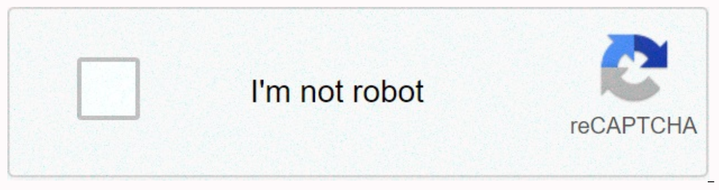

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Cardiovascular drugs pharmacology pdf

There are several classes of established lipid levels, or antihyperlipemic drugs available as a prescriber. Choosing which agent to use depends to a large extent on the patient's cholesterol profile, cardiovascular, liver and kidney function. Statins are designed to be ldl, bad cholesterol most strongly associated with vascular disease. Notable side effects include myopathy and rhabdomyolysis. Some evidence suggests that statins should not be used in patients over 75 years of age who have not had a history of heart disease or stroke. Statins inhibit the enzyme hydroxymethylglutaryl-CoA reductase (HMGCR). Approved statins include atorvastatin, cerivastatin, fluvastatin, lovastatin, pravastatin, rosuvastatin and simvastatin. Fibaate is prescribed to reduce hypercholesterolaemia in patients who are not tolerated or are not suitable for statin therapy. Fibrates raises HDL (good cholesterol) and lower triglyceride levels. A reduction in fibrate-induced insulin resistance is beneficial when dyslipidaemia is associated with other metabolic syndrome parameters (e.g. hypertension and type 2 diabetes mellitus). Treatment with Fibrate is not suitable for patients with low HDL levels and treatment should be discontinued if HDL-C levels are tolerated shortly after initiation of treatment. Fibrates is recommended as a first line treatment only in patients with very high triglycerides. Fibrates activates peroxidoma proliferator-activated receptors (PPARs), especially PPARα. They are metabolised by cytochrome P450 3A4 (CYP3A4). Approved fibrates include, for example, besafibrate, ciprobrate, clofibrate, fenofibrate and gemfibrozil. Niocin (nicotinic acid or vitamin B3) is used as a vitamin supplement. It lowers both cholesterol and triglycerides concentrations by inhibiting synthesis; it also increases HDL cholesterol. In addition, statin therapy is used, or alone, when statins are not tolerated. Do not use if the patient has a history of peptic ulcer or arterial haemorrhage. Nicotinic acid derivative acipimox can be used in similar situations. Inositolnikotite can be used to treat peripheral vascular diseases, but not in acute phase of cerebrovascular accident or in patients with recent myocardial infarction. NICE does not recommend the use of inositol nicotine for the treatment of intermittent limping in patients with peripheral arterial disease. Bile acid sequestrants are synthetic polymeric resins that prevent the intestinal reabsorption of bile components, thus acting on hypolipidic substances. Also used for other purposes, such as the treatment of chronic diarrhea due to malabsorption of bile acids and the prevention of itching in patients with chronic liver disease. As hypolipidemic agents, they are less effective than statins. Do not use if blood triglycerides are elevated. For example, cholestyramine, colestipol and colesevelaam. Ezetimibe inhibits intestinal cholesterol intake protein Niemann-Pick C1-like protein 1, which is absorption of intestinal cholesterol. There is only a modest effect of mono-therapy, but it can be used additionally with or without dietary measures to treat primary hypercholesterolaemia and homozygous familial hypercholesterolaemia. In patients with moderate and severe hepatic impairment. Lomitapide inhibits microsomal triglyceride transfer protein (MTTP), resulting in decreased lipoprotein secretion and reduced concentration of lipoprotein-borne lipids such as cholesterol and triglycerides. Only be used under expert supervision in patients with homozygous familial hypercholesterolaemia, in addition to diet and other lipid-regulating medicinal products. Since lomitapine may interfere with the absorption of fat soluble nutrients, vitamin E and fatty acid supplements are essential. Phytosterols (plant sterols and stanols) are naturally present steroid-like compounds similar to cholesterol. Stanols are saturated sterols with no double bonds in the structure of the sterol ring. Despite being effective in reducing LDL cholesterol, the benefits of foods and supplements enriched with phytosterol have not yet been proven [Genser et al. (2012)]. The most common form of phytosterols in human food β sitosterol, campesterol and stigmasterol; the most common stanols are sitostanol and campestanol. Orlistat inhibits pancreatic lipase, thereby reducing the absorption of fats from food. Used in addition to a reduced calorie diet as an anti-obesity treatment in obese patients with additional risk factors such as type 2 diabetes, hypertension or hypercholesterolaemia. Fibrinolytic and thrombolytic drugs are used to break down blood clots (blood clots) to limit the occlusion of blood vessels. Fibrinolytic medicinal products act as thrombolytics by activating plasminogen, forming plasmin, which breaks down the clot fibrin. These types of drugs are used to treat myocardial infarction, thromboembolic strokes, deep vein thrombosis and pulmonary embolism to limit perfused tissue damage and ultimately prevent the death of these conditions. They are most effective when administered as soon as the diagnosis determines their use is beneficial. Often synergistically anticoagulants such as heparin are used. Fibrinolytics are contraindicated in haemorrhagic stroke and other indications for which bleeding is a risk factor (including borate lung disease, acute pancreatitis, aneurysm, aortic dissection, bleedingdialysis, coagulation defects, severe vaginal bleeding, history of cerebrovascular disease or recent bleeding, oesophageal veins, peptic ulcers, recent trauma and severe hypertension). Thrombolytic medicinal products are: Recombinant tissue plasminogen activator proteins (r-tPAs) such as alteplase, reteplase and tenecteplase. All three are indicated for acute myocardial infarction (AMI), with alteplase also indicated for the treatment of (PE), stroke and thrombolytic thrombolytic thrombolytic central venous access devices. anistreplase (anisoyated plasminogen streptokinase activator complex (APSAC) - an acylated complex of purified human plasminogen and bacterial streptokinase. After hydrolysis of the acyl group, the activator complex converts plasminogen into plasminogen, which breaks down fibrin. streptokinase is a bacterial enzyme that activates plasminogen to produce thrombolytic action. Ami, deep vein thrombosis (DVT), PE, acute arterial thromboembolism and central retinal venous or arterial thrombosis are indicated. urokinase (urokinase type plasminogen activator (uPA)) - serine protease, which activates plasminogen to break down blood clots. Indicated for DVT, PE, occlusive peripheral arterial disease, occlusive central venous coverings and occlusive arteriovenous hemodialysis. The summary table below is presented in the Pharmafactz.com. FIBRINOLYTIC MEDICINAL PRODUCTS Summary of fibrinolytics used in the clinic. Fibrinolytic drugs increase the normal process of clot decomposition, through the activation of plasminogen, an enzyme important for clot decomposition. Mechanically they are in fact recombinant versions of tissue plasminogen activator (t-PA), an enzyme that converts plasminogen plasminogen plasmin to plasmin is largely responsible for the breakdown of blood clots. Alteplase is a genetically modified recombinant version of t-PA that binds to fibrinogen and fibrinin. Tenecteplase is a recombinant modified t-PA with better fibrin specificity and a longer duration of action than t-PA. Reteplase is