

Effects of cardiovascular drugs on the eyeball

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Acronyms

WHO: World Health Organization

ACE: angiotensin converting enzyme

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ABSTRACT

Introduction and Objective: There is a high incidence of cardiovascular conditions among the patients who visit the ophthalmology offices, and many of drugs used for these conditions may cause undesirable effects on the eyeball. The objective of this research was to determine the adverse reactions caused by the consumption of these drugs in the visual organ, and highlight their contraindications in people affected by eye disease.

Method: A literature search was performed using specialized texts, and the drugs that could produce ocular adverse reactions were identified, as well as those that were contraindicated in ophthalmic diseases.

Results: A total of 276 medications were reviewed and 72 (26.08%) were selected. Blurred vision (38/72), decreased visual acuity (21/72) and dizziness (16/72) were the most common adverse reactions associated with the use of cardiovascular drugs. The six medications that are contraindicated in these patients are exposed, as well as the 14 that should be prescribed with extreme caution in diseases such as glaucoma, optic atrophy, hypertensive retinopathy and migraine, among others.

Conclusions: It was found that 72 drugs (26.08%) used in cardiovascular disease may produce some ocular symptoms as an adverse reaction. Blurred vision, decreased visual acuity and dizziness were predominant. It is extremely important to conduct a good medical interview to know the patient's medical history and avoid the use of drugs that are useful for a disease but harmful for another one. The doctor, knowingly, will weigh the risk/benefit of those drugs that are essential.

Key words: Cardiovascular Agents/ adverse effects, Cardiovascular Agents/ contraindications; Eye Diseases/ chemically induced, Eye Diseases/ etiology

Efectos de los medicamentos cardiovasculares sobre el globo ocular

RESUMEN

Introducción y objetivo: A las consultas de Oftalmología acuden pacientes con una alta incidencia de enfermedades cardiovasculares y muchos de los fármacos útiles para este tipo de afecciones pueden producir efectos indeseables sobre el globo ocular. El objetivo de esta investigación fue determinar las reacciones adversas que,

sobre el órgano visual, provoca el consumo de estos medicamentos, y señalar sus contraindicaciones en personas afectadas por alguna enfermedad ocular.

Método: Se realizó una búsqueda bibliográfica en textos especializados y se seleccionaron los medicamentos que podían producir reacciones adversas oculares, así como los que estaban contraindicados en las enfermedades oftalmológicas.

Resultados: Se revisaron 276 medicamentos y se seleccionaron 72 (26,08 %). La visión borrosa (38/72), la disminución de la agudeza visual (21/72) y el vértigo (16/72) fueron las reacciones adversas más frecuentes asociadas al uso de los medicamentos cardiovasculares. Se exponen los 6 medicamentos que están contraindicados en este tipo de pacientes y los 14 que deben prescribirse con gran precaución en enfermedades como: el glaucoma, la atrofia óptica, la retinopatía hipertensiva y la migraña, entre otras.

Conclusiones: Se encontró que 72 medicamentos (26,08 %) utilizados en las enfermedades cardiovasculares presentan, dentro de sus reacciones adversas, alguna sintomatología ocular. Predominan la visión borrosa, la disminución de la agudeza visual y el vértigo. Es de extrema importancia realizar un buen interrogatorio a los pacientes para conocer sus antecedentes patológicos personales y así evitar el uso de fármacos que sean útiles para una enfermedad y perjudiciales para otra. El médico, con conocimiento de causa, valorará el riesgo/beneficio en aquellos fármacos imprescindibles.

Palabras clave: Fármacos cardiovasculares/ efectos adversos, Fármacos cardiovasculares/ contraindicaciones; Oftalmopatías/ etiología, Oftalmopatías/ inducido químicamente.

INTRODUCTION

From as far back as 1500 B.C., in the Ebers papyrus (ancient Egypt), there is recorded evidence on the use of substances to treat diseases. The Greek word *φάρμακον* was used to refer to both, the drugs used as medications and those used for other purposes. Today, the term drug, when it means medicament, refers to that purified chemical substance used in the prevention, diagnosis, treatment, mitigation and cure of a disease¹.

