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Review Article

AN OVERVIEW OF MANAGEMENT OF HYPERTENSION WITH ANGIOTENSIN-CONVERTING ENZYME INHIBITORS

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ABSTRACT

Blockage of the renin-angiotensin system (RAS) is now recognized as an effective approach to the treatment of hypertension and congestive heart failure. Today, it is possible to antagonize the effects of angiotensin II (AT-II) more specifically by blocking its receptors by using non peptide receptor antagonists. AT-II-receptor antagonists were developed as agents that would more completely block the RAS and thus decrease the adverse effects seen with Angiotensin Converting Enzyme (ACE inhibitors). AT-II-receptor antagonists include losartan, valsartan, irbesartan, candesartan, eprosartan and telmisartan. The adverse effects of AT-II-receptor antagonists dizziness, headache, upper-respiratory- tract infection, cough, and gastrointestinal disturbances occur at about the same rate as with placebo. Four of them have recently been launched on the market and several others are preregistered for the treatment of hypertension. These new molecules are as effective as ACE inhibitors, calcium antagonists and beta-blockers in lowering blood pressure in hypertensive patients. When compared to ACE inhibitors, they appear to have comparable favorable effects on systemic and renal hemodynamic properties. All available AT-II-receptor antagonists seem to be equally effective in reducing both systolic and diastolic blood pressure. Currently, AT-II-receptor antagonists are used either as mono therapy in patients who cannot tolerate ACE inhibitors or in combination with other antihypertensive agents. In this review we summarize the combined therapy of ACE inhibitors and AT-IIreceptor antagonists play in ischemic heart disease.

KEYWORDS: Renin-angiotensin system, Hypertension, Angiotensin II receptor, Angiotensin Converting Enzyme inhibitors

1. INTRODUCTION

ACE inhibitors, or inhibitors of **A**ngiotensin-**C**onverting **E**nzyme, are a group of pharmaceuticals that are used primarily in treatment of hypertension and congestive heart failure, in some cases as the drugs of first choice. [1, 2]

The first step in the development of (ACE) inhibitors was the discovery of angiotensin converting enzyme (ACE) in plasma by Leonard T. Skeggs and his colleagues in 1956. The conversion of the inactive angiotensin I to the potent angiotensin II was thought to take place in the plasma. However, in 1967, Kevin K. F. Ng and John R. Vane showed that the plasma (ACE) was too slow to account for the conversion of angiotensin I to angiotensin II *in vivo*. Subsequent investigation showed that rapid conversion occurs during its passage through the pulmonary circulation. [3-4]

Bradykinin is rapidly inactivated in the circulating blood and it disappears completely in a single passage through the pulmonary circulation. Angiotensin I also disappears in the pulmonary circulation due to its conversion to angiotensin II. Furthermore, angiotensin II passes through the lungs without any loss. The inactivation of bradykinin and the conversion of angiotensin I to angiotensin II in the lungs were thought to be caused by the same enzyme. In 1970, Ng and Vane using bradykinin potentiating factor (BPF) provided by Sérgio Henrique Ferreira showed that the conversion of angiotensin I to angiotensin II was inhibited during its passage through the pulmonary circulation. [5]

Bradykinin potentiating factor (BPF) is derived from the venom of the pit viper (*Bothrops jararaca*). It is a family of peptides and its potentiating action is linked to inhibition of bradykinin by ACE. Molecular analysis of BPF yielded a nonapeptide BPF teprotide (SQ 20,881) which showed the greatest (ACE) inhibition potency and hypotensive effect *in vivo*. Teprotide had limited clinical value, due to its peptide nature and

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lack of activity when given orally. In the early 1970s, knowledge of the structure-activity relationship required for inhibition of ACE was growing. David Cushman, Miguel Ondetti and colleagues used peptide analogues to study the structure of ACE, using carboxypeptidase A as a model. Their discoveries led to the development of captopril, the first orally-active ACE inhibitor in 1975. [4]

Captopril was approved by the United States Food and Drug Administration in 1981. The first non-sulfhydryl-containing (ACE) inhibitor enalapril was marketed two years later. Since then, at least twelve other ACE inhibitors have been marketed.

2. RENIN ANGIOTENSIN SYSTEM:

The **renin-angiotensin system** (RAS) [8-10] or the **renin-angiotensin-aldosterone system** (RAAS) is a hormone system that regulates blood pressure and water (fluid) balance.