a recombinant t-PA that binds less to fibrinogen and fibrinin but has a longer duration of action than an endogenous enzyme. Streptokinase is derived from hemolytic streptococci. It is inactive until it binds to circulating plasminogen. Adverse reactions Bleeding - especially intracerebral bleeding occurs in ~1% of patients. Hypotension-dose-dependent and more frequently with streptokinase. Allergic reactions of streptokinase. All fibrinolytic medicinal products are administered iv or intra-arterially. The half-life of streptokinase (1h) is longer than alteplase or reteplase (0.5h), but similar to tenecteplase. The purpose of antiplatelet drugs is to reduce platelet aggregation to inhibit the formation of blood clots in the arterial bloodstream. Used to treat patients with cardiac and cerebrovascular conditions. They are classified according to their mechanism of action: irreversible cyclooxygenase inhibitors- aspirin, used for primary (cardiac) vascular disease prevention in older at-risk patients, acute indications and secondary prophylaxis Adenosine diphosphate (ADP) receptor inhibitors- clopidogrel, which are used for acute indications and secondary prevention; prasugrel (plus aspirin) used to prevent atherothrombotic events in patients with acute coronary syndrome who are percutaneous coronary artery (PCI); ticagrelor (plus aspirin), used to prevent atherothrombotic complications in patients with acute coronary syndrome; canretor (plus aspirin) is used to treat patients who are undergoing PCI and who have not received clopidogrel, prasugrel or ticagrelor in the past and who are not eligible for these medicinal products. Phosphodiesterase inhibitors- cilostazol are indicated for improving maximum and pain-free walking distance in intermittently limp patients. Dose reduction is recommended in patients receiving medicinal products that inhibit Cyp3A4 and CYP2C19. Cilostazol is contraindicated in patients with moderate or severe hepatic impairment and in patients with a creatinine clearance ≤ 25 ml/min. Protease-activated receptor 1 (PAR1) antagonists- vorapaxar are not approved in the United Kingdom, but are used elsewhere to reduce the risk of thrombotic cardiovascular events in patients with a history of myocardial infarction (MI) or peripheral arterial disease (PAD). Contraindicated in patients with a history of stroke, transient ischaemic attack (TIA) or intracranial haemorrhage (ICH), or in patients with active bleeding. Metabolism is mainly hepatic, therefore it is not recommended to use in patients with severe hepatic impairment. Glycoprotein IIB/IIIA inhibitors block the binding of fibrinogen to platelet receptors- arbaxib, which is used in addition to unfractionated heparin and aspirin to prevent ischaemic complications in high-risk patients undergoing percutaneous transluminal coronary experience as a single treatment; eptifibatide (plus unfractionated heparin and aspirin) and tirofibane (plus unfractionated heparin, aspirin and clopidogrel) are used to prevent early myocardial infarction in patients with unstable angina or non-ST segment elevation myocardial infarction, and the combination of tirofibane may be used in patients with non-ST segmental myocardial infarction who are undergoing PCI. Adenosine reuptake inhibitors- dipyridaamol, used in addition to oral anticoagulation for the prophylaxis of thromboembolism associated with cardiac valves, and secondary prevention of ischaemic stroke and transient ischaemic seizures. Thromboxane receptor antagonists- none of them have been approved, but see Davı et al. (2012) for the reasons behind their development Thromboxane synthesis inhibitors- none have been approved, but see Davı et al. (2012) anticoagulants are used to prevent the formation or growth of fibrin/erythrocyced blood clot in the venous bloodstream. They are not useful for the treatment of arterial blood clots, which consist mainly of platelet aggregations. Anticoagulants can be administered parenterally or orally. Parenteral anticoagulants: heparin (unfractionated or standard heparin) works quickly, but also has a short time of action. This characteristic allows heparin infusion to be used in patients at high risk of bleeding, as the anticoagulation effect ends quickly after the end of the infusion. Low molecular weight heparins are effective as unfractionated heparin, but have a lower risk of causing heparin-induced thrombocytopenia. They are also more convenient to use as they than unfractionated heparin, and is therefore the preferred option for preventing venous thromboembolism, such as deep vein thrombosis (DVT), pulmonary embolism (PE), myocardial infarction (MI), the prevention of unstable coronary artery disease and the prevention of clotting in extra-body blood circulation procedures. For example, the drugs are dalteparin sodium, enoxaparin sodium, and tinzaparin sodium heparinides, such as danaparoid sodium, are mixtures of heparin derivatives called glycosaminoglycans, such as heparan, dermatane, and chondroitin sulphates. SS is used to reduce the risk of surgical patients. Argatroban is an oral anticoagulant that acts as a thrombin inhibitor. It is indicated for the prevention or treatment of thrombosis with heparin-induced thrombocytopenia (HIT) or at risk. Hirudins such as desirudin, lepirudin and bivalirudin are derivatives of saliva anticoagulant found in the leech. These compounds are direct thrombin inhibitors. Bivalirudin is indicated for the treatment of unstable angina or ST segment elevation MI in patients who are designed for rapid or early intervention and as anticoagulant in patients undergoing percutaneous coronary intervention. Epoprostenol (prostacycline PGI2) can be used to prevent platelet aggregation during renal dialysis when heparins are not suitable or contraindicated. The half-life of epoprostenol is very short and should therefore be administered as a continuous intravenous infusion. May also be used in combination with oral anticoagulant to treat primary pulmonary hypertension resistant to other treatments, special medical care. Fondaparinux inhibits activated factor X and is indicated for the prevention of venous thromboic events in different at-risk groups Oral anticoagulants: coumarin (warfarin and acenocoumarol) and fenindion an antagonise the action of vitamin K, but are slow to achieve complete anticoagulant action (48 to 72 hours). From this group of drugs, warfarin is the drug of choice. Warfarin is used to prevent venous thromboembolism in patients at risk. Keeling D et al. (2011, PMID: 21671894) provides instructions for the use of warfarin anticoagulation. Dabigatran, rivaroxaban and apixaban are oral anticoagulants that are alternatives to warfarin. Rivaroxaban and apixaban inhibit platelet activation and fibrin blood clots by direct, selective and reversible factor Xa inhibition. Dabigatran foreline is a protege that is converted to active dabigatran in vivo. Dabigatran is a specific reversible direct thrombin inhibitor. Regular laboratory tests are not necessary for either of these medicines. In addition, there are fewer drug-food interactions with these oral anticoagulants. These represent the advantages of these drugs when using warfarin. Nitrates include glyceryl trinitrate (GTN), isosorbide di nitrate and isosorbide mononitrate, which are intended under a number of trade names. Nitrates vasodilatation by activating soluble guanylyl guanylyl Used to treat