Prescribe, dispense or suggest the use of a drug has always been a therapeutic procedure used by the healthcare professional, with beneficial effects for human beings. Currently, a wrong trend has emerged, where common people who are not specialists "suggests" taking a drug without having the basic knowledge of its use and no information about its adverse reactions. This conduct has led to an epidemic of diseases which increase adverse reactions and health expenditures. The correct selection of a drug should be made by qualified personnel taking into account the criteria of efficacy, safety, convenience and cost².

The rational use of drugs has become an important strategy of the World Health Organization (WHO), and

of many countries, including Cuba, which aims to get the best effect with the least quantity of drugs during a short period of time and at a reasonable cost, to avoid temporary or permanent disability and the economic burden it means to society. Recent drug-epidemiology studies show that the use of medications is already a major cause of death in the developed world^{2,3}.

The twentieth century was characterized in terms of health and medicine by the eradication of diseases, increased life expectancy, the emergence of powerful drugs and the appearance of adverse reactions. In the last 50 years, and associated with the development of the pharmaceutical industry, there has also been an increase in the use of drugs, and thus the likelihood of unwanted effects, as well as iatrogenic diseases caused by the misuse of them².

The ophthalmology offices are visited by large numbers of adults who express, in their personal or family medical history, the presence of cardiovascular diseases, among which are: angina, hypertension, heart failure, arrhythmias, cardiomyopathy, myocardial infarction, peripheral vascular disease and valvular heart disease, just to name a few. These people are medicated with various drugs, which are within

the three groups most commonly used in routine clinical practice. Since the 1960s, there has been a worldwide increased in the use of cardiovascular and psychiatric medications due to the emergence of propranolol and benzodiazepines²⁻⁴.

Motivated by knowing the behavior of the consumption of these drugs in the population treated in a health area, this research was conducted in order to determine the possible adverse reactions that the use of cardiovascular drugs causes in the visual organ, and their contraindications in people living with some eye disease.

METHOD

A document research was conducted through a literature search of cardiovascular drugs in national and international treatment guidelines, and Pharmacy, Pediatrics and Internal Medicine books, during the first quarter of 2012. As a preamble to the study, cardiovascular medications were organized according to the different pharmacological actions and grouped in a classification (Appendix). Subsequently, those that could produce ocular adverse reactions were identified, as well as those that were contraindicated in eye diseases. Medications that had two pharmacological actions were processed only once to avoid false conclusions.

Data were recorded and processed using Microsoft Excel 2007, making it possible to devise the frequency distribution tables and graphics of the research.

RESULTS

A total of 276 cardiovascular drugs were reviewed³⁻¹⁸, and 72 (26.08%) were selected as they met the selection criteria (Figure 1).

Figure 2 is based on a frequency distribution of the ocular adverse reactions present in these drugs. Blurred vision, decreased visual acuity and dizziness are the three most common reactions that can occur when taking these drugs. Blurred vision is present in 38 medications (52.8%), decreased visual acuity in 21 (29.2%) and dizziness in 16 (22.2%).

Tables were made according to the mechanism of action, contraindications and adverse reactions of cardiovascular drugs. Table 1 shows the antiarrhythmics. As it can be seen, only nitroglycerin is contraindicated in people with narrow-angle glaucoma. However, although it is included in this category, this drug is rarely used by cardiologists in patients with cardiac

arrhythmias; instead, it is very useful in the ischemic patient. When analyzing the adverse reactions of the 24 antiarrhythmic drugs, it can be noticed that the visual impairment occurs in 20 of them (83.3%), either as decreased visual acuity, color vision or lights, diplopia, scotoma and blurred vision

