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A Current Review on Animal Screening Methods of Anti-Hypertensive Drugs

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Abstract
Hypertension is a major factor in heart attack, stroke, and kidney failure-related death or disability. The evaluation of antihypertensive medications and the aetiology, pathophysiology, implications, and treatment of hypertension have all benefited greatly from the use of experimental animal models. Genetically hypertensive rats come in a variety of strains these days, and most labs employ these models to study hypertension therapeutically. In-Vitro Animal Models provides a concise summary of the traits, importance, and traditional and genetic models of hypertension in animals. Three models exist for hypertension: transgenic models, chronic nitric oxide inhibition-induced hypertension, and monkey hypertension model (renin inhibition in monkeys). The most common animal models, their traits, and their importance are briefly summarised in this article on experimental models of hypertension, both traditional and genetic.

Keywords: Heart attack, Hypertension, Fatigue, Heart, Anti-hypertensive drugs

I. INTRODUCTION

Hypertension, sometimes referred to as high blood pressure, is a chronic medical disorder characterized by a continuously raised blood pressure within the arteries [1]. Typically, hypertension is asymptomatic [2]. However, it poses a significant risk for cardiovascular disease, peripheral artery disease, Alzheimer, tachycardia, cardiac arrest, cerebral infarction, a chronic renal condition, and peripheral arterial diseases [3-5]. Globally, one of the main causes of early mortality is hypertension. Initial (critical) hypertension and second-degree hypertension are two categories for high blood pressure [6]. Most cases between 93 to 96 % are initial, which is high blood pressure brought on by a non-specific lifestyles and genes. Dietary habits that raise the possibility involve eating too much sodium, being overweight, smoking, not exercising, and drinking beer 6]. Another 5–10% of scenes are classified as second-degree hypertension, which is high blood pressure brought on by an obvious reason, such as the intake of contraceptives, renal artery constriction, chronic renal failure, or a hormonal problem [6]. Systolic (higher level) and diastolic (fewer level) readings of blood pressure are used to classify hypertension [1]. Many people have average resting hypertension, which ranges from between 60 and 80 mmHg diastolic and 100 to 130 mmHg systolic. Medicine and lifestyle modifications can reduce hypertension and lessen the possibility of medical problems. A healthier nutrition, reduced alcohol consumption, losing weight, fitness, and reduced use of salt are examples of modifications to lifestyles [6-7]. Medicines for hypertension are prescribed if lifestyle modifications are insufficient. Worldwide, about 16 to 37% of people suffer from arterial hypertension [7].

SCREENING METHODS OF HYPERTENSION

The identification of people with elevated pressure by screening techniques is essential for quick diagnosis and care to avoid problems.

IN VIVO SCREENING MODELS

A) ACUTE RENAL HYPERTENSION IN RATS [8]

RATIONALE

The induction of acute renal hypertension in rats is a common experimental approach aimed at

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understanding the immediate effects of elevated blood pressure on renal function. This model allows researchers to investigate the pathophysiological changes that occur in the kidneys in response to a sudden increase in blood pressure. Understanding the acute responses is crucial for elucidating the early mechanisms involved in hypertensive kidney injury and for the development of potential therapeutic interventions [8].

PRINCIPLE

The principle of inducing acute renal hypertension involves raising the blood pressure rapidly and studying the immediate impact on renal hemodynamics, filtration, and other functional parameters. Various methods can be employed, such as the administration of vasoconstrictors like angiotensin II or norepinephrine, or through renal artery manipulation. These approaches trigger a quick and controlled increase in blood pressure, allowing researchers to observe and measure immediate changes in renal function

PROCEDURE

a) Animal Preparation

- Use healthy adult rats, preferably of a standardized strain.
- Ensure ethical compliance and obtain necessary approvals.
- Fast the rats for an appropriate duration before the experiment.

b) Anesthesia And Surgical Preparation

- Anesthetize the rats using an appropriate anesthetic agent.
- Secure the rat on a surgical platform, ensuring proper maintenance of body temperature.
- Perform aseptic surgery to expose the renal arteries or for the administration of vasoconstrictors.

c) Induction Of Acute Hypertension

- Administer vasoconstrictors (e.g., angiotensin II or norepinephrine) intravenously or through other routes.
- Alternatively, induce acute hypertension by renal artery clamping or other surgical manipulations.

d) Blood Pressure Monitoring

- Continuously monitor blood pressure using appropriate techniques (e.g., telemetry, intra-arterial catheterization, or tail-cuff methods).