When blood volume is low, the kidneys secrete renin. Renin stimulates the production of angiotensin. Angiotensin causes blood vessels to constrict resulting in increased blood pressure. Angiotensin also stimulates the secretion of the hormone aldosterone from the adrenal cortex. Aldosterone causes the tubules of the kidneys to retain sodium and water. This increases the volume of fluid in the body, which also increases blood pressure.
If the renin-angiotensin-aldosterone system is too active, blood pressure will be too high. There are many drugs which interrupt different steps in this system to lower blood pressure. These drugs are one of the main ways to control high blood pressure (hypertension), heart failure, kidney failure, and harmful effects of diabetes.

2.1. Activation

The system can be activated when there is a loss of blood volume or a drop in blood pressure (such as in hemorrhage). [2-4]

1. If the perfusion of the juxtaglomerular apparatus in the kidneys decreases, then the juxtaglomerular cells release the enzyme renin.
2. Renin cleaves an inactive peptide called *angiotensinogen*, converting it into *angiotensin I*. [1,3,7]
3. Angiotensin I is then converted to *angiotensin II* by angiotensin-converting enzyme (ACE) which is found mainly in lung capillaries.
4. Angiotensin II is the major bioactive product of the renin-angiotensin system. Angiotensin II acts as an endocrine, autocrine/ paracrine, and intracrine hormone. [19]
5. Patil Jaspal et al. have shown local synthesis of Angiotensin II in neurons of sympathetic ganglia.

2.2. Effects

It is believed that Angiotensin I may have some minor activity, but angiotensin II is the major bio-active product. Angiotensin II has a variety of effects on the body: [11-17]

- Throughout the body, it is a potent vasoconstrictor of arterioles.
- In the kidneys, it constricts glomerular arterioles, having a greater effect on efferent arterioles than afferent. As with most other capillary beds in the body, the constriction of afferent arterioles increases the arteriolar resistance, raising systemic arterial blood pressure and decreasing the blood flow. However, the kidneys must continue to filter enough blood despite this drop in blood flow, necessitating mechanisms to keep glomerular blood pressure up. To do this, Angiotensin II constricts efferent arterioles, which forces blood to build up in the glomerulus, increasing glomerular pressure. The glomerular filtration rate (GFR) is thus maintained, and blood filtration can continue despite lowered overall kidney blood flow.
- In the adrenal cortex, it acts to cause the release of aldosterone. Aldosterone acts on the tubules (e.g the distal convoluted tubules and the cortical collecting ducts) in the kidneys, causing them to reabsorb more sodium and water from the urine. Potassium is secreted into the tubules in exchange for the sodium, which is excreted. Aldosterone also acts on the central nervous system to increase an individual's appetite for salt, and to stimulate the sensation of thirst.
- Release of Anti-Diuretic Hormone (ADH), also called vasopressin - ADH is made in the hypothalamus and released from the posterior pituitary gland. As its name suggests, it also exhibits vaso-constrictive properties, but its main course of action is to stimulate reabsorption of water in the kidneys.

These effects directly act in concert to increase blood pressure.
The renin-angiotensin system is often manipulated clinically to treat high blood pressure.

- Inhibitors of angiotensin-converting enzyme (ACE inhibitors) are often used to reduce the formation of the more potent angiotensin II. Captopril is an example of an ACE inhibitor.
- Alternatively, angiotensin receptor blockers (ARBs) can be used to prevent angiotensin II from acting on angiotensin receptors.
- Direct renin receptor inhibitors are aliskiren[5] and the investigational remikiren[6].
- As of November 2008, a vaccination against angiotensin II, codenamed CYT006-AngQb, is undergoing clinical trials.

2.3. Effects of ACE inhibitors:

Mechanism of action

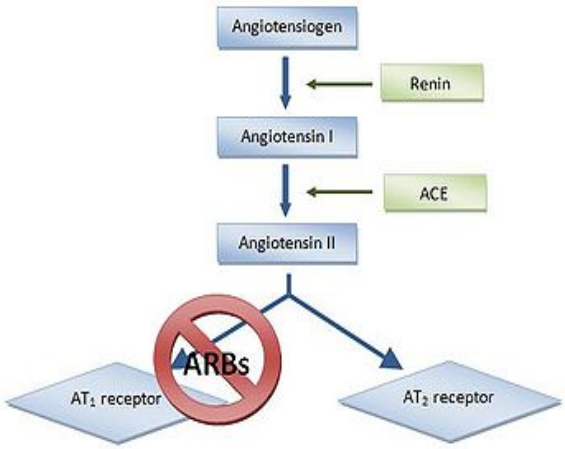

Figure 1: Renin angiotensin pathway

Blood pressure and fluid and electrolyte homeostasis is regulated by the renin-angiotensin-aldosterone-system.[1] Renin, an enzyme released from the kidneys, converts the inactive plasma protein angiotensinogen into angiotensin I (Ang I). Then Ang I is converted to Ang II with angiotensin converting enzyme (ACE). Ang II in plasma then binds to AT-receptors.