Table 2 shows the antihypertensive medications. In total, we found 40 medications, but only 26 were analyzed because the rest had been analyzed in previous tables. Of these, only sodium nitroprusside (mixed vasodilator) is contraindicated in Leber optic atrophy and fenoldopam is contraindicated in glaucoma. With regard to adverse reactions in this group of drugs, dizziness was the most common one. It was present in 13 of them (50%), followed by visual disorders in 12 drugs (46.1%) and eye redness in 23 % (6 drugs)

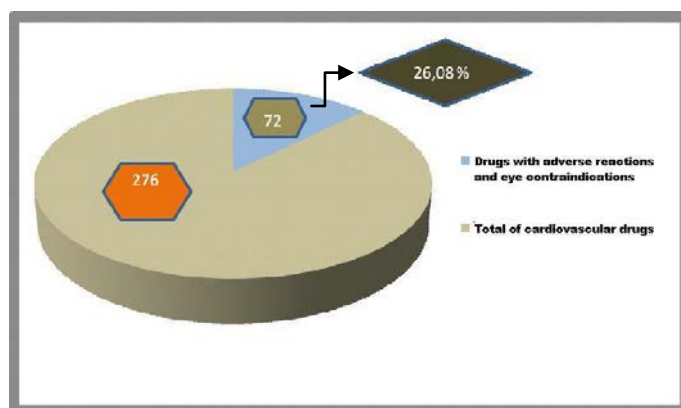


Figure 1. Percentage of cardiovascular drugs with adverse reactions and eye contraindications.

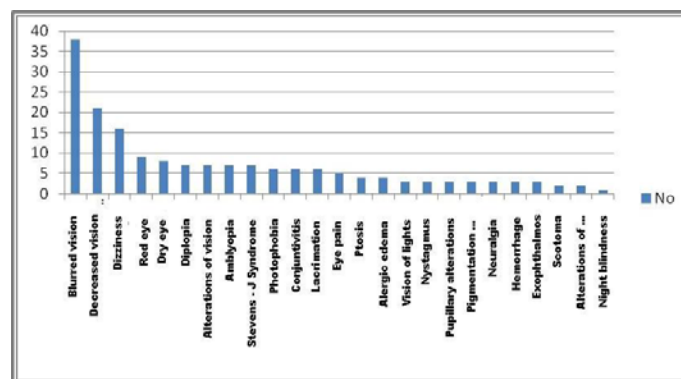


Figure 2. Eye adverse reactions due to the use of cardiovascular drugs.

Table 1. Contraindications and adverse eye reactions of antiarrhythmic drugs.

Mechanism of action and drug	Contraindication	Adverse Reactions
Class Ia. Antagonistas del sodio		
Disopyramide	-	Blurred vision and diplopia
Quinidine Sulfate	-	Blurred vision, photophobia, mydriasis, impaired color vision, diplopia, night blindness, scotomata, optic neuritis and decreased visual field
Class Ib		
Lidocaine	-	Blurred vision and diplopia
Mexiletine	-	Blurred vision and nystagmus
Class Ic		
Flecainida, Clorhidrato de propafenona y Encainida	-	Blurred vision
Class II. Beta Blockers		
Atenolol, Metoprolol, Esmolol and propranolol hydrochloride	-	Decreased vision
Acebutolol	-	Blurred vision
Nadolol	-	Dry eye and blurred vision
Oxprenolol hydrochloride	-	Keratoconjunctivitis
Timolol maleate	-	Decreased vision, diplopia, ptosis, red eye, dry eye
Metipronolol	-	Dry eye and vertigo
Class III. Potassium antagonists		
Amiodarone	-	Corneal pigmentation, photophobia, colored visual halo, decreased visual acuity
Sotalol	-	Decreased vision
Class IV. Calcium antagonists		
Verapamil	-	Stevens-Johnson Syndrome
Nifedipine	-	Eye pain
Others		
Digoxin	-	Trigeminal Neuralgia, dyschromatopsia (yellow-green), blurred vision, vision of lights, photophobia, amblyopia
Glycerol trinitrate (nitroglycerin)	Narrow-angle glaucoma	Blurred vision
Phenytoin sodium	-	Diplopia, nystagmus, blurred vision, Stevens-Johnson syndrome
Adenosine	-	Blurred vision and scotomas

Table 2. Contraindications and adverse eye reactions of antihypertensive drugs.