e) Renal Function Assessments

- Measure parameters such as glomerular filtration rate (GFR), urine output, urinary protein excretion, and other markers of renal function.
- Use clearance techniques or biomarkers to assess renal function.

f) Histological Examination

- Collect renal tissue samples for histological examination to observe immediate changes in renal architecture, such as glomerular and tubular alterations.

g) Hemodynamic Measurements

- Assess hemodynamic parameters, including renal blood flow, vascular resistance, and renal perfusion pressure.

h) Data Collection

- Record data at specific time points to capture the dynamic changes induced by acute hypertension.
- Include control groups for comparison [8].

EXPECTED RESULTS

The results of inducing acute renal hypertension in rats may include:

a) Immediate Changes in Blood Pressure

Rapid elevation in systemic blood pressure.

b) Renal Hemodynamic Alterations

Changes in renal blood flow and perfusion pressure.

c) Functional Changes

Immediate alterations in glomerular filtration rate, urine output, and other renal function parameters

d) Histological Changes

Evidence of acute injury, such as glomerular congestion, tubular dilation, or vascular changes.

e) Hemodynamic Responses

Changes in systemic and renal hemodynamics, such as increased vascular resistance.

B) CHRONIC RENAL HYPERTENSION IN RATS [9]

RATIONALE

The induction of chronic renal hypertension in rats serves as a valuable model to study the long-term effects of sustained elevated blood pressure on renal function and structure. This model is particularly relevant for understanding the progression of hypertensive kidney injury, mimicking conditions seen in chronic hypertension in humans. Investigating chronic responses provides insights into the development and progression of renal damage, aiding in the identification of potential therapeutic interventions [9].

PRINCIPLE

The principle of inducing chronic renal hypertension involves maintaining elevated blood pressure over an extended period. This can be achieved through various methods, such as the two-kidney, one-clip (2K1C) model, chronic angiotensin II infusion, or other approaches that result in sustained

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hypertension. The focus is on studying the long-term consequences on renal hemodynamics, function, and morphology [9].

PROCEDURE

a) Animal Preparation

- Use healthy adult rats, preferably of a standardized strain.
- Obtain ethical approvals for the study.

b) Anesthesia And Surgical Preparation

- Anesthetize the rats using appropriate agents.
- Perform aseptic surgery for the chosen method of inducing chronic hypertension.

c) Induction Of Chronic Hypertension

- Perform renal artery clipping (2K1C model) or administer agents like angiotensin II chronically to sustain elevated blood pressure.
- Ensure continuous or periodic monitoring to maintain hypertensive conditions.

d) Blood Pressure Monitoring

- Regularly monitor blood pressure using appropriate techniques (telemetry, intra-arterial catheterization, or tail-cuff methods).

e) Renal Function Assessments

- Periodically assess key parameters such as glomerular filtration rate (GFR), urine output, and urinary protein excretion to track long-term changes in renal function.

f) Histological Examination

- Collect renal tissue samples at various time points for histological examination to observe chronic changes in renal architecture, such as fibrosis, glomerulosclerosis, and interstitial damage.
- Stain tissues for detailed evaluation.

g) Hemodynamic Measurements

- Assess chronic effects on renal blood flow, vascular resistance, and perfusion pressure.

h) Data Collection

- Record data over an extended period to capture the progressive changes induced by chronic hypertension.
- Include appropriate control groups for comparison

EXPECTED RESULTS

The results of inducing chronic renal hypertension in rats may include:

a) Sustained High Blood Pressure

Confirmation of stable and elevated blood pressure over the chronic period.

b) Long-Term Renal Hemodynamic Alterations

Changes in renal blood flow, vascular resistance, and perfusion pressure over time.

c) Progressive Functional Changes

Gradual alterations in glomerular filtration rate, urine output, and other renal function parameters

d) Chronic Histological Changes

Evidence of chronic injury, such as fibrosis, glomerulosclerosis, and tubulointerstitial damage

e) Hemodynamic Responses Over Time

Evaluation of systemic and renal hemodynamics during the chronic phase.