angina symptoms, not the root cause. The use of all nitrates is contraindicated in patients with aortic stenosis, cardiac tampons, anaestural pericarditis, hypertrophic cardiomyopathy, hypovolaemia, hypovolaemia, noticeable anaemia, mitral stenosis, increased intracranial pressure due to brain haemorrhage, intracranial pressure or toxic pulmonary oedema. Prescribers should be aware of tolerability in patients taking long-acting or transdermal nitrate and should monitor blood nitrate levels to ensure low levels of 4 to 12 hours per day to maintain efficacy. Common side effects for all nitrates include dizziness, postural hypotension, tachycardia and throbbing headache. Glyceryl trinitrate (GTN): administered as sublingual tablets, as sublingual aerosol aerosol, transdermal patches or as an intravenous infusion for the treatment and prophylaxis of angina. GTN can also be used to calm unstable angina and congestive heart failure. Isosorbide dinitrate: administer as immediate-release sub-tongue tablets, as an under-linguistic aerosol dispenser or intravenous infusion for the prevention or treatment of angina. Immediate-release and intravenous formulations may be used to treat left ventricular insufficiency. Modified-release formulations are used for the prophylaxis of angina. Isosorbide dinivre is slower than GTN. Isosorbide mononitrate: administered as sublingual tablets for the prophylaxis of angina Calcium channel blockers (CCBs) is intended for the treatment of hypertension. These medicines interfere with the inward movement of calcium ions through slow channels between myocardial cells, AV node cells and smooth muscle cells in blood vessels. The overall effect is to reduce myocardial contractile resistance, the formation and spread of electrical impulses within the heart, and the tone of blood vessels. There is a variety of CCB drugs available to prescribers, including single drug and fixed-dose combination drugs. Common side effects include dizziness, flushing, headache, swelling and palpitations. For all CCBs, prescribers should be alert to the possibility of overdose (CCB poisoning) with symptoms such as nausea, vomiting, dizziness, agitation, confusion, coma in case of severe intoxication, metabolic acidosis and hyperglycaemia. It is recommended that treatment be discontinued gradually as sudden withdrawal may be associated with exacerbation of myocardial ischaemia. All CCBs should be avoided during pregnancy unless the risk of uncontrolled maternal hypertension outweighs the risk to the foetus. Dose reduction may be necessary due to hepatic metabolism. Monotherapy medicinal products: Amlodipine: oral dihydropyridine type CCB prescribed for angina and hypertension. Contraindicated in patients with cardiogenic shock, significant aortic stenosis or unstable Felodipine: oral dihydropyridine type CCB prescribed for angina and hypertension. Use is contraindicated in cardiac cardiac vascular obstruction (e.g, aortic stenosis), uncontrolled heart failure, unstable angina or within 1 month after myocardial infarction. Isradipine: oral CCB prescribed for hypertension. The use is contraindicated in acute porphyria, cardiogenic shock, during or during 1 month myocardial infarction or unstable angina. Lacidipine: oral dihydropyridine type CCB prescribed for hypertension. Contraindicated in the same patients as isradipine. Lercanidipine: oral dihydropyridine type CCB prescribed for mild to moderate hypertension. Contraindicated in the same patients as isradipine. Nicardipine: prophylaxis of mild to moderate hypertension and angina in the form of an oral dihydropyridine type CCB. May be administered intravenously in patients with life-threatening hypertension in 6-patients (postoperative, hepatic or renal impairment or acute life-threatening hypertension during pregnancy). The use is contraindicated in acute porphyria, cardiogenic shock, significant or advanced aortic stenosis or unstable or acute angina attack. Oral administration should be avoided from 1 month after myocardial infarction (MI), intravenous administration, which should be avoided within 8 days after MI. Prophylaxis of angina is not generally recommended. It may be used off-label to delay premature work. Contraindicated in the same patients as isradipine. Nisoldipine: (not available in the United Kingdom) Oral dihydropyridine type CCB is indicated for the treatment of hypertension, which may be used alone or in combination with other antihypertensive agents. Avoid co-administration with CYP3A4 modulating medicinal products. Nimodipine: dihydropyridine type CCB (administered or administered intravenously) is indicated for the treatment or prevention of ischaemic neurological defects in aneurysm subarachnoid haemorrhage. Contraindicated in acute porphyria or unstable angina or for 1 month after myocardial infarction. Diltiazem: oral CCB, indicated for the treatment of angina and mild to moderate hypertension in prolonged-release formulations. Contraindicated in acute porphyria, left ventricular insufficiency and pulmonary edulation, second or third degree AV block (if a pacemaker is installed), severe bradycardia and sinus weakness syndrome. Verapamil: indicated for the treatment of supraventricular arrhythmias (oral or slow intravenous injection), paroxysmal tachyarrhythmias (slow intravenous injection), angina pectoris (oral), hypertension (immediate-release oral medicines) and cluster headache prophylaxis (initiated under the supervision of a specialist using rapidly releasing oral medicines). Oral verapamil can also be used for prophylaxis after myocardial infarction in patients for whom beta-blockers are not suitable. The use is acute atrial flutter or fibrillation related to the pathways of accessories (e.g. Wolff-Parkinson-White syndrome), bradycardia, cardiogenic shock, history of heart failure (even if it is controlled), a history of severely impaired left ventricular function (even if it is controlled), hypotension, second- and third-degree AV block, sinus syndrome weakness or sino-atrial block. Constipation is a common side effect. Fixed-dose combination medicines: Nifedipine with atenolol: CCB in combination with a beta-adrenoceptor antagonist (beta-blocker) designed to treat hypertension and angina. Indicated only when calcium channel blockers or beta-blockers alone prove insufficient with Amlodipine and valsartan: CCB in combination with angiotensin I1 receptor antagonist for the treatment of hypertension in patients who have already stabilised at the same doses as individual medicinal products. Amlodipine in combination with olmesartan: CCB in combination with angiotensin AT1 receptor antagonist for the treatment of hypertension in patients who have already stabilised at the same doses with individual medicinal products. Amlodipine in combination with olmesartan and hydrochlorothiazide: CCB in combination with an angiotensin AT1 receptor antagonist and a thiazide diuretic prescribed in patients who have already stabilised at the same doses as individual medicinal products or whose hypertension is not adequately controlled by olmesartan and amlodipine. Felodipine in combination with ramipril: CCB in combination with an angiotensin converting enzyme (ACE) inhibitor for patients who have already stabilised at the same doses with individual medicinal products. Stable angina usually results from atherosclerotic patches of the coronary arteries. It limits blood flow and oxygen supply to the heart. Stable angina is often predessed by exertion and relieve rest. Stable angina medications include nitrates (medication of choice), calcium channel blockers (CCBs), beta-blockers