Mechanism of action and drug	Contraindication	Adverse Reactions
Arterial vasodilators		
Dihidralazina Hydrochloride	-	Lacrimation, conjunctivitis and exophthalmos
ACE inhibitors		
Captopril	-	Blurred vision
Enalapril	-	Blurred vision, Stevens-Johnson Syndrome
Fosinopril sodium	-	Decreased vision and red eye
Ramipril	-	Conjunctivitis
Mixed vasodilator		
Sodium Nitropruside	Leber optic atrophy	
Angiotensin-II receptor antagonists		
Candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan and valsartan	-	Dizziness
Modifiers adrenergic		
a) Alpha adrenergic receptor blockers		
Terazosin	-	Blurred vision and dizziness
Prazosin	-	Dizziness, blurred vision and red eye
b) Alpha 2 agonists		
Clonidine, guanabenz y guanfacine	-	Dizziness
Methyldopa	-	Dizziness and blurred vision
c) Adrenergic Blockers		
Reserpine	-	Blurred vision, redness, lacrimation, miosis and ptosis.
d) Beta Blockers	-	See Table 1
Diuretics		
a) With action in the loop of Henle		
Furosemide	-	Blurred vision
b) Thiazides		
Hydrochlorothiazide	-	Vertigo and xanthopsia
Chlorthalidone	-	Decreased vision
Calcium antagonists		
a) Derivatives of benzodiazepines		
Diltiazem	-	Amblyopia and red eye
b) Derivatives difenilquilamina		
Verapamil	-	See Table 1
c) Dihydropyridines		
Nifedipine	-	See Table 1
Other drugs of hypertensive emergency		
Fenoldopam	Glaucoma	Eye pain, ocular hypertension
Nitroglycerine	Narrow-angle glaucoma	Blurred vision
Esmolol	-	See Table 1

Table 3 shows the cardiovascular drugs most commonly used in heart disease. Beta-blockers, the non-nitrate antianginals, nitroglycerine among the nitrates and calcium antagonists are shown in detail in Tables 1 and 2. Those that can cause tension decomposition in patients with narrow-angle glaucoma are the antianginals of nitrate type (isosorbide dinitrate, nitropental and nitroglycerin), and streptokinase that should not be used in patients with hypertensive retinopathy. Of the drugs discussed in this table, it can be seen that allergy reaction are present in 4 of them (30.7%), and visual disorders and lacrimation appear in 3 (23%).

Cardiac glycosides, the hypolipidemic and vasodila-

tors in general are shown in Table 4. The rest of the groups set forth in the classification (Appendix) were not included because their adverse reactions do not include eye problems. In the 9 remaining drugs, after excluding those described in the above mentioned tables, it can be seen that visual disorders, in all its variations, are the predominant reaction, with 7 drugs (77.7%)

Table 5 presents the possible precautions doctors should take to indicate the use of cardiovascular drugs in relation to eye conditions. It is important to note that of the 14 drugs shown, 7 (50%) may affect the different types of glaucoma.

Table 3. Contraindications and adverse eye reactions of coronary artery disease drugs.