C) NEUROGENIC HYPERTENSION IN DOGS [10]

RATIONALE

Neurogenic hypertension in dogs serves as a model to study the influence of the nervous system on blood pressure regulation. This model helps mimic conditions where alterations in neural control contribute to sustained high blood pressure. Investigating neurogenic hypertension in dogs provides insights into the underlying mechanisms and potential therapeutic interventions for hypertensive states related to neural dysfunction

PRINCIPLE

The principle involves inducing neurogenic hypertension in dogs by manipulating the neural control mechanisms that regulate blood pressure. This can be achieved through various methods such as nerve stimulation, lesions, or pharmacological interventions targeting neural pathways. The focus is on understanding how alterations in neural regulation led to sustained increases in blood pressure [10].

PROCEDURE

a) Animal Selection and Preparation

- Use healthy adult dogs, ensuring ethical compliance and obtaining necessary approvals.
- Conduct pre-experimental health assessments.

b) Anesthesia and Surgical Preparation

- Anesthetize the dogs using appropriate agents.
- Perform aseptic surgery for the chosen method of inducing neurogenic hypertension.

c) Induction of Neurogenic Hypertension

- Implement techniques such as nerve stimulation, lesions, or pharmacological agents

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targeting neural pathways to induce neurogenic hypertension.

- Ensure continuous monitoring to maintain hypertensive conditions.

d) Blood Pressure Monitoring

- Regularly monitor blood pressure using appropriate techniques (intra-arterial catheterization, telemetry, or Oscillo metric methods).

e) Neurological Assessments

- Evaluate neural responses, such as sympathetic activity, using techniques like nerve recordings or biochemical markers.

f) Renal Function and Hemodynamic Measurements

- Assess the effects of neurogenic hypertension on renal blood flow, vascular resistance, and perfusion pressure.

g) Data Collection

- Record data over the experimental period to understand the impact of neurogenic factors on blood pressure regulation.
- Include appropriate control groups for comparison

EXPECTED RESULTS

The results of inducing neurogenic hypertension in dogs may include:

a) Sustained High Blood Pressure

Confirmation of stable and elevated blood pressure resulting from neurogenic manipulations.

b) Altered Neural Responses

Changes in neural activity, such as increased sympathetic tone, indicating the success of the neurogenic induction.

c) Renal Hemodynamic Alterations

Effects on renal blood flow, vascular resistance, and perfusion pressure due to neurogenic influences

d) Hypertensive Phenotype

Development of a hypertensive phenotype characterized by persistent high blood pressure.

D) DOCA-SALT INDUCED HYPERTENSION IN RATS [11]

RATIONALE

The DOCA-salt induced hypertension model in rats is employed to study the hypertensive effects of mineralocorticoid excess, particularly with deoxycorticosterone acetate (DOCA) administration along with a high-salt diet. This model mimics certain aspects of human hypertension associated with mineralocorticoid excess, such as hyperaldosteronism, and allows researchers to investigate the pathophysiological mechanisms underlying salt-sensitive hypertension and its impact on the cardiovascular and renal systems [11].

PRINCIPLE

The principle involves the chronic administration of DOCA along with a high-salt diet to induce hypertension in rats. DOCA, a mineralocorticoid, mimics the actions of aldosterone, leading to sodium retention and potassium excretion. The high-salt diet exacerbates sodium retention, resulting in increased blood volume and elevated blood pressure. The model is designed to study the progression of hypertension, renal injury, and other cardiovascular consequences associated with mineralocorticoid excess [11].

PROCEDURE

a) Animal Selection and Preparation

- Use healthy adult rats, preferably of a standardized strain.
- Obtain ethical approvals for the study.

b) Anesthesia and Surgical Preparation

- Anesthetize the rats using appropriate agents.
- Implant DOCA pellets subcutaneously, typically in the neck or back region, to provide a slow release of the mineralocorticoid.

c) High-Salt Diet Administration:

- Feed the rats a high-salt diet to promote sodium retention and exacerbate the hypertensive effects of DOCA.

d) Blood Pressure Monitoring

- Regularly monitor blood pressure using appropriate techniques (tail-cuff, telemetry, or intra-arterial catheterization).

e) Renal Function Assessments

- Periodically assess renal function parameters, such as glomerular filtration rate (GFR), urine output, and urinary protein excretion, to track changes over time.

f) Histological Examination

- Collect renal tissue samples at various time points for histological examination to observe changes in renal architecture, including fibrosis, glomerulosclerosis, and tubular damage.
- Stain tissues for detailed evaluation.

g) Cardiovascular Assessments

- Evaluate cardiovascular parameters, such as cardiac function and vascular responses, to understand the systemic effects of DOCA-salt-induced hypertension.

h) Data Collection

- Record data over the experimental period to capture the progression of hypertension and associated changes.