and potassium channel activators. These drugs for families have vasodilator effects that reduce blood pressure. Arteriolar dilation reduces peripheral vascular resistance and left ventricular pressure during systol, resulting in an improvement in cardiac output. In patients who do not have intolerance or contraindication to either nitrates, beta-blockers or CCBs, the listed drugs may be used as alternative antianginal agents. Potassium channel activators: Niorandil: a nitrate-component potassium channel activator with both arterial and venous vasodilatation properties. Approved for the prevention and long-term treatment of angina. Medicinal products with other mechanisms of action: Ivabradine: Ivabradine inhibits the initials (mixed Na+-K+ inward flow, activated by hyperpolarisation and modulated by an autonomous nervous system) in sinoatritrione (pacemaker) (PMID: 15301560). Heart rate decreases without myocardial contractility or ventricular repolarisation. Ivabradine oral medicinal product is indicated for the treatment of patients with angina pectoris mild to severe chronic heart failure. Contraindicated in patients with an acute myocardial infarction or slowing heart rate (<70bpm), immediately after cerebrovascular accident, patients dependent on pacemaker, second and third degree heart block, severe hypotension, sinus syndrome, sinoatrial block, unstable angina or unstable or acute heart failure. Common side effects include atrial fibrillation, blurred vision, bradycardia, dizziness, first degree heart block, headache, phosphenes, ventricular extrasystolids and visual disturbances. Ranolazine: It is likely to work through the sodium channels of the heart to modulate the permeability and cellular excitability of sodium ions. Indicated as adjun adjunstition in patients with stable angina who are not adequately controlled or tolerated in the first line of antianginal therapy. Caution should be exercised in patients with low body weight, moderate to severe congestive heart failure, QT prolongation and elderly patients. Avoid use in patients with moderate and severe hepatic or renal impairment. Common side effects include asthenia, constipation, dizziness, headache, nausea and vomiting. Angiotensin receptor antagonists are used to treat hypertension, diabetic nephropathy and congestive heart failure. As a group, these drugs are called sartans, and it forms a stem with their non-proprietary names. Clinical angiotensin receptor antagonists inhibit the activation of the angiotensin II-induced AT1 receptor, thereby modulating the renin-angiotensin system. This effect inhibits angiotensin II-mediated effects, mainly vasoconstriction and aldosterone and vasopressin secretion, which is clinically manifested as a decrease in blood pressure and vascular resistance. The efficacy of each sartan depends on inhibition of the pressor (inhibition of the effect of angiotensin II blood pressure increases), the affinity of its AT1 receptor and the biological half-life. Angiotensin receptor antagonists may be prescribed as individual medicinal products or fixed dose combinations with other antihypertensive medicinal products, in particular thiazide diuretic hydrochlorothiazide. All angiotensin receptor antagonists are contraindicated in patients with aliskiren, a direct renin inhibitor, diabetes mellitus or kidney disease with eGFR <60. All these medicines should be avoided in patients with severe hepatic impairment and during pregnancy unless this is important as they may impair the control of the blood pressure and renal function of the foetus and newborn. Use with caution in patients with renal impairment, starting with a low dose, and titrated according to response. For monotherapy medicinal products: telmisartan: indicated for the prevention of hypertension (20-40 mg once daily, titration up to 80 mg if necessary), for the prevention of cardiovascular events in patients with atherosclerotic diabetic organ damage (80 mg once daily). Common side effects include arthralgia, back pain, chest pain, eczema, gastrointestinal tract symptoms, leg cramps, myalgia, pharyngitis, sinusitis and urinary tract infection. Olmesartan/Olmesartan medoksomil: Indicated for the treatment of hypertension, starting with a daily dose of 10 mg, if necessary by increasing the dose to 20 mg. The maximum dose is 40mg per day. Contraindicated in patients with biliary obstruction. Adverse reactions include arthritis, chest pain, cough, fatigue, indigestion, haematuria, hypertriglyceridaemia, hyperuricaemia, flu-like symptoms, musculoskeletal pain, peripheral oedema, pharyngitis, rhinitis and urinary tract infection. Valsartan: indicated for the treatment of hypertension, heart failure when ACE inhibitors cannot be used, or in combination with an ACE inhibitor when a beta-blocker cannot be used, and myocardial infarction with left ventricular insufficiency or left ventricular systolic dysfunction. Additional specific contraindications are biliary cirrhosis and cholestasis. Common side effects include kidney damage. Losartan: potassium: indicated for the treatment of heart failure when ACE inhibitors cannot be used, and diabetic nephropathy in type 2 diabetes mellitus. An additional specific contraindication is severe in heart failure. Vertigo is a common side effect. The manufacturer recommends avoiding Irbesartan: indicated in patients with hypertension, patients on haemodialysis and type 2 diabetes mellitus. Common side effects include fatigue, musculoskeletal pain, nausea and vomiting. Azosartan/azosartan medoksomil: indicated for the treatment of hypertension and recommended in patients with hypertension and intravascular volume depletion. Common side effects include diarrhoea and increased creatine kinase levels. The manufacturer recommends avoiding patients with severe hepatic impairment or with low dose and close monitoring in patients with mild to moderate hepatic impairment. Proprosartan: Indicated for the treatment of hypertension with an adult dose of 600 mg once daily. Common side effects include headache, nausea, rhinitis, diarrhoea, malaise and vomiting. Candromycin/candromycin zigettil: indicated for hypertension (usual dose 8 mg once daily), intravascular volume of hypertension (usual dose 8 mg once daily), heart failure with left ventricular systolic dysfunction, if ACE inhibitors are tolerable and heart failure with left ventricular systolic dysfunction in combination with an ACE inhibitor (dose starts at 4 mg once daily, increasing to 32 mg once daily or maximum tolerated dose for two weeks). Contraindicated in patients with cholestasis. Often there are other sartans, common side effects of headache and dizziness. Avoid prescribing to patients with severe hepatic impairment and be careful in patients with renal impairment (eGFR under 15). Fixed-dose combined medicinal products: losartan and hydrochlorothiazide irbesartan and amlodipine with valsartan valsartan and hydrochlorothiazide Olmesartan and amlodipine amlodipine blocker) Telmisartan with hydrochlorothiazide Olmesartan with amlodipine and hydrochlorothiazide Angiotensin II (ATII) is a very potent endogenous vasoconstrictor. It is formed from angiotensin I in the blood by an angiotensin converting enzyme (ACE). The modulating effects of atii renin-angiotensin-aldosterone system (RAAS) are mediated by angiotensin receptors AT1 and AT2. ACE inhibitors partially prevent ATI from switching to ATII. As a result, blood vessels expand, and blood pressure decreases. Lowering blood pressure makes it easier to