Mechanism of action and drug	Contraindication	Adverse Reactions
Antiplatelet		
Acetylsalicylic acid	-	Angioneurotic edema, ocular hemorrhages
Dipyridamole	-	Allergic edema
Clopidogrel	-	Stevens-Johnson Syndrome
Anticoagulants		
Heparin calcium, sodium and Fraxiparine	-	Lacrimation
Acenocumarol	-	Ocular bleeding
Warfarin sodium	-	Yellow conjunctival pigmentation
Fibrinolytic		
Streptokinase	Hypertensive retinopathy	
Beta-blockers	-	See Table 1
Opiates		
Morphine	-	Blurred vision, nystagmus, diplopia, miosis
Non-nitrate Antianginals		
Verapamil, nifedipine, atenolol, nadolol, metoprolol, timolol maleate, propranolol hydrochloride and amiodarone	-	See Table 1
Diltiazem and captopril	-	See Table 2
Antianginal nitrates		
Isosorbide dinitrate, pentaerythritol tetranitrate (nitropental) and glycerol trinitrate (nitroglycerin)	Narrow-angle glaucoma	Blurred vision

Table 4. Contraindications and eye adverse reactions of cardiac glycosides, lipid lowering drugs and vasodilators.

Mechanism of action and drug	Contraindication	Adverse Reactions
Cardiac glycosides (Digitalis)		
Digoxin and Digitoxin	-	Trigeminal neuralgia, yellow-green vision, blurred vision, vision of lights, photophobia, amblyopia
Hypolipidemics		
a) HMG-CoA Reductase inhibitors		
Simvastatin and Lovastatin	-	Blurred vision
b) Unknown Mechanism		
Nicotinic acid	-	Blurred vision
c) Fibrates		
Gemfibrozil	-	Blurred vision
Hemorheologicals		
Pentoxifylline	-	Retinal hemorrhages
Coronary vasodilators		
Nifedipine and Nitroglycerin	See Table 1	See Table 1
Diltiazem	-	See Table 2
Dipyridamole	-	See Table 3
Peripheral and coronary vasodilator		
Hydralazine, Enalapril and Diltiazem	-	See Table 2
Diazoxide	-	Optic nerve infarction, papilledema, cataract, blurred vision
Isosorbide	-	Blurred vision and diplopia

DISCUSSION

The increasing number of drugs available and the increasing information on their effectiveness and safety are a result of the scientific and technological development and the globalization of nowadays society³. It is the responsibility of the physician to maintain a good doctor-patient relationship that allows time for a proper explanation of the importance of treatment, its benefits, risks, including the adverse reactions, in order to perform an adequate drug prescription.

When making a comprehensive analysis of cardiovascular drug adverse reactions and contraindications for patients with eye diseases, it is striking how often those of ocular cause appear (26.08%).

What is meant by an adverse reaction?

The WHO defines it as any harmful response, that was not sought, and that appears at doses normally used in humans for the treatment, prevention or diagnosis of disease. The effects induced by drug abuse, accidental consumption or suicide attempts are not included^{3,4,14}. Example of adverse reactions may include the following: hypersensitivity reactions (acetylsalicylic acid and digitalis), idiosyncratic side effect (sympathetic-mimetic amines, diuretics and nitroglycerin), toxic effects (digitalis), teratogenic effects [digoxin, dihydroergotamine, phenytoin, warfarin, angiotensin converting enzyme (ACE) inhibitor], paradoxical effect (antiarrhythmics), rebound phenomenon (propranolol), tachyphylaxis, tolerance (propranolol

Table 5. Ophthalmic Precautions to consider when prescribing cardiovascular drugs.

Drug	Mechanism of action	Precautions
Disopyramide	Antiarrhythmic, sodium antagonist	Migraine and Glaucoma
Nadolol	Beta Blocker	Amblyopia
Ramipril	ACE inhibitor	
ASA, dipyridamole and clopidogrel	Antiplatelet	Bleeding risk
Nicotinic acid	Hypolipidemic	Glaucoma
Nitroglycerine	Coronary vasodilator	Migraine
Nifedipine		Narrow-angle glaucoma
Dipyridamole		Migraine
Epinephrine, metaraminol, methoxamine and phenylephrine		Narrow-angle glaucoma

and hydralazine), dependency, resistance, intolerance, Herxheimer reaction, reaction due to drug-viral infection interaction⁴.