ARBs are blocking the last part of the renin-angiotensin pathway and block the pathway more specifically than ACE inhibitors.

The AT_1 receptor mediates Ang II to cause increased cardiac contractility, sodium reabsorption and vasoconstriction which all lead to increased blood pressure. By blocking AT_1 receptors, ARBs lead to lower blood pressure.

An insurmountable inhibition of the AT_1 receptor is achieved when the maximum response of Ang II cannot be restored in the presence of the ARB, no matter how high the concentration of Ang II is. The angiotensin receptor blockers can inhibit the receptor in a competitive surmountable, competitive insurmountable or noncompetitive fashion, depending upon the rate at which they dissociate from the receptor.

ACE inhibitors lower arteriolar resistance and increase venous capacity; increase cardiac output and cardiac index, stroke work and volume, lower renovascular resistance, and lead to increased natriuresis (excretion of sodium in the urine).

Normally, angiotensin II will have the following effects: (13-16)

- vasoconstriction (narrowing of blood vessels), which may lead to increased blood pressure and hypertension
- Specifically, angiotensin II constricts the efferent arterioles of the kidney, leading to increased perfusion pressure in the glomeruli.
- Ventricular remodeling of the heart, which may lead to ventricular hypertrophy and CHF
- Stimulate the adrenal cortex to release aldosterone, a hormone that acts on kidney tubules to retain sodium and chloride ions and excrete potassium. Sodium is a "water-holding" molecule, so water is also retained, which leads to increased blood volume, hence an increase in blood pressure.
- Stimulate the posterior pituitary into releasing vasopressin (also known as anti-diuretic hormone (ADH)) which also acts on the kidneys to increase water retention.
- decrease renal protein kinase C

With ACE inhibitor use, the effects of angiotensin II are prevented, leading to decreased blood pressure.

Epidemiological and clinical studies have shown that ACE inhibitors reduce the progress of diabetic nephropathy independently from their blood pressure-lowering effect. This action of ACE inhibitors is utilised in the prevention of diabetic renal failure.

ACE inhibitors have been shown to be effective for indications other than hypertension even in patients with normal blood pressure. The use of a maximum dose of ACE inhibitors in such patients (including for prevention of diabetic nephropathy, congestive heart failure, prophylaxis of cardiovascular events) is justified because it improves clinical outcomes,

independent of the blood pressure lowering effect of ACE inhibitors. Such therapy, of course, requires careful and gradual titration of the dose to prevent the effects of rapidly decreasing blood pressure (dizziness, fainting, *etc*).

3. Classicfication: [5, 15-20]

ACE inhibitors can be divided into three groups based on their molecular structure:

Sulfhydryl-containing agents

- Captopril (trade name Capoten), the first ACE inhibitor
- Zofenopril

Dicarboxylate-containing agents

This is the largest group, including:

- Enalapril (Vasotec/Renitec)
- Ramipril (Altace/Tritace/Ramace/Ramiwin)
- Quinapril (Accupril)
- Perindopril (Coversyl/Aceon)
- Lisinopril (Lisodur/Lopril/Novatec/Prinivil/Zestril)
- Benazepril (Lotensin)

Phosphonate-containing agents

- Fosinopril (Monopril) is the only member of this group

Naturally occurring

Casokinins and lactokinins are breakdown products of casein and whey that occur naturally after ingestion of milk products, especially cultured milk. Their role in blood pressure control is uncertain. The tripeptides Val-Pro-Pro and Ile-Pro-Pro produced by the probiotic Lactobacillus helveticus have been shown to have ACE-inhibiting and antihypertensive functions.

4. Adverse effects associated with ACE Inhibitors:

Common adverse drug reactions [17-20] (less than 1% of patients) include: hypotension, cough, hyperkalemia, headache, dizziness, fatigue, nausea, renal impairment.

