Intern Med.* 252.6 (2002): 497-503.
32. Mori TA, Bao DQ, Burke V, et al. "Docosahexaenoic acid but not eicosapentaenoic acid lowers ambulatory blood pressure and heart rate in humans." *Hypertension.* 43 (1999): 253-260.
33. Williams C, Kingwell BA, Burke K, McPherson J, Dart AM. Folic acid supplementation for 3 wk reduces pulse pressure and large artery stiffness independent of MTHFR genotype. *Am J Clin Nutr.* 82.1 (2005): 26-31.
34. UNESCO (1996). *Culture and Health, Orientation Texts – World Decade for Cultural Development 1988 – 1997, Document CLT/DEC/PRO – 1996, Paris, France, pgs. 129.*
35. UNESCO (1998). *FIT/504-RAF-48 Terminal Report: Promotion of Ethnobotany and the Sustainable Use of Plant Resources in Africa, pgs. 60, Paris, 1998.*

\*\*\*\*\*