



Pharmacogenetics of anti -hypertensive drugs

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DESCRIPTION

Antihypertensive drugs are used for the treatment of high blood pressure, and more specifically, the primary and secondary hypertension. The complications of high blood pressure might trigger and/or cause several complex systematic cardiovascular disorders or syndromes such as stroke, unstable angina and myocardial infarction. Antihypertensive therapy seeks to prevent the complications of high blood pressure, such as stroke and myocardial infarction. Evidence suggests that reduction of the blood pressure by 5 mmHg can decrease the risk of stroke by 34%, of ischaemic heart disease by 21%, and reduce the likelihood of dementia, heart failure, and mortality from cardiovascular disease. There are many classes of antihypertensive, which lower blood pressure by different means. The most important and widely used drugs include thiazide diuretics, calcium channel blockers, ACE inhibitors, and Angiotensin II Receptor Blockers (ARBs), and beta blockers. Antihypertensive drugs are used to treat hypertension, one of the most common symptoms of patients suffering from cardiovascular diseases such as heart attack and stroke. In the current pharmacology of cardiovascular disease, four drug clusters, angiotensin-converting enzyme inhibitors, beta blockers, calcium channel blockers, and diuretics, cover the main therapeutic properties of most antihypertensive drugs. The pharmacokinetic and especially metabolic profiles of antihypertensive drugs have been intensively studied due to the large inter-subject variability of plasma concentrations and the diversity of efficacy responses, especially the P450-dependent metabolic states they exhibit.

Beta-blockers

Beta-adrenergic blockers first cause a decrease in cardiac output, followed by a decreased peripheral vascular resistance and decrease in plasma renin.

The majority of the beta-blockers are metabolized by P450 reactivity deriving dealkylated and hydroxylated metabolites and they appear to have similar metabolic characteristics. The elimination of the most of them occurs through hepatic metabolism and/or renal excretion of the unchanged drug. Phase II glucuronidation reactions take place also in the most beta-blockers metabolic pathways. Atenolol and nadolol are the only beta-blockers that appear to be excreted in the unchanged form by the kidneys, while CYP1A₂ and CYP2D₆ seem to affect the propranolol biotransformation.

Calcium channel blockers

The dihydropyridine group calcium channel blockers, such as nifedipine, amlodipine and felodipine and the non-dihydropyridine group calcium channel blockers such as phenylalkylamine verapamil and benzothiazepine diltiazem. These drugs are able to decrease the concentration of free intracellular calcium ions leading to decreased contraction and vasodilation and they inhibit the aldosterone secretion. They also present diuretic activity through an increase in renal blood flow and glomerular filtration rate.

Antihypertensive drugs metabolism

Drug discovery and development are risky initiatives that require significant investment in capital, time and scientific expertise. Foreign metabolism research is one of the major topics in the research and development of pharmaceuticals, cosmetics and dietary supplements. Antihypertensive drugs are used to treat hypertension, one of the most common symptoms of patients suffering from cardiovascular diseases such as myocardial infarction and stroke.

In the current pharmacology of cardiovascular disease, four drug clusters, angiotensin-converting enzyme inhibitors, beta blockers, calcium channel blockers, and diuretics, cover the main therapeutic properties of most antihypertensive drugs. The pharmacokinetic and especially metabolic profiles of antihypertensive drugs have been intensively studied due to the large inter-subject variability of plasma concentrations and the diversity of efficacy responses, especially the P450-dependent metabolic states they exhibit. Improving modeling and understanding of human drug metabolism. Improve experimental studies of small xenobiotic molecule metabolism.

The main predictive tools that use these methods are rule-based approaches, quantitative structure-activity relationships, and docking approaches. This review provides a detailed metabolic profile of the major groups of antihypertensive drugs, including metabolites and metabolic enzymes, and also provides specific information on the computational approach used to predict the metabolic profile of some antihypertensive drugs.