A persistent dry cough is a relatively common adverse effect believed to be associated with the increases in bradykinin levels produced by ACE inhibitors, although the role of bradykinin in producing these symptoms remains disputed by some authors. Patients who experience this cough are often switched to angiotensin II receptor antagonists.

Rash and taste disturbances, infrequent with most ACE inhibitors, are more prevalent in captopril and is attributed to its sulfhydryl moiety. This has led to decreased use of captopril in clinical setting, although it is still used in scintigraphy of the kidney.

Renal impairment is a significant adverse effect of all ACE inhibitors. The reason for this is still unknown. Some suggest that it is associated with their effect on angiotensin II-mediated homeostatic functions such as renal blood flow. Renal blood flow may be affected by Angiotensin II because it vasoconstricts the efferent arterioles of the glomeruli of the kidney, thereby increasing glomerular filtration rate (GFR). Hence, by reducing angiotensin II levels, ACE inhibitors may reduce GFR, a marker of renal function. However this is actually untrue as whilst the efferent arteriole is more relaxed, so too is the afferent arteriole which acts to increase GFR in a compensatory manner. Specifically, ACE inhibitors can induce or exacerbate renal impairment in patients with renal artery stenosis. This is especially a problem if the patient is also concomitantly taking an NSAID and a diuretic - the so-called "triple whammy" effect - such patients are at very high risk of developing renal failure.

ACE inhibitors may cause hyperkalemia. Suppression of angiotensin II leads to a decrease in aldosterone levels. Since aldosterone is responsible for increasing the excretion of potassium, ACE inhibitors ultimately cause retention of potassium.

A severe allergic reaction can occur that rarely can effect the bowel wall and secondarily cause abdominal pain. This "anaphylactic" reaction is very rare as well.

Some patients develop angioedema due to increased bradykinin levels. There appears to be a genetic predisposition towards this adverse effect in patients who degrade bradykinin slower than average.

5. Clinical use:

Indications for ACE inhibitors include: (12, 19-23)

- Prevention of cardiovascular disorders
- Congestive heart failure (CHF)
- Hypertension
- Left ventricular dysfunction
- Prevention of nephropathy in diabetes mellitus

In several of these indications, ACE inhibitors are used first-line as several agents in the class have been clinically shown to be superior to other classes of drugs in the reduction of morbidity and mortality.

ACE inhibitors are often combined with diuretics in the control of hypertension (usually a thiazide), when an ACE inhibitor alone proves insufficient; and in chronic heart failure (usually furosemide) for improved symptomatic control. Thus there exist, on the market, combination products combining an ACE inhibitor with a thiazide (usually hydrochlorothiazide) in a single tablet to allow easy administration by patients.

6. General Properties of ACE Inhibitors (4, 15, 22-16)

6.1. Lisinopril (Prinivil)

General Uses

Lisinopril (Prinivil - the brand name) is a drug used for treating high blood pressure and other ailments that deal with the circulatory system. It works by decreasing certain chemicals that tighten the blood vessels, so blood flows more smoothly and the heart can pump blood more efficiently. Specifically, the effects of "loosening" the blood vessels can aid in ways other than easing high blood pressure. Lisinopril can also treat congestive heart failure and improve a patient's chances for survival after a heart attack.

Potential Problems

Lisinopril is in a class of drugs called ACE Inhibitors, which have been found to carry several dangerous side effects in recent studies. If you are not pregnant, lisinopril can cause heavy sweating, vomiting, diarrhea, or other types of fluid loss that may lead to very low blood pressure, dizziness, and fainting.

The consequences of taking this drug while pregnant are even worse, as ACE Inhibitors have been shown to cause serious birth defects in unborn children, specifically to their brains and hearts, and can also cause fetal death.

If you've suffered any consequences as a result of taking this drug, see your doctor and contact an attorney immediately.

6.2. Benazepril (Lotensin)

Intended Uses and Benefits

Benazepril is a generic form of an ACE Inhibitor, which is a class of drugs manufactured and prescribed primarily for the treatment of high blood pressure and hypertension. ACE Inhibitors tend to reduce the amount of chemicals in the human body that work against the circulatory system by narrowing blood vessels, making it much more difficult for blood to flow smoothly to and from the heart.

Typically, the long term result of this narrowing of blood vessels can lead to high blood pressure, heart attacks and even strokes. ACE Inhibitors also tend to help patients recover from a heart attack by minimizing the structural damage done to the heart immediately after an attack.