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- Include appropriate control groups for comparison

EXPECTED RESULTS

The results of DOCA-salt-induced hypertension in rats may include:

a) Sustained High Blood Pressure

Confirmation of stable and elevated blood pressure resulting from DOCA administration and the high-salt diet.

b) Renal Hemodynamic Alterations

Changes in renal blood flow, vascular resistance, and perfusion pressure over time.

c) Progressive Renal Dysfunction

Gradual alterations in glomerular filtration rate, urine output, and other renal function parameters

d) Chronic Histological Changes

Evidence of chronic renal injury, such as fibrosis, glomerulosclerosis, and tubulointerstitial Damage

e) Cardiovascular Consequences

Impacts on cardiac function and vascular responses indicative of systemic effects.

E) FRUCTOSE INDUCED HYPERTENSION IN RATS [12]

RATIONALE

Fructose-induced hypertension in rats is a model designed to study the effects of excessive fructose consumption on blood pressure regulation. This model is relevant to understanding the impact of high fructose intake, commonly found in modern diets, on the development of hypertension. Investigating fructose-induced hypertension provides insights into the underlying mechanisms, including changes in insulin sensitivity, oxidative stress, and vascular function [12].

PRINCIPLE

The principle involves exposing rats to a high-fructose diet, leading to increased fructose consumption and metabolic alterations. Excessive fructose intake can contribute to insulin resistance, dyslipidemia, and other metabolic disturbances, potentially leading to elevated blood pressure. The model allows researchers to explore the links between fructose metabolism and the development of hypertension

PROCEDURE

a) Animal Selection and Preparation

- Use healthy adult rats, preferably of a standardized strain.
- Obtain ethical approvals for the study.

b) Dietary Intervention

- Feed rats a high-fructose diet, typically in the form of fructose-enriched water or a diet with elevated fructose content.

c) Blood Pressure Monitoring

- Regularly monitor blood pressure using appropriate techniques (tail-cuff, telemetry, or intra-arterial catheterization).

d) Metabolic Assessments

- Assess metabolic parameters, including insulin sensitivity, glucose tolerance, and lipid profiles, to understand the metabolic changes associated with fructose consumption.

e) Vascular Function Assessments

- Evaluate vascular responses to assess endothelial function and the impact of fructose on blood vessel reactivity.

f) Oxidative Stress Measurements

- Measure oxidative stress markers to investigate the potential role of oxidative stress in fructose-induced hypertension.

g) Renal Function Assessments

- Assess renal parameters, such as glomerular filtration rate (GFR) and urinary protein excretion, to understand the renal consequences of fructose-induced hypertension.

h) Data Collection

- Record data over the experimental period to capture the progression of fructose-induced hypertension and associated changes.
- Include appropriate control groups for comparison

EXPECTED RESULTS

The results of fructose-induced hypertension in rats may include:

a) Elevated Blood Pressure

Confirmation of increased blood pressure resulting from the high-fructose diet.

b) Metabolic Disturbances

Evidence of insulin resistance, dyslipidemia, and altered glucose metabolism associated with fructose consumption.

c) Vascular Dysfunction

Impaired endothelial function and altered vascular reactivity indicative of the impact on blood vessels.

d) Oxidative Stress

Increased oxidative stress markers suggesting a potential role in the development of hypertension.

e) Renal Consequences

Changes in renal function parameters, such as altered glomerular filtration rate and urinary protein excretion.

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F) GENETIC HYPERTENSION IN RATS [13]

RATIONALE

Genetic hypertension in rats serves as a valuable model to study the hereditary factors contributing to elevated blood pressure. This model involves selectively breeding rats with a genetic predisposition to hypertension, allowing researchers to investigate the underlying genetic mechanisms and study the progression of hypertension over generations. Genetic hypertension models are crucial for understanding the genetic basis of hypertension and exploring potential therapeutic interventions

PRINCIPLE

The principle involves selectively breeding rats with a hypertensive phenotype, usually identified based on elevated blood pressure levels. The selective breeding process focuses on transmitting the genetic traits associated with hypertension from one generation to the next. This model is designed to mimic the hereditary aspects of hypertension observed in certain human populations [13].