pump blood into the heart and can improve heart function. Additional clinical intervention of ACE inhibitors slows the progression of kidney disease due to high blood pressure or diabetes. ACE inhibitors are the first choice for hypertension treatment, especially under 55 years old. The use of ACE inhibitors to treat heart failure is not so age-related and the level of benefit achieved appears to be increasing with age. Angiotensin receptor antagonists are commonly used in patients who cannot tolerate ACE inhibitors and are useful because they inhibit the residual ATII activity of a series of residual ATII in the blood due to incomplete ACE inhibition. The combination of angiotensin receptor antagonists and ACE inhibitors may be better than either medicine alone. ACE inhibitors are administered as prodrugs or a prodrug of conjugates, which are metabolized in the liver by the active compound. Ace inhibitor prodrug is the common name stem suffophilia -pril and the active compound is stem-prilat. Captopril had the first ACE inhibitor approved but has since been replaced by alternatives with improved duration and less harmful effects. There is a wide range of ACE inhibitors available as a prescriber, but all have similar antihypertensive effects at equivalent doses. The main difference between the different medicines is the duration of their action. Some of them are listed below with an equivalent dose. Name Eq. daily dose Start dose Usual dose Max. dose ACE inhibitors dosages for hypertension benazepril 10mg 10mg 20-40mg 80mg captopril 50mg (25mg bid) 12.5-25mg bid-tid 25-50mg bid-tid 450mg /day enalapril 5mg 5mg 10-40mg 40mg 40mg fosinopril 10mg 10mg 20-40mg 80mg lisinopril 10mg 10mg 10-40mg 80mg moexipril 10mg 10mg 10-40mg 80mg moexipril 7.5mg 7.5mg 7.5-30mg 30mg perindopril 4mg 4mg 4-8mg 16mg ramipril 2.5mg 2.5mg 2.5-20mg 20mg trandolapril 2mg 1mg 2-4mg 8mg quinapril 10mg 10mg 20-80mg 80mg tid = three times a day bid = two times a day All ACE inhibitors are contra-indicated in patients with previous ACE inhibitor-induced angiodema, or hypersensitivity to the drug. Prescribers should be wary of prescribing ACE inhibitors in patients with renal impairment, aortic valve stenosis or cardiac outflow obstruction, hypovolaemia, dehydration or haemodialysis (using high-flow polyacryl lytrile membrane). Administration of Ace women who are likely to become pregnant, as well as use during pregnancy due to the risk of birth defects caused by the medicine. Mnemonic contributes to acetic inhibitor contraindications of rectsidivitis U: Pregnancy, allergy/ angiodema, Renal failure, K-hyperkalaemia (potassium>55). Side effects include dry, irritating cough and less frequent renal stenosis or allergic reaction. Alpha-blockers, α-blockers or α-adrenergic antagonists are pharmacological agents that act as α-adrenoceptor antagonists. Medicinal products may be non-selective, antagonising both α1 and α2 receptor subtypes, or may be selective over one subtype to another. α-blockers are most commonly used to treat hypertension, but are also widely used to treat symptoms of BPH (benign prostatic hyperplasia). The symptoms of Raynaud's disease also α treatment with the drug-blocker, although the efficacy of this condition has not been clearly demonstrated. Common α with all other blockers are the risk of hypotension (especially after the first dose), dizziness, drowsiness, dry mouth and headache. Many side effects decrease over time. Non-selective α anti-blockers for controlling hypertensive episodes associated with phenozocytoma) α1-selective blockers for control of hypertensive episodes associated with phenotopoma (symptomatic relief in benign prostatic hyperplasia, (BPH) prazosin (BPH, hypertension) doxazosin (BPH, hypertension) steelosine (BPH, hypertension) silodosin (BPH) tamsulosin (BPH) indomine (BPH) α2-selective blockers mirtazapine (treatment of episodes of depression) Beta-blockers, beta-adrenoceptors blockers are pharmaceutical agents that act as competing antagonists of β-adrenoceptors, which are activated by the endogenous endogenous catecholamines epinephrine (adrenaline) and norepinephrine (norepinephrine). Beta-blocking medicines used to treat conditions such as angina, heart failure, irregular heartbeat, swelling and high blood pressure, and which can also be used to treat glaucoma and anxiety. Side effects are generally not serious and decrease when the body adjusts to treatment. Hypotensive effects (especially after the first dose), fatigue, dizziness and cold hands and feet are quite common side effects. In men, the use of a beta-blocker may cause erectile dysfunction. Beta-blockers are contraindicated in patients with asthma, cardiogenic shock, hypotension, pronounced bradycardia, metabolic acidosis, pheochromocytoma (excluding special use with alpha-blockers), Prinzmetal angina, grade 2 and 3 AV block, severe peripheral arterial disease, sinus syndrome or uncontrolled heart failure. In addition, beta-blockers, including patients considered to be cardio-selective, should be avoided where possible. patients with a history of asthma, bronchospasm or a history of obstructive respiratory disease. If there is a cardio-selective beta-blockers may prescribe special medical care for patients, with particular attention to bronchospasm induction. There is a risk of sade heart failure when beta blockers and calcium channel blocker (antiarrhythmic), verapamil, used in combination with ischemic heart disease. Ike α-blockers, beta-blockers may be selective or non-selective β-adrenoceptor tealatypes. β1-selective drugs are considered cardio selective because the heart and kidneys are the main sites of β1-adrenoceptor expression. β2-adrenoceptor is expressed in the lungs, gastrointestinal tract, liver, uterus, smooth muscles of blood vessels and skeletal muscles, and β3-adrenoceptor is found in fat cells. Non-selective beta-blockers timolol (hypertension, prevention of angina, migraine, prophylaxis after myocardial infarction, glaucoma reduces intraocular pressure) pindolol (hypertension, angina) propranolol (hypertension, angina, anxiety, essential tremor, migraine prophylaxis, arrhythmias, prophylaxis after myocardial infarction, treatment of symptoms of thyrotoxicosis) levobunolol (glaucoma- reduces increased intraocular pressure) carteolol (hypertension, increased intraocular pressure) sotalol (artyroxy) oxotrophy (angina, hypertension and cardiac athyroidism) nadolol (angial hypertension, migraine pain and tremor) Selective beta-blockers (β 1 selective beta-blockers) , cardio-selective) atenolol (hypertension, angina, arrhythmias) esmomol (tachycardia and hypertension in the perioperative period, short-term treatment of supraventricular arrhythmias) metoprolol (hypertension, angina pectoris, arrhythmias, early intervention within 12 hours after a heart attack, prevention of migraine) coeliac prolool (mild-to-moderate hypertension) kotenidone (hypertension), kotenidone is a 4:1 mixture of atenolol and carbonic anhydrase inhibitor, chlorthalidone bisoprolol (hypertension, steno cardiol) antentolol (hypertension) antentolol (hypertension) , angina, arrhythmias) nebivolol (essential hypertension, hypertension in patients with renal impairment, in addition to stable mild to moderate heart failure) betaxolol (hypertension , primary open-angle glaucoma) indicate that β1 selectivity is not absolute, and some inhibitory action β2-adrenoceptor is exhibited at higher doses. Antiarrhythmics are a group of medicines used to suppress cardiac arrhythmias (cardiac