Inherent Risks

Although ACE Inhibitors hit the market with much fanfare, studies have shown that there are substantial risks involved with this class of medication. Side effects in typical patients range from minor to severe, particularly if there is an allergic reaction. These side effects include dizziness, coughing, loss of the sense of taste and swelling in the throat and facial areas.

Pregnant women are taking on potentially grave danger if they use an ACE Inhibitor. Many authorities have discovered that ACE Inhibitors can lead to serious birth defects that involve unspeakable damage to the child's brain and heart, and many instances have shown that ACE Inhibitors can lead to fetal death.

If you have suffered as a result of taking an ACE Inhibitor, you only have a certain amount of time to take action. In order to make sure that your rights are protected and asserted, contact an experienced attorney today.

6.3. Captopril (Capoten)

General Uses

Captopril is a generic drug that belongs to a class of medications called ACE Inhibitors. Its main purpose is to help treat patients with high blood pressure, hypertension or those who have recently suffered heart attacks. The specific function it performs is to eliminate and/or minimize the chemicals in the human body that narrow the blood vessels, as this narrowing phenomenon makes it much more difficult for blood to circulate.

If blood cannot circulate, it creates an untenable amount of stress on the heart, and the consequences of this condition are severe. Narrow blood vessels can directly lead to heart attacks and strokes, and many of each is fatal, if not completely debilitating.

Risks Involved

Unfortunately, several studies in recent years have created a high level of concern regarding the use of ACE Inhibitors. In regards to side effects, patients can suffer from such conditions as a persistent, hacking cough, spells of dizziness, loss of the sense of taste, swelling in the throat, neck and face and many other previously unforeseen consequences.

The greatest risk involves pregnant women. Additional studies have shown that the risk of birth defects nearly doubles in pregnant women who are taking ACE Inhibitors. These birth defects generally destroy the fetus' brain and/or heart. There are also several instances on record where the fetus has died in the womb.

6.4. Ramipril (Altace)

General Use

Ramipril (Altace - Brand Name) is used for the treatment of hypertension.

Potential Problems

Taking Ramipril may cause a variety of adverse reactions depending on your age and health history. Head and neck angioedema can result after taking this drug. This can be a serious side effect since swelling of the tongue or throat can cause airway blockages and difficulty in breathing.

A patient taking Ramipril may also experience impaired renal function, hyperkalemia, cough, or impaired liver functions.

This drug, as for many ACE (angiotensin converting enzyme) Inhibitors should not be taken during pregnancy. Cease use of Ramipril upon detecting pregnancy. Taking Ramipril during pregnancy creates risk of injury or death to the developing fetus.

If you have experienced any adverse reaction or had any issues with your pregnancy after or during your use of Ramipril, you need to contact your physician and contact an attorney as soon as possible.

6.5. Trandolapril (Mavik)

Uses and Potential Benefits

Trandolapril is a generic form of a drug that fits into the medical class of medication known as angiotensin-converting enzyme inhibitors, or "ACE" Inhibitors. ACE Inhibitors reduce the amount of angiotensin in the body, which is a benefit because this chemical tends to narrow the blood vessels. Narrower blood vessels increase blood pressure, as the blood has less space in which to travel to get to and from the heart as part of a properly-functioning circulatory system.

The consequences of having narrow blood vessels and increased blood pressure is that this added stress on the body can ultimately lead to serious medical events, such as a heart attack and/or a stroke when not enough blood is reaching these vital areas.

Problems Recently Discovered

Even though early results with ACE Inhibitors were encouraging, recent research has uncovered serious, or sometimes even grave, consequences for those taking ACE Inhibitors. Pregnant women were particularly vulnerable, as ACE Inhibitors are suspected of causing a number of serious side effects. A general rule is that a pregnant woman should not take these drugs.

The result of taking these medications by pregnant women is either serious, irreversible birth defects in the form of damaged hearts and brains of the children or even death. Even more research has shown that regardless of the trimester, these drugs can pose a significant threat to the unborn child.

If you have suffered as a result of taking an ACE Inhibitor, you only have a pre-defined amount of time to protect your rights. Therefore, you're taking an enormous and unnecessary risk by not contacting an attorney immediately.

6.6. Capoten

General Use

Capoten is an ACE (angiotensin converting enzyme) Inhibitor drug used to treat hypertension.