PROCEDURE

a) Animal Selection

- Choose rat strains with a known genetic predisposition to hypertension, such as spontaneously hypertensive rats (SHR).

b) Selective Breeding

- Select breeding pairs with a hypertensive phenotype.
- Breed these pairs to produce offspring with a higher likelihood of developing hypertension.

c) Blood Pressure Monitoring

- Regularly monitor blood pressure in the selected breeding pairs and subsequent generations using appropriate techniques (tail-cuff, telemetry, or intra-arterial catheterization).

d) Phenotypic Assessments

- Assess other phenotypic characteristics associated with hypertension, such as cardiac hypertrophy, vascular remodeling, and renal function.

e) Genetic Analysis

- Conduct genetic analyses to identify specific genetic markers or loci associated with the hypertensive phenotype.
- Use molecular biology techniques to study gene expression and regulation.

f) Therapeutic Interventions

- Implement therapeutic interventions to explore potential treatments or preventive measures for genetic hypertension.

g) Data Collection

- Record data over multiple generations to observe the hereditary transmission of hypertension and any changes in the hypertensive phenotype.

EXPECTED RESULTS

The results of genetic hypertension in rats may include:

a) Hereditary Transmission

- Confirmation of the hereditary transmission of the hypertensive phenotype over successive generations.

b) Elevated Blood Pressure

- Consistently elevated blood pressure levels in rats with the genetic predisposition to hypertension.

c) Phenotypic Changes

- Evidence of cardiac hypertrophy, vascular remodeling, and alterations in renal function associated with hypertension.

d) Genetic Markers

- Identification of specific genetic markers or loci associated with the hypertensive phenotype through genetic analysis.

e) Response to Interventions

- Assessment of the efficacy of therapeutic interventions in mitigating or preventing hypertension in the genetically predisposed rats.

➢ *IN VITRO* SCREENING MODELS

A) ALPHA 2 ADRENORECEPTOR BINDING [14]

RATIONALE

The study of alpha-2 adrenergic receptor binding is crucial for understanding the physiological and pharmacological aspects of adrenergic signaling. These receptors are involved in the regulation of various physiological processes, including blood pressure, heart rate, and neurotransmitter release. Investigating the binding of ligands to alpha-2 adrenergic receptors can provide insights into potential therapeutic targets for conditions such as hypertension, anxiety, and pain

PRINCIPLE

The principle of alpha-2 adrenergic receptor binding assays involves the use of radio labeled ligands (e.g., tritiated norepinephrine or other specific agonists) to measure the binding affinity and density of alpha-2 receptors. Competitive binding assays can also be employed, where unlabeled ligands or compounds are tested for their ability to compete with the radiolabeled ligand for binding to the receptors [14].

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PROCEDURE

a) Preparation Of Membrane Homogenate

- Isolate tissues or cells expressing alpha-2 adrenergic receptors.
- Homogenize the tissues or cells to obtain a membrane preparation containing the receptors.

b) Radioligand Binding Assay

- Incubate the membrane homogenate with a radiolabeled ligand specific for alpha-2 receptors.
- Allow the ligand to bind to the receptors under various conditions (e.g., different concentrations of ligand, time points).

c) Separation of Bound and Free Ligand

- Separate the bound ligand from the free ligand using techniques such as filtration or centrifugation.

d) Quantification of Binding

- Measure the radioactivity associated with the bound ligand.

e) Data Analysis

- Calculate binding parameters, such as binding affinity (Kd) and receptor density (Bmax), using saturation binding curves

EXPECTED RESULTS

The results of alpha-2 adrenergic receptor binding assays typically include:

Saturation binding curves illustrating the relationship between radio ligand concentration and binding. Scatchard plots for a more detailed analysis of binding kinetics. Values for binding affinity (Kd) and receptor density (B_{max}).

B) ANGIOTENSIN 2 RECEPTOR BINDING [15-16]

RATIONALE

The rationale behind angiotensin II receptor binding assays lies in understanding the specific interaction between Ang II and its receptors. These assays help researchers and clinicians study the pharmacological properties of compounds that modulate the renin-angiotensin-aldosterone system, which is involved in cardiovascular regulation [15][16].

PRINCIPLE

The principle of angiotensin II receptor binding assays involves using radiolabeled angiotensin II or other labeled ligands to measure their binding affinity and specificity to the angiotensin II receptors on cell membranes or tissue preparations. The binding is typically competitive, where the test substance competes with a known concentration of radiolabeled ligand for binding sites on the receptors.