Adverse reactions to one type of drug or substance depend on various factors, among which we have the subject's particular characteristics (age, sex, race, body weight, comorbidities, genetic predisposition, and nutritional status), route of administration, absorption and elimination rate, the dosage of the drug and drug combinations. That is why such reactions occur more frequently in children, women and seniors, and during the first or third quarter of pregnancy¹⁴.

In all groups of drugs studied, except in antithrombotics, visual disorder predominates, with all its variants, as the most common adverse reaction that may occur; antiarrhythmics 83.3%, antihypertensives 46.1%, medications used in coronary disease 23% and cardiac glycosides, hypolipidemics and vasodilators 77.7%. Only six cardiovascular drugs are contraindicated in eye diseases: nitroglycerin, isosorbide dinitrate, nitropental, fenoldopam, streptokinase and sodium nitroprusside.

It is important to instill in health professional, particularly in young people, the need to conduct a good medical interview, because this way, they can get the information about what conditions the patients suffer from and thus make an adequate pres-

cription for eliminating or at least minimizing the occurrence of adverse reactions in people who come to receive a health service in any of our health institutions.

CONCLUSIONS

Seventy-two cardiovascular drugs present adverse reactions involving some kind of ocular symptoms. Only 6 are contraindicated. Blurred vision, decreased visual acuity and dizziness are the three most common reactions that may occur with their use. It is extremely important to conduct a good interview of patients to know their medical history and the illnesses they suffer from, and avoid as much as possible the use of the 6 contraindicated drugs and the 14 drugs that require special caution because they can cause decompensation in patients with eye diseases such as glaucoma, optic atrophy, migraine and risk of developing intraocular hemorrhage.

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APPENDIX. List of cardiovascular drugs by mechanism of action⁶⁻¹⁸

1. ANTIARRHYTHMIC DRUGS (Vaughan Williams Classification)

- **Class I. Sodium channel blockers**
- **Class Ia:** Disopyramide, Procainamide, Quinidine Sulfate, Ajmaline, Prajimalina
- **Class Ib:** Lidocaine, Mexiletine, Tocainide, Phenytoin
- **Class Ic:** Flecainide, Propafenone, Encainide, Loricainide, Aprindina, Moricizine
- **Class II. Beta blockers:** Atenolol, Carvedilol, Acebutolol, Betaxolol, Bisoprolol, Esmolol, Metoprolol, Nadolol, Propranolol, Pindolol, Carteolol, Labetalol, Penbutolol, Timolol Maleate, Oxyprenolol Hydrochloride, Metipronolol
- **Class III. Potassium channel blockers:** Amiodarone, Acimilida, Bretylium, Dofetilide, Ibutilide, Sotalol
- **Class IV. Calcium channel blockers:** Diltiazem, Verapamil, Nifedipine, Nicardipine, Amlodipine, Isradipine, Nisoldipine, Felodipine, Nimodipine
- **Class V. Parasympathetic stimulation:** Digoxin, Edrophonium
- **Others:** Adenosine, Nitroglycerin, Diphenylhydantoin (Phenytoin Sodium), Magnesium Sulfate, Aramine, Metaraminol

2. ANTIHYPERTENSIVES

- **Arterial Vasodilators:** Hydralazine, Dihydralazine Hydrochloride, Minoxidil, Fenoldopam, Nicorandil, Diazoxide
- **ACE inhibitors:** Captopril, Enalapril, Lisinopril, Quinapril, Fosinopril Sodium, Cilazapril, Perindopril, Ramipril, Benazepril, Alazapril, Moexipril, Trandolapril