Potential Problems

Capoten's has side effects related to renal, hematological, and dermatological functions. Patients using this ACE inhibitor have had renal insufficiency or renal failure, nephritic syndrome, polyuria, oliguria, and urinary frequency. Some patients

suffered other side effects such as anemia, rashes, and fever.

Patients taking Capoten also experienced angioedma which is swelling involving lips, tongue, face, mucous membranes, glottis or larynx. This can be serious since airway swelling can cause difficulty in breathing. Never take Capoten while pregnant or nursing. As with other ACE Inhibitors, Capoten is known to cause injury or death to a fetus if taken during the second and third trimester of pregnancy. Discontinue use of Capoten immediately upon detection of pregnancy.
Contact your physician and an attorney immediately, if you have experienced any of these or other adverse side effect or used Capoten during pregnancy.

6.7. Lotensin

General Use

Lotensin is a drug that is used to lower your blood pressure. Lotensin relaxes arteries that will lower blood pressure, but also help improve the pumping of a failing heart and improve cardiac output with those with heart failure.Lotensin can also be used to treat congestive heart failure.

Potential Problems

ACE (angiotensin converting enzyme) Inhibitors like Lotensin can cause severe side effects like swelling of the facial tissue and upper airways leading to serious breathing difficulties. Although rare, other serious side effects include abdominal pain, constipation, diarrhea, dizziness, loss of taste, headache, loss of appetite, fatigue, nausea, chest pain, vomiting, chills, fainting, fever, breathing difficulties, numbness or tingling in the hands or feet, rash, or a sore/swollen throat.

Using Lotensin during the second and third trimester of pregnancy can result in injury or even death to the developing baby. If you are pregnant, nursing, or think you may be pregnant, discontinue use of Lotensin as soon as possible.

Treatment under Lotensin can also cause a mild side effect such as a dry, persistent cough which resolves after you stop taking the drug

If you have experienced any of these side effects or experienced any issues with your pregnancy while taking Lotensin, consult with your physician and contact an attorney immediately.

6.8. Vasotec

General Use

Vasotec is a drug that lowers your blood pressure by allowing the production of angiotensin II, thereby relaxing the arteries. Relaxed arteries will not only lower blood pressure, but help improve the pumping of a failing heart and improve cardiac output in people with heart failure.
Vasotec can be used alone to treat high blood pressure. In addition, Vasotec is useful for treating congestive heart failure. [12]

Potential Problems

If you have a known allergy to ACE (angiotensin converting enzyme) Inhibitors, do not take this drug. On very rare occasions, ACE Inhibitors like Vasotec can cause swelling of the facial tissue and upper airways leading to serious breathing difficulties.
Patients with severe heart failure or a pre-existing kidney disease can incur further damage to kidney functions while taking this drug.

Do not take Vasotec while pregnant or nursing.
Using Vasotec has mild side effects such as a dry, persistent cough which resolves after you stop taking the drug. However, although rare, there are more serious side effects which include abdominal pain, constipation, diarrhea, dizziness, loss of taste, headache, loss of appetite, fatigue, nausea, chest pain, vomiting, chills, fainting, fever, breathing difficulties, numbness or tingling in the hands or feet, rash, or sore/swollen throat.

6.9. Aceon

General Use

Aceon is an ACE (angiotensin converting enzyme) Inhibitor drug that is used to lower high blood pressure and reduce the risk of cardiovascular mortality or non-fatal hear attacks.

Potential Problems

Taking Aceon may increase the risk of dangerous allergic reactions such as swelling of your lips or throat. This may result in difficulty in breathing.
Aceon can cause dizziness or drowsiness. Using Aceon can also cause dehydration since its side effects include heavy sweating, vomiting, or diarrhea.
Do not take Aceon if you are pregnant or think you may be pregnant. Aceon is known to cause injury or

death to the developing baby while taken during the second and third trimesters of pregnancy.
If you experienced any adverse reaction or were pregnant during treatment under Aceon, you need to contact your physician and contact an attorney as soon as possible.

6.10. Accupril

General Use

Accupril is an ACE (angiotensin converting enzyme) Inhibitor drug used for treating hypertension (high blood pressure) and congestive heart failure.

Potential Problems

Accupril can cause a variety of serious side effects including dehydration. Since you may experience heavy sweating, vomiting, diarrhea, or other causes of fluid loss, take plenty of fluids to prevent dehydration. Other side effects may include but are not limited to dizziness or drowsiness.