PROCEDURE

a) Preparation Of Membrane or Cell Homogenates

- Isolate cell membranes or homogenize tissues containing angiotensin II receptors.
- Centrifuge the homogenate to obtain a membrane fraction.

b) Radiolabeling of Ligands

- Radiolabel angiotensin II or other ligands with a suitable radioactive isotope (e.g., tritium, iodine).

c) Binding Assay

- Incubate the membrane or cell homogenate with a fixed concentration of radiolabeled ligand and varying concentrations of the test compound (or Ang II).
- The binding reaction is allowed to reach equilibrium.

d) Separation of Bound and Free Ligand

a) Use a separation technique, such as filtration or centrifugation, to separate bound and free radiolabeled ligands.

e) Detection and Quantification

b) Measure the radioactivity associated with the bound ligand using a scintillation counter or autoradiography.

f) Data Analysis

c) Calculate the binding affinity (Kd), maximum binding (Bmax), and other parameters using standard binding equations. .

EXPECTED RESULTS

The results of angiotensin 2 receptor binding studies provide information about the affinity of Ang 2 for its receptor, the concentration of receptor, and the competitive binding of Ang 2 analog or potential therapeutic agents. These finding contribute to the understanding of the physiological and pharmacological aspects of the renin-angiotensin system.

C) ACE INHIBITION IN GUENIA PIG ILEUM

RATIONALE

ACE is an enzyme that plays a crucial role in the renin-angiotensin-aldosterone system, which regulates blood pressure and fluid balance. Inhibiting ACE can lead to vasodilation and decreased blood pressure. Studying the effects of ACE inhibitors on the guinea pig ileum helps researchers understand the role of ACE in smooth muscle contraction and the potential impact of ACE inhibitors on these processes.

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PRINCIPLE

The guinea pig ileum is often used in pharmacological studies as it contains smooth muscle that responds to various neurotransmitters and drugs. ACE inhibitors interfere with the conversion of angiotensin I to angiotensin II, a potent vasoconstrictor. By inhibiting this conversion, ACE inhibitors cause vasodilation, and their effects on smooth muscle, including the guinea pig ileum, can be studied.

PROCEDURE

a) Tissue Preparation

- Guinea pig ileum is isolated and prepared for experimentation.

b) Baseline Contractions

- Baseline contractions of the ileum are recorded to establish a control.

c) Application of ACE Inhibitor

- An ACE inhibitor is applied to the tissue. Common ACE inhibitors include captopril or enalapril.

d) Recording Contractions

- Changes in smooth muscle contractions in response to the ACE inhibitor are recorded.

e) Analysis

- The data obtained is analyzed to understand the impact of ACE inhibition on the guinea pig ileum.

EXPECTED RESULTS

The results would typically show a reduction in smooth muscle contractions in the guinea pig ileum following the application of an ACE inhibitor. This reflects the vasodilatory effect of ACE inhibition, as well as potential implications for gastrointestinal smooth muscle function.

D) INHIBITION OF ANGIOTENSIN CONVERTING ENZYME [17]

RATIONALE

The inhibition of angiotensin-converting enzyme (ACE) is a pharmacological strategy commonly used in the treatment of cardiovascular diseases, particularly hypertension and heart failure. ACE is an enzyme that plays a crucial role in the renin-angiotensin-aldosterone system (RAAS), which regulates blood pressure and fluid balance. The primary function of ACE is to convert angiotensin I, an inactive precursor, into angiotensin II, a potent vasoconstrictor. Angiotensin II also stimulates the release of aldosterone, which promotes sodium and water retention. By inhibiting ACE, the production of angiotensin II is reduced, leading to vasodilation, decreased blood pressure, and reduced aldosterone release

PRINCIPLE

The principle of ACE inhibition involves blocking the enzymatic activity of ACE. This can be achieved using ACE inhibitors, which are a class of drugs that specifically target and inhibit the ACE enzyme. Common ACE inhibitors include enalapril, lisinopril, and ramipril

PROCEDURE

a) Patient Assessment

- Before prescribing ACE inhibitors, a thorough patient assessment is necessary, including medical history, blood pressure measurements, and laboratory tests.

b) Prescription

- Based on the assessment, if hypertension or heart failure is diagnosed, a healthcare provider may prescribe an ACE inhibitor.

c) Administration

- The patient takes the prescribed ACE inhibitor medication orally, usually once or twice a day. The medication may be in the form of tablets or capsules.