arrhythmias) such as atrial fibrillation, atrial flutter, ventricular tachycardia and ventricular fibrillation. Class I antiarrhythmics interfere with the function of the sodium channel and are broken down by the effect they affect on their potential for action (AP) — see Section 1, and in cardiopulmonary redares when amiodarone is not available) class Ic antiarrhythmics such as flecainid (used to treat different arrhythmias: AV nodal reciprocating tachycardia, arrhythmias associated with Wolff-Parkinson-White syndrome and supraventricular arrhythmias) and propafenone (used primarily under special supervision in hospital for the treatment of supraventricular arrhythmias and paroxysmal supraventricular tachyarrhythmias, including paroxysmal atrial flutter or fibrillation and paroxysmal tachycardia, which includes AV nodule or akssuar treatment is not effective or contraindicated). Class II antiarrhythmics are common beta-blockers- See the subject of beta-adrenoceptor blocking medicinal products over one class III antiarrhythmic (mainly affecting potassium (K+) outflow, prolonging repolarisation), e.g. dronedarone (used to treat atrial flutter and fibrilation and to maintain the simulant rhythm after cardioversion) and amiodarone (used to treat angina and arrhythmias). Note that amiodarone should not be co-administered with sofosbuvir with daclatasvir, sofosbuvir and ledipasvir and simeprevir in combination with sofosbuvir due to the risk of severe bradycardia and cardiac block. Class IV antiarrhythmics (are slow calcium channel blockers, reduce av node conduction and shorten the AP plateau) e.g. verapamil and diltiazem Class V (other) antiarrhythmics, e.g. digoxin (reduces conduction rate via AV node, used to treat congestive heart failure and atrial fibrillation), adenosine (used intravenously for supraventricular tachycardia, magnesium sulphate (used to treat torsades de pointes) Compared to the above classification, and treatment of atrial fibrillation, Class I and III antiarrhythmics are used as rhythm control medical cardioversion agents while class II and IV antiarrhythmics are used as means of rate control. Diuretics are especially useful in treating water and salt retention caused by heart failure. Common side effects such as muscle cramps result from the loss of too much sodium, potassium or magnesium. Prescribers should be aware of the risk of diuretic-induced hypokalaemia. There are three main types of diuretics, each affecting a different part of the kidneys: Lingu diuretics– prescribed for the treatment of fluid retention (oedema), especially in the lungs. These drugs are very fast acting, but short-lived and cause dramatic water loss. e.g. furosemide, bumetanid and uncommon torasemide. Furosemide may be determined with potassium chloride to maintain potassium content. Thiazide diuretics- fast-acting but longer duration than loop diuretics, less dramatic water loss. They are often used to treat low-dose hypertension. for example, bendroflumethiazide, hydrochlorothiazide and indapaid Potassium-sparing diuretics – these are weaker diuretic types that increase water loss but prevent high potassium loss. Potassium-sparing diuretics are usually for the treatment of water retention due to heart failure, e.g. spironolactone and eplerenone (aldosterone antagonists), triamterene and amilorid (epithelial sodium channels, ENaC) Potassium-sparing diuretics are not usually necessary in routine treatment of hypertension unless hypokalaemia develops. Other o diuretics Osmotic diuretics, such as mannitol, given as an intravenous infusion (IV) may be used to treat increased brain oedema and intraocular pressure (e.g. in patients with glaucoma). Carbonic anhydrase inhibitors such as acetazolamide (administered orally or intravenously) and dorzolamide and brinzolamide (topically) are diuretics used to treat glaucoma. Medications from these different families can be prescribed fixed-dose combinations that can be used when compliance with separate medications is an issue. For example, furosemide with triamtene or spironolactone, cotriamteride (triamterene and hydrochlorothiazide), concomitant amiloferus (amiloride plus furosemide) and co-mism (amiloride plus hydrochlorothiazide). Dorzolamide and brinzolamide may be prescribed at fixed doses in combination with timolol beta-blocker, intraocular pressure increase and glaucoma in patients for whom beta-blocker monotherapy is inadequate. Diuretics are especially useful in treating water and salt retention caused by heart failure. Common side effects such as muscle cramps result from the loss of too much sodium, potassium or magnesium. Prescribers should be aware of the risk of diuretic-induced hypokalaemia. There are three main types of diuretics, each affecting a different part of the kidneys: Lingu diuretics– prescribed for the treatment of fluid retention (oedema), especially in the lungs. 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For example, furosemide with triamtene or spironolactone, cotriamteride (triamterene and hydrochlorothiazide), concomitant amiloferus (amiloride plus furosemide) and co-mism (amiloride plus hydrochlorothiazide). Dorzolamide and brinzolamide may be prescribed at fixed doses in combination with timolol beta-blocker, intraocular pressure increase and glaucoma in patients for whom beta-blocker monotherapy is inadequate. Positive inotropic agents increase myocardial contractile concentration by increasing calcium levels in the cytoplasm of muscle cells or by increasing cardiac sensitivity to calcium. Positive inotropes are indicated for acute conditions with low cardiac output (CO), such as cardiogenic shock after myocardial infarction, acute decompensated heart failure, low CO countries after heart surgery, cardiogenic shock, septic shock, and cardiomyopathy. By contrast, negative inotropes weaken the force of contraction of the heart's evidence that one specific positive inotrope is better than the other. The choice of which medicine to provide depends on factors such as the patient's underlying condition and the doctor's preference. Drugs that act as positive inotropes include catecholamines (dobutamine and isoprerenaline [synthetic catecholamines] and adrenaline and norepinephrine [endogenous catechomines]) and phosphodiesterase type-3 (PDE3) inhibitors. The cardiac effects of catecholamines are associated with their effect as alpha and beta adrenoceptor agonists, in particular the activation of the ß1-adrenoceptor increases cardiac contractability and heart rate. Dobutamine is mainly a ß1 agonist, but its effect on ß2 receptors causes vasodilatation (and reduces afterload), which can be compensated by the administration of a vasopressor such as norepinephrine. Isoprenaline has a similar profile to dobutamine, but tends to cause more tachycardia. Norepinephrine, which works mainly by α1-adrenoceptors, is mainly used as a vasopressor (increasing afterload to maintain medium arterial pressure) rather than inotrope. It is often used in combination with other inotropes, such as dobutamine, to maintain adequate perfusion (supra). Since adrenaline is activity at all adrenoceptor other more specific inotropes are often preferred adrenaline. The main use of adrenaline is a bolus dose given during re-life after cardiac arrest. Inhibition of PDE3 increases intracellular calcium, causing vasodilatation and myocardial contractile resistance, and is a causal mechanism of action for enoxidone of PDE3 inhibitors, milrinone and a non-selective phosphodiesterase inhibitor. Positive inotropic agents increase myocardial contractile concentration by increasing calcium levels in the cytoplasm of muscle cells or by increasing cardiac sensitivity to calcium. 