There is an increased risk of dangerous allergic reactions while taking Accupril. These allergic reaction symptoms could include swelling of the lips, face, and tongue. You may also experience difficulty in breathing.
Accupril is known to cause injury or even death to an unborn baby when used during the second and third trimesters of pregnancy. Do not take Accupril if you are pregnant or could become pregnant.
If you were pregnant while taking treatment under Accupril or experienced any other side effects, contact a physician and an attorney as soon as possible.

6.11. Univasc

General Use

Univasc is used to treat hypertension (high blood pressure).

Potential Problems

There are several serious side effects that can result from taking Univasc, including allergic reactions. These could include the closing of the throat, swelling of the face, lips or tongue, or hives. You may experience dizziness, fainting, little to no urine, chest pain, or irregular/changes in your heartbeat. You should also be wary of any sign of an infection that would include symptoms of a sore throat and/or fever. [17, 21]

Univasc is known to cause injury or even death to a developing fetus when used during the second and third trimesters of pregnancy. Do not take Univasc if you are pregnant or could become pregnant.
If you have experienced any serious side effect or used Univasc while pregnant, contact your physician and attorney immediately.

6.12. Mavik

General Uses

Mavik is a drug that's a member of the class of medication called ACE Inhibitors, and these drugs are generally used to help patients deal with hypertension, high blood pressure, recovery from heart attacks and in some cases diabetes.
In a physiological sense, Mavik and other ACE Inhibitors help to decrease the amount of chemicals in the body that tend to tighten blood vessels, as tighter blood vessels make it more difficult for blood to flow freely, thereby creating a higher blood pressure. ACE Inhibitors have also been shown to help patients recover from heart attacks by reducing the amount of damage that's done to the heart as a result of the attack.

Risks Involved

Studies have shown that there are substantial risks involved with taking ACE Inhibitors. Among them are side effects that include coughing, dizziness, skin rashes, swelling of the face, neck and throat and an increase in the level of potassium in the blood.
The risks are most substantial in pregnant women. ACE Inhibitors have shown a tendency to greatly increase the risk of birth defects and prenatal death. These birth defects, if the child survives, include serious and irreparable damage to the child's heart and brain and the systems surrounding these organs.
If you have suffered as a result of taking ACE Inhibitors, you have no time to waste - contact an attorney today to see if you have a claim against the manufacturer as a result of the damages you suffered. There's only a certain amount of time available to assert your claim, so time is of the essence.

6.13. Monapril

General Uses

Monapril is a prescription drug that belongs to the class of medications called ACE Inhibitors. ACE

Inhibitors are drugs that are designed to help patients suffering from high blood pressure, hypertension, recent heart attacks and even diabetes.

ACE Inhibitors are designed to reduce the amount of chemicals produced by the body that have the effect of narrowing blood vessels. Narrow blood vessels, in essence, create a smaller space for blood to circulate, thereby increasing blood pressure. Increased blood pressure creates several potential problems, including much higher risks for heart attacks, kidney problems and strokes.

6.14. Aliskiren: a novel renin inhibitor for hypertension.

Hypertension is one of the major causes of cardiovascular morbidity. Most patients who are on treatment for hypertension fail to achieve adequate control with the existing therapy and rates of cardiovascular morbidity remain high. As the renin-angiotensin-aldosterone system is strongly implicated in the development of hypertension-related target organ damage, intensive efforts have been devoted towards the development of drugs targeting this system. In addition to angiotensin converting enzyme inhibitors and angiotensin receptor blockers, inhibition of renin has also become a clinical reality. Aliskiren, a novel renin inhibitor, has overcome a number of shortcomings of existing drugs and is now available to address angiotensin production directly at its rate-limiting step.

CONCLUSION:

Angiotensin II antagonists signify a key new advance in the management of hypertension and probably congestive heart failure and chronic renal failure. These agents are very effective in lowering blood pressure and present a unique tolerability profile. Additional studies are now necessary to evaluate their impact on the long-termmorbidity and mortality of patients with various cardiovascular diseases. Several large trials are underway in various populations. The LIFE study (Losartan Intervention for End-point reduction in hypertension) is evaluating the effect of losartan on cardiovascular morbidity and mortality in hypertensive patients and the RENAAL study examine the renal protective effect of losartan in patients with type II diabetes. The ELITE trial (Evaluation of Losartan in the Elderly) has compared the safety and efficacy of losartan and captopril in elderly patients with heart failure.

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