d) Monitoring

- Regular monitoring of blood pressure and other relevant parameters is essential to assess the effectiveness of ACE inhibition and to detect any potential side effects.

e) Adjustment of Dosage

- The healthcare provider may adjust the dosage based on the patient's response and tolerance to the medication

EXPECTED RESULTS

The results of ACE inhibition include:

a) Blood Pressure Reduction

- ACE inhibitors effectively lower blood pressure by reducing the production of angiotensin II and promoting vasodilation.

b) Improved Cardiac Function

- In heart failure patients, ACE inhibition can improve cardiac function by reducing the workload on the heart and enhancing its pumping ability.

c) Reduced Aldosterone Release

- ACE inhibitors decrease the release of aldosterone, leading to decreased sodium and water retention, which is beneficial in heart failure and hypertension.

d) Potential Side Effects

- While ACE inhibitors are generally well-tolerated, they may cause side effects such as cough

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and elevated levels of potassium in some individuals.

E) ANGIOTENSIN- II INDUCED CONTRACTION [18-19]

RATIONALE

The rationale behind using Ang II to induce contraction in isolated rabbit aorta is to study its vasoconstrictor effects. Ang II acts on angiotensin receptors on vascular smooth muscle cells, leading to an increase in intracellular calcium levels and subsequent contraction of the smooth muscle, ultimately causing vasoconstriction

PRINCIPLE

The principle of the experiment involves isolating a segment of the rabbit aorta and subjecting it to Ang II to observe its contractile response. Ang II acts on angiotensin receptors, particularly AT1 receptors, leading to activation of signaling pathways that result in smooth muscle contraction

PROCEDURE

- The procedure involves isolating the rabbit aorta and mounting it in an organ bath filled with a physiological solution to maintain tissue viability.
- The aorta is connected to a force transducer, and changes in tension are recorded using a data acquisition system.
- Angiotensin II is then applied to the bath, and the resulting contraction of the aorta is measured over time

EXPECTED RESULTS

- The addition of angiotensin II should lead to a dose-dependent contraction of the isolated rabbit aorta.
- The contractile response can be measured as an increase in tension, and the concentration-response curve can be plotted to analyze the potency and efficacy of angiotensin II.
- The results may vary based on experimental conditions, the health of the isolated tissue, and the specific concentrations of angiotensin II used.

F) MONOCROTALINE INDUCED PULMONARY HYPERTENSION [20-23].

RATIONALE

Monocrotaline is an alkaloid toxin derived from certain plants, and it is known to induce pulmonary hypertension in animals. The model is used to mimic certain aspects of human pulmonary arterial hypertension (PAH), allowing researchers to investigate the pathophysiology and potential treatments for this condition. Monocrotaline-induced PH involves vascular remodeling, inflammation, and increased pulmonary vascular resistance, which are key features of PAH

PRINCIPLE

Monocrotaline is administered to experimental animals, typically rodents, leading to damage and remodeling of pulmonary vessels. The toxin disrupts the pulmonary endothelium and smooth muscle cells, initiating a cascade of events that result in increased pulmonary arterial pressure and right ventricular hypertrophy

PROCEDURE

- The procedure involves the injection of monocrotaline into the animals. The route of administration (intravenous, intraperitoneal) and dosage may vary based on the specific experimental design.
- Animals are monitored over time to assess the development of pulmonary hypertension and associated changes in cardiovascular parameters.
- Techniques such as echocardiography, hemodynamic measurements, and histological analysis are commonly employed to evaluate the severity of PH and its impact on the cardiovascular system.

EXPECTED RESULTS

- Monocrotaline-induced pulmonary hypertension results in increased pulmonary arterial pressure, right ventricular hypertrophy, and vascular remodeling.
- Hemodynamic changes include elevated right ventricular systolic pressure and increased pulmonary vascular resistance.
- Histological analysis typically reveals thickening of the pulmonary arteries, inflammatory cell infiltration, and other signs of vascular remodeling.
- This model allows researchers to test the efficacy of potential therapeutic interventions for pulmonary hypertension.

II. CONCLUSION

The study of the pathophysiology of persistent hypertension and its consequences uses various animal models of experimental hypertension. More and more, novel chemical entities are tested using these animal models. The creation of new models that take into account recent developments in the biology of hypertension can speed up research into the disease's aetiology and the creation of novel hypertension therapeutics. Different animal Models of hypertensions are utilized for different categorical novel antihypertensive pharmacological drug screening.

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None

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