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Inhibition of PDE3 increases intracellular calcium, causing vasodilatation and myocardial contractile resistance, and is a causal mechanism of action for enoxidone of PDE3 inhibitors, milrinone and a non-selective phosphodiesterase inhibitor. Digoxin belongs to a class of medicines called cardiac glycosides, which also includes digital toxin and ouabain. Cardiac glycosides occur naturally in plants called Genera Digital, such as fox gloves and Strophanthus. Clinically, only digoxin and very rarely digital toxin are used. Such agents increase the force of contraction of the heart, a positive inotropic activity that is the basis of their use in some cases of heart failure. They also have a significant effect on electrical conductivity in the heart, especially at the speed at which the operational potential is carried out at the atrioventricular (AV) node. Digoxin is used clinically in severe heart failure, but usually as a third line when other medicines, including ACE inhibitors, low-dose β-blockers and aldosterone receptor antagonists, or angiotensin receptor blockers, or angiotensin receptor blockers do not provide sufficient benefits. However, as explained below, digoxin can be used at an earlier stage if the patient has atrial flutter as a concomitant morbidity. The relevant chemistry structurally, observed here, cardiac glycosides (carneolides) consist of a steroid ring to which lactone and sugar residues (β configuration) are attached in C17 (D ring) and C3 (Ring) positions respectively. Unsaturated lactone ring is important for the pharmacodynamic activity of cardiac glycosides, as are steroid-B and C/D ring cis-fusion, B/C ring transfusion and β-hydroxyl presence in C14. Sugar groups (which are different in nature and number, e.g. one rhamnosis in ouabin or dig triple toxin and digital toxin digitisation) affect the efficacy and pharmacokinetics of individual compounds. The nature of sugar also contributes to the modest selectivity of cardiac glycosides between isoforms at their primary molecular target Na+/K+-ATPas. The latter is considered classically heterodichom 1:1 in α stoöhhimetry with regulatory subunits (β phosphorus at the heart) Cardiac mechanism of action Cardiac glycosides associated with Catalytic α subunit of Na+/K+-ATPase (sodium pump) that inhibits its effect when transporting Na+ out of the heart muscle cell and K+ to the heart muscle cell. Therefore, the therapeutic concentration of digoxin in the heart muscle is associated with the proportion of Na+/K+-ATPas pumps, reducing overall pumping activity. Excessive pump inhibition is the basis for many serious side effects of digoxin that limit its use (see below). Digoxin binds to the extracellular side of the pump, which competes with K+, at least partially explaining the clinically relevant phenomenon that decreased K+ concentrations in plasma (hypokalaemia) increase the effect of digoxin, which may lead to serious toxicity. In addition, decreased plasma K+ may result in the phosphorylation of Na+/K+-ATPase, which increases its affinity for digoxin binding and thus pump occupancy. The isoforms of Na+/K+-ATPase α1β and α2β are related to the inotropic activity of cardiac glycosides. Tolerance of the heart muscle, which, due to its high electrical activity, is particularly dependent on Na+/K+-ATPase to maintain suitable ion inclination elevations throughout the plasma membrane, causes pump inhibition na+ ([Na+]i intracellular concentration increase). This is accompanied by a slight reduction in the potential of the membrane of the resting agent (diastolic) of heart muscle cells because the pump is electrogenic (i.e. pumps 3 Na+ out: 2 K+ per transport cycle at the expense of one AtP molecule hydrolysed ADP and Pi). The subsequent decrease in electrochemical gradute in Na+ wearing secondarly reduces ca2+ expulsion from the cytoplasm during diastol with stochiometry 3 Na+ by the na+/Ca2+ heat exchanger (NCX1) operating each transport cycle. This occurs because of the Na+/K+-ATPase (primary active transport) operation to maintain ncx1 mediated secondary active transport. Excess Ca2+ is separated by the smagnifying cell of sarkiplasmic reticulum (SR) by Ca2+-ATPase (SERCA2a) in its organelle membrane. Thus, an additional free Ca2+ ventricular activity potential is available for release from sR lume (stage 2) by calcium calcium release (CICR). The last process has been developed in the text box. Cytoplasm Ca2+ transient, which is followed and generates systolic is thus increased and increased occupation of the cardiac isoform troponin-C (TNNC1) ca2+ means increased cardiac contractileity. The effect of digoxin on the electrical activity of the heart is complex and consists of several direct and indirect activities. Directly, inhibition of Na+/K+-ATPase causes a small depolarisation of the heart muscle (see above) that promote the abnormal release of heart muscle cells and, consequently, ectopic shocks in heart muscle cells and consequent ectopic beats (see below). Acting directly on the heart control system, slows down the speed of the conduction pathways through the atrioventricular (AV) node, prolonging the refractory period. The latest action is useful and the underlying use of the drug in patients with atrial fibrillation or flutter comes with high ventricular rates, usually when combined with heart failure. Although digoxin does not correct atrial fibrillation or flutter, it inhibits aberrant impulses through the AV node to trigger ventricular arrhythmias. By contrast, excessive suppression of av conductiveness causes cardiac block, which is one of the characteristics of digoxin toxicity. Indirectly, but again by inhibition of na+/K+-ATPase, digoxin stimulates parasympathetic neural supply to the heart by acting on the central vagal nucleus (i.e. increasing the vagal tone), which strengthens its inhibitory effect on the speed of conduction of the AV node and also reduces the autosing of the sinoatic (SA) node, thus reducing the rate of discharge. The last action slows down the heart rate in the siar rhythm. Pharmacokinetics Digoxin may be administered orally or if rapid action by slow intravenous injection is required. When administered orally, the bioavailability of digoxin affects the pharmaceutical form (tablets, or liquid). The drug has a large volume of distribution, mainly due to binding of skeletal muscle Na+/K+-ATPase, with a elimination half-life of approximately 36 hours (with normal renal function, see below), a loading dose is usually required orally if urgent action is required. It can be taken with or without food. Digoxin is a polar molecule and the main elimination pathway (approximately 70% of the drug does not change) is renal excretion, which includes both glomerular filtration and active tubular secretion. Therefore, the dose of digoxin should be reduced in case of significant renal impairment, especially in view of the very low therapeutic index. Dose reduction is proportional to the reduction in glomerular filtration rate (GFR). Hepatic metabolism contributes to elimination to a much lower extent than renal excretion. Drug interactions Safety margins between digoxin doses produced therapeutic or toxic effects (plasma concentrations approximately 1 to 100 mg/ day) have been reported as therapeutic or toxic. In