EFFECTS OF DRUGS USED FOR CARDIAC DISEASES ON LUNGS

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Many drugs used to treat cardiac diseases can directly or indirectly alter lung function. Their effects may either be irreversible, partially reversible or totally reversible depending upon type of drug, its mechanism of action and duration of usage.

Their effect may be apparent within hours, days, weeks, months or even after years depending upon mechanism of action of drug and individual variability and susceptibility.
Drug reactions may present to the clinician as a syndrome and several drugs may produce different syndromes in different subjects.

The overall incidence is unknown. Though clinical presentation, laboratory studies, pulmonary function studies, radiological studies, nuclear studies and lung biopsy may be helpful in supporting the diagnosis of drug induced lung disease or in limiting the differential diagnosis, but the discontinuation of the culprit drug is the first step in both diagnosis and the treatment. The patients response to discontinuation of drug may not be immediate, it may take days, weeks or even months to reverse physiological and pathological changes and in some cases changes may be irreversible. They may produce bronchoconstriction, fibrosing alveolitis, pulmonary oedema, cough, lupus syndrome, PIE syndrome, pleural effusion, alveolar haemorrhages, vasculitis and fibrosis.

Bronchoconstriction can be aggravated by a number of medications. Beta blockers blocks the beta receptors of bronchial smooth muscle, thereby promoting bronchoconstriction or bronchospasm. Beta blockers whether cardio-selective or non-selective should be avoided in patients with bronchospastic diseases like bronchial asthma and COPD. The usual pattern of response is gradual worsening of breathlessness and failure to respond to beta agonist.

Asthmatic reaction to aspirin was described long ago. A well known syndrome comprising asthma, nasal polyps and aspirin sensitivity has been recognized since the 1920s. It provoked bronchospasm by inhibiting cyclo oxygenase. This response is seen in 2-4% of asthmatics.

Adenosine is used as an anti-arrhythmic drug. Most patients feel a sense of chest fullness and dyspnoea at therapeutic dosage of 6-12 mg. Rarely adenosine bolus can precipitate bronchospasm.

Cough is a recognized complication of all the angiotensin converting enzyme (ACE) inhibitors. 5-20% of patients experience dry cough. It is usually not dose related, most frequently seen in women than men, develops between one week to six months of therapy. This may be mediated by accumulation of bradykinin, substance P and/or prostaglandin in lungs. It resolves with discontinuation of offending drug usually within four days, but it may take weeks.

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Haemorrhage into the lung is reported with thrombolytic and anticoagulant therapies

Interstitial pneumonatis or fibroses is a common manifestation of drug induced lung disease. Different drugs may cause very different reactions and indeed the same drug may provoke different responses in different individual. The reaction leading to alveolitis are direct toxic effects of drug, idiosyncratic reaction or related to drug induced lupus erythematosus (SLE).

Cardiac drugs may be responsible for SLE; Procainamide and Hydralazin are most common offenders. Pleuropulmonary manifestation are very common. Diagnosis is based on drug history and manifestations of SLE. Anti nuclear antibody (ANA) is usually positive homogenous but the anti-ds (double standard) DNA antibody negative. ANA positivity may persists for several months, but the symptoms usually reverse within

two months of discontinuation of drug. Steroid may be beneficial. Drug, induced SLE is usually totally reversible.

Pleural effusion, pleural thickening and pleuritis may occur because of a drug induced serositis, cardiac decompensation with associated pulmonary oedema, constrictive pericarditis, pulmonary emboli or vasculitis.

Pulmonary edema both cardiogenic and non-cardiogenic may be induced by number of drugs for example, Thiazide diuretics. Recognition of drug induced pulmonary edema may be difficult in a patient with underlying cardiac dysfunction unless hemodynamic measurements are made.

Systemic Vasculitis is reported with Hydralazin and Quinidine

Pulmonary infiltrates with eosinophilia syndrome (PIE) is attributed to many drugs. Presentation is dyspnoea, cough with or without fever with abrupt or insidious onset. Chest x-ray shows fleeting bilateral patchy alveolar infiltrates and there is peripheral eosinophilia (upto 80%). Recovery occurs rapidly after discontinuation of the culprit drug. Steroid may hasten the recovery.

Coughing, wheezing, pulmonary edema is noted in patients treated with Ca++ channel blockers due to vasodilatation.

Acetazolamide is used for the treatement of edema due to CCF and for drug induced edema. It worsens respiratory acidosis, so the drug is contra-indicated in severe COPD patients.

TABLE – 1

Drugs used for Cardiac Disease Effecting Lungs

I	**Beta Blockers** (adrenergic antagonists)		
	Selective:	• Atenolol	• Metoprolol
		• Betaxolol	• MetoprololXL
		• Bisoprolol	
	Non-Selective:	• Nadolol	• Propranolol LA
		• Propranolol	• Timolol
	Selective with Intrinisic Sympathetic Activity (ISA):	• Acebutolol	
	Intrinisic Sympathetic Activity:	• Labetolol	• Carvediolol
II	**Angiotensin Converting Enzyme Inhibitors**		
		• Benazepril	• Moexipril
		• Captopril	• Quinapril
		• Enalapril	• Ramipril
		• Fosinopril	• Trandolopril
		• Lisinopril	
III	**Calcium Channel Blockers (Antagonist)**		
		• Amlodipine	• Nicardipine
		• Diltiazem, SR, CD, XR	• Nifedepine, XL, LL
		• Isradipine	• Nisoldipine
		• Mibefradil	• Verepamil, SR, COER
IV	**Diuretics**		
	Thiazide:	• Bendroflumethiazide	• Indapamide
		• Benzthiazide	• Methyclothiazide
		• Chlorothiazide	• Metolazone
		• Chlorthaladone	• Polythiazide
		• Hydrochlorothiazide	• Quinethazone
		• Hydroflumethiazide	• Trichloromethiazide
	Carbonic Anhydrase Indibitors:	• Acetazolamide	
V	**Centrally Acting Adqenergic Agent**	• Methyl Dopa	
VI	**Direct Acting Vasodilators**	• Hydralazine	
VII	**Cardiac Glycosides**	• Digoxin	
VIII	**Miscellaneous**	• Adenosine	• Aspirin
		• Amiodarone	• Opiates – Pethidine
		• Tocainide	• Oxygen
		• Procainamide	• Prazocin
		• Quinidine	• Lidocaine
		• Reserpine	•Anti-coagulant/thrombolytic

TABLE – 2

Different Effects of Cardiac Drugs on Lungs

Bronchoconstriction	• Beta blockers • Aspirin	• Adenosine • Pethidine/Morphine
Fibrosing Alveolitis	• Amiodarone • Tocainide • Procainamide	• Quinidine • Hydralazine • Methyl Dopa
Cough	• ACE Inhibitors	
Pleural Fibrosis	• Practolol • (Beta blockers)	
Lupus Syndrome	• Procainamide • Hydralazine • Chlorthaladone • Methyl Dopa • Reserpine	• Thiazides • Proctolol • Prazocin • Digoxin
PIE Syndrome (Pulmonary Infiltrates with Eosinophilia)	• Hydralazine • Aspirin	• Amiodarone
Pulmonary Oedema	• Tocainide • Terbutaline • Albuterol • Thiazide diuretics	• Ca++ Channel blocker • Over dose of Opiates • Over dose of Aspirin • Amiodarone

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