- **Mixed vasodilators:** Sodium Nitroprusside
- **Angiotensin II receptor antagonists:** Candesartan, Eprosartan, Irbesartan, Losartan, Olmesartan, Telmisartan, Valsartan, Versartan
- **Adrenergic Modifiers**
 - ✓ **Alpha adrenergic receptor blocker (Sympatholytics):** Doxazosin, Prazosin, Terazosin, Phenoxybenzamine
 - ✓ **Alpha 2 agonists:** Clonidine, Guanabenz, Guanfacine, Methyldopa
 - ✓ **Adrenergic blockers (sympathoplegics):** Rauwolfia Alkaloids, Guanethidine, Guanadrel Sulfate, Reserpine
 - ✓ **Beta receptor blockers:** Timolol Maleate, Nadolol, Oxyprenolol Hydrochloride, Metoprolol, Bisoprolol, Atenolol, Acebutolol, Betaxolol, Carteolol, Penbutolol, Pindolol, Propranolol, Metipranolol, Nebivolol
 - ✓ **Alpha and beta blockers:** Labetalol Hydrochloride, Carvedilol
- **Diuretics**
 - ✓ **With action in the loop of Henle:** Ethacrynic Acid, Furosemide, Bumetanide, Torasemide, Piretanide
 - ✓ **Thiazides:** Hydrochlorothiazide, Chlorthalidone, Chlorothiazide, Hydroflumethazide, Indapamide, Methyclothiazide, Metolazone, Benzthiazide, Polythiazide Bendroflumetazida, Xipamide
 - ✓ **Potassium sparing. Inhibitor of sodium channels:** Triamterene, Amiloride, Eplerenone
 - ✓ **Mineralocorticoid inhibitor (potassium-sparing):** Spironolactone, Canrenone
 - ✓ **Osmotics:** Mannitol

- ✓ **Carbonic anhydrase inhibitor:**
Acetazolamide, Methazolamide
- ✓ **Xanthine:** Theophylline
- ✓ **Acidifiers:** Ammonium chloride
- **Calcium channel blockers**
 - ✓ **Benzodiazepine derivatives:** Diltiazem
 - ✓ **Diphenylkylamine derivatives:** Verapamil
 - ✓ **Dihydropyridines:** Amlodipine, Delodipino, Isradipine, Nicardipine, Nifedipine, Nisoldipine, Felodipine, Nitrendipine, Nimodipine
- **Endothelin inhibitors:** Bosentan, Vasopressin Antagonists (Conivaptan and Tolvaptan) Imidazoline Receptors (Hiperium, Moxonidine)
- **Agonists for opening potassium channels:** Pinacidil, Nicorandil, Cromakalina
- **Serotonin Antagonist:** Ketanserin
- **Renin inhibitors:** Pepsatina and Statin
- **Vasopeptidase inhibitors:** Bradykinin and Atrial Natriuretic Factor
- **Vasodilators of ganglionic blocking agent (ganglioplegics):** Trimethaphan
- **Drugs used in hypertensive emergencies:** Sodium Nitroprusside, Nicardipine, Fenoldopam, Nitroglycerin, Enalapril, Hydralazine, Labetalol, Esmolol, Phentolamine, Diazoxide

3. CORONARY DISEASE

- **Antiplatelet drugs:** ASA, Dipyridamole, Indobufen, Rigodel, PG12
 - ✓ **Antagonist of adenosine biphosphate receptors:** Clopidogrel, Ticlopidine
 - ✓ **Antagonist of the receptor of glycoprotein IIb / IIIa platelet:** Abciximab, Eptifibatide, Tirobifan
- **Antithrombotic:** Heparin calcium, Heparin sodium, Low molecular weight heparin (Fraxiparine), Acenocoumarol, Warfarin sodium, Hirudin, Hirulog, Hirugen, Reapina, Enoxaparin, Lepidurin, Ticlopidine, Nadroparin, Dalteparin. Dextran 40, Dipyridamole
- **Thrombolytic / Fibrinolytic:** Streptokinase, Alteplase recombinant, APSAC (Anisoylated plasminogen streptokinase activator complex) Reteplase, Anistreplase, Tecneplase, Lanoteplase
- **Beta blockers:** Atenolol, Metoprolol
- **Opiates:** Morphine