addition, digoxin has important pharmacodynamic and pharmacokinetic interactions with a wide range of medicinal products, including some used to treat heart disease. Some important examples are: Pharmacodynamic – these are largely predictable basic knowledge of cardiac pharmacology: β-adrenoreceptor antagonists: AV node conduction rate has facilitated noradrenaline (and adrenaline) acting as agonists β1-adrenoceptor nodal tissue. Blockade of this effect by β1-antagonists with the degree of conductive conductability of the DIGOne-negative AV node may result in high grade AV blockade. In addition, β negative inotropic effects that physiologically antagonised the inotropic effect of digoxin. ca2+ channel blockers: Ca2 + channel blockers, which have a certain selectivity of L-type Ca2 + channels in the heart muscle (e.g. verapamil) can produce a negative inotropic effect, denying the beneficial positive inotropic effect of digoxin. thiazide and loop diuretics: both classes cause potassium loss from the body, leading to hypokalaemia. As explained above, it potentiates the effect of digoxin, which leads to potential toxicity. Pharmacokinetic – these are less easily understood knowledge of the mechanism and are probably best consulted in comprehensive textbooks on basic and clinical pharmacology and national and local formulas: drugs that increase the absorption of digoxin from the gastrointestinal tract. Many antibiotics (e.g. erythromycin) can cause this by shrinking the intestinal flora that metabolize part of the drug before it is absorbed over the mucous membrane. volume of distribution of digoxin or medicinal products that alter renal clearance. Verapamil, quinidine, amiodarone and spironolactone are particularly important due to cardiovascular/renal activity. Adverse reactions The main side effects of digoxin are: bradükardia AV node conduction block (see above): digoxin is contraindicated in patients with grade 2 cardiac block or intermittent complete heart block, which triggers a variety of arrhythmias, including ectopic shocks (see above): after delay in depolarisation (DAD) may result from associated shocks ca2+ overload (bigeminy) Digoxin is contraindicated in patients with or at risk of ventricular arrhythmias such as anorexia, nausea, vomiting and neurological disorders such as yellow vision (likely due to retinal effects), fatigue, malaise and confusion. Digoxin toxicity may be induced by electrolyte imbalances involving hypokalaemia (see above), hypomagnesaemia and hypercalcaemia. Treatment of digoxin toxicity includes drug prevention, potassium supplementation to correct hypokalaemia and, in severe cases, the administration of digoxin-specific antibody fragments. John Peters Digoxin belongs to a class of drugs known as cardiac glycosides, which also includes digital toxin and

ouabain. Cardiac glycosides occur naturally in plants called Genera Digital, such as fox gloves and Strophanthus. Clinically, only digoxin and very rarely digital toxin are used. Such agents increase the force of contraction of the heart, a positive inotropic activity that is the basis of their use in some cases of heart failure. They also have a significant effect on electrical conductivity in the heart, especially at the speed at which the operational potential is carried out at the atrioventricular (AV) node. Digoxin is clinically used in severe heart failure, but usually as a third line when other medicines, including ACE inhibitors, β of blockers and aldosterone receptor antagonists or angiotensin receptor blockers is not sufficient. However, as explained below, digoxin can be used at an earlier stage if the patient has atrial flutter as a concomitant morbidity. 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The latter is considered α heterodichograph (α1, α2, α3 and α4) β (β1, β2 and β3) subunits 1:1 stoöhhimetry in stoihachimetric subunits with regulatory subunits (phosolemman in the heart) Mechanism of action Cardiac glycosides are bound by the catalytic α subunit of Na+/K+-ATPase (sodium pump), which inhibits its effect when transporting Na+ from the heart muscle cell and the cell of the K+ heart muscle. Therefore, the therapeutic concentration of digoxin in the heart muscle is associated with the proportion of Na+/K+-ATPas pumps, reducing overall pumping activity. Excessive pump inhibition is the basis for many serious side effects of digoxin that limit its use (see below). Digoxin binds to the extracellular side of the pump, which competes with K+, at least partially explaining the clinically relevant phenomenon that decreased K+ concentrations in plasma (hypokalaemia) increase the effect of digoxin, which may lead to serious toxicity. 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In addition, digoxin has important pharmacodynamic and pharmacokinetic interactions with a wide range of medicinal products, including some used to treat heart disease. Some important examples are: Pharmacodynamic – these are largely predictable basic knowledge of cardiac pharmacology: β-adrenoreceptor antagonists: AV node conduction rate has facilitated noradrenaline (and adrenaline) acting as agonists β1-adrenoceptor nodal tissue. Blockade of this effect by β1-antagonists with the degree of conductive conductability of the DIGOne-negative AV node may result in high grade AV blockade. In addition β-blockers exert a negative inotropic effect, which physiologically antagonises the inotropic effect of digoxin. ca2+ channel blockers: Ca2 + channel blockers, which have a certain selectivity of L-type Ca2 + channels in the heart muscle (e.g. verapamil) can produce a negative inotropic effect, denying the beneficial positive inotropic effect of digoxin. thiazide and loop diuretics: both classes cause potassium loss from the body, leading to hypokalaemia. As explained above, it potentiates the effect of digoxin, which leads to potential toxicity. Pharmacokinetic – these are less easily understood knowledge of the mechanism and are probably best consulted in comprehensive textbooks on basic and clinical pharmacology and national and local formulas: drugs that increase the absorption of digoxin from the gastrointestinal tract. Many antibiotics (e.g. erythromycin) can cause this by shrinking the intestinal flora that metabolize part of the drug before it is absorbed over the mucous membrane. volume of distribution of digoxin or medicinal products that alter renal clearance. Verapamil, quinidine, amiodarone and spironolactone are particularly important due to cardiovascular/renal activity. Adverse reactions The main side effects of digoxin are: bradycardia AV node conduction block (see above): digoxin is contraindicated in patients with second degree heart block or intermittent complete heart block, which triggers a variety of arrhythmias, including ectopic shocks (see above): delayed after depolarisation (DAD) may result from associated beats (bigeminy) digoxin is contraindicated in patients with or if you are at risk of ventricular arrhythmias gastrointestinal disorders such as anorexia, nausea, vomiting and diarrhoea neurological disorders such as yellow vision (probably due to retinal action), tiredness, malaise and confusion. Digoxin toxicity may be induced by electrolyte imbalances involving hypokalaemia (see above), hypomagnesaemia and hypercalcaemia. Treatment of digoxin toxicity includes drug prevention, potassium supplementation to correct hypokalaemia and, in severe cases, the administration of digoxin-specific antibody fragments. John Peters Peters