• Antianginals

- ✓ **Non-nitrate:** Molsidomine, Nicorandil, Diltiazem, Timolol Maleate, Nifedipine, Amiodarone Hydrochloride, Captopril, Nadolol, Verapamil, Diisopropylammonium. Dobutamine Hydrochloride, Isosorbide, Propranolol, Dipyridamole, Metoprolol Tartrate, Glyceryl Triacetate, Amiodipina Besylate, Felodipine, Gallopamil Hydrochloride, Nicardipine, Nisoldipine, Streptokinase-Streptodornase, Atenolol, Pindolol, Glucose-Insulin-Potassium
- ✓ **Nitrates:** Venous coronary vasodilators: Glycerol trinitrate (nitroglycerin), isosorbide dinitrate, isosorbide mononitrate, nitroglycerin patches, pentaerythritol tetranitrate (nitropental)
- **Calcium channel blockers:** See Antiarrhythmics

4. CARDIAC GLYCOSIDES OR CARDIOTONIC

- **Non-digitalis:** Very brief action: Ouabain
- **Digitalis**
 - ✓ Prolonged action: Digitoxin
 - ✓ Brief action: Digoxin
 - ✓ Very brief action: Deslanoside C or Cedilanid

5. HYPOLIPIDEMICS

- **HMG-CoA reductase inhibitors (statins):** Lovastatin (Mevacor), Pravastatin (Pravachol), Simvastatin (Zocor) and Fluvastatin (Lescol)
- **Bile acid sequestering resins:** cholestyramine, colestipol (Colestid), Probuco
- **Unknown mechanism:** Nicotinic Acid
- **Fibrates (fibric acid derivatives):** Gemfibrozil (Lopid), Clofibrate (Atromid-S), Bezafibrate, Fenofibrate, Ciprofibrate
- **Fish oil (Omega 3, 6, 9)**
- **Postmenopausal hormones:** Estrogen with or without progestin
- Policosanol or PPG
- Acipimox

6. BETA AGONIST AGENTS:

- **Sympathomimetic amines:** Dobutamine, Dopamine, Epinephrine, Norepinephrine, Phenylephrine, Metaraminol, Methoxamine, Isoprenaline, Levarterenol, Salbutamol, Ibupamina, Isoproterenol, Epinephrine,

Norepinephrine

7. *PHOSPHODIESTERASE INHIBITORS*: Amrinone, Milrinone, Enoximone, Vesnarinone, Levosimendan

8. *ANTI-ARTERIOSCLEROTICS, ANTIATHEROSCLEROTICS AND HEMORHEOLOGICALS*: Pentoxifylline, Diisopropylammonium Cinnarizine

9. *SPECIFIC BRAIN OXYGENATORS*: Pyritinol, Piracetam, Nicergoline, Cinnarizine, Ginkgo Biloba, Vincamine

10. *VASODILATORS*

- **Brain**: Buphenine Hydrochloride, Codergocrina (Hidergin), Buflomedil, Nimodipine, Isoxsuprine
- **Coronary**: Nifedipine, Diltiazem, Nitrendipine, Dipyridamole, Nitroglycerine, Isosorbide, Amrinone, Felodipine, Amlodipine, Azapetina, Troxerutin, Nesiritide

- **Peripheral**: Tolazoline, dihydroergotoxin, isoxuprine nicotinic acid, cyclandelate, adenosine triphosphoric acid, Hydralazine, buphenine, Isradipine, Flunarizine, Enalapril, Codergocrina mesylate, diazoxide, Buflomedil, Azpetina, Troxerutin

- **Inotropic**: Aminophylline

11. *PHLEBOTROPICS*: Diosmin, Calcium dobesilate, Venaton, Rutascorbin

12. *ANTICONVULSANTS*: Magnesium sulfate, Diazepam, Convulsin

13. *METABOLIC SUPPORT*: Alfa-carnitine

14. *PARASYMPATHOLYTIC*: Atropine

15. *OTHERS*: Prostaglandin E₁ (Alprostadil), Prostacyclin (Epoprostenol)