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THE POWERFUL DRUGS PULLING PEOPLE TO CARDIAC FAILURE

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ABSTRACT

Heart failure is a clinical syndrome that is predominantly caused by cardiovascular disorders such as coronary heart disease and hypertension. However, several classes of drugs may induce heart failure in patients without concurrent cardiovascular disease or may precipitate the occurrence of heart failure in patients with pre-existing left ventricular impairment. We reviewed the literature on drug-induced heart failure, using the MEDLINE database and lateral references. Successively, we discuss the potential role in the occurrence of heart failure of cytostatics, immunomodulating drugs, antidepressants, calcium channel blocking agents, nonsteroidal anti-inflammatory drugs, anti-arrhythmic, beta-adrenoceptor blocking agents, anaesthetics and some miscellaneous agents. Drug-induced heart failure may play a role in only a minority of the patients presenting with heart failure. Nevertheless, drug-induced heart failure should be regarded as a potentially preventable cause of heart failure, although sometimes other priorities do not offer therapeutic alternatives (e.g., anthracycline-induced cardiomyopathy). The awareness of clinicians of potential adverse effects on cardiac performance by several classes of drugs, particularly in patients with pre-existing ventricular dysfunction, may contribute to timely diagnosis and prevention of drug-induced heart failure.

Key words: cardiac failure-drugs for treatment- diclofenac-NSAID's.

INTRODUCTION

Heart Attack - Drugs for its Treatment

A complete obstruction to blood flow in a coronary artery may result in myocardial infraction (MI) commonly called as heart attack. Infraction means the death of an area of tissue because of interrupted blood supply. It is mainly caused by

- diminished coronary blood flow,
- Increased myocardial demand.
- Hypertrophy of the heart.
- Thrombotic diseases,trauma
- Obesity, high B.P, cholesterol, rheumatoid arthritis, smoking, several drugs etc.

Figure 1. Chest Pain

Some of the Drugs used for treatment of Heart attacks are;

Aspirin

Aspirin is an analgesic and antipyretic, prescribed for pain, heart attack and fever. The drug decreases the substances that cause pain and inflammation.

Valsartan

Valsartan is an angiotensin II receptor blocker, prescribed for hypertension, congestive heart failure and myocardial infarction (heart attack).

Dalteparin

Dalteparin is an anticoagulant (blood thinner) that prevents blood clots in persons undergoing surgery. Along with aspirin this medication is prescribed for heart attack, unstable angina (chest pain).

Epinephrine

Epinephrine is a hormone, recommended for cardiac arrest (to restart the heart beat), dilation of

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blood vessels, increase of diastolic blood pressure, increasing the flow of blood to heart and anaphylactic shock (allergic reactions).

Eptifibatide

Eptifibatide is an antithrombotic agent, prescribed for the treatment of patients with acute coronary syndrome (heart condition), and those undergoing percutaneous coronary intervention (angioplasty), and stenting (placing of a cylindrical device within vessels). It prevents platelets in the

Glyceryl Trinitrate

Glyceryl Trinitrate is an organic nitrate, prescribed for angina and heart failure.

Isoproterenol Inhalation

Isoproterenol Inhalation is a sympathomimetic compound, prescribed for asthma, heart attack and shock. This medication relaxes the muscles in the airways and aid in breathing.

Perindopril

Perindopril is a long-acting ACE inhibitor, prescribed for high blood pressure, heart attack and heart failure.

Heparin

Heparin is an anticoagulant, prescribed for deep venous thrombosis, arterial embolism and pulmonary embolism. It is also used for prevention of blood clot in heart surgery.|

Streptokinase

Streptokinase is an enzyme, prescribed for heart attack, pulmonary embolism and deep vein thrombosis. It breaks up and dissolves blood clots that can block arteries.

Tenecteplase

Tenecteplase is a tissue plasminogen activator (tPA), prescribed for preventing death from acute myocardial infarction (sudden heart attack).

Ticagrelor

Ticagrelor is a platelet aggregation inhibitor, prescribed for reducing death rate in patients with myocardial infarction and angina pectoris.

Trandolapril

Trandolapril is an angiotensin-converting enzyme (ACE) inhibitor, prescribed for high blood pressure either alone or with other medications. Lowering high blood pressure helps prevent strokes, heart attacks and kidney problems. This medication is also used to improve survival after an acute heart failure.

Nitroglycerin Tablets, Capsules and Spray

Nitroglycerin Tablets, Capsules and Spray is an organic nitrate, prescribed for chest pain.

Eplerenone

Eplerenone is a mineral corticoid receptor antagonist, prescribed for high blood pressure and heart attack. It blocks the action of aldosterone, which aids in the regulation of blood pressure.

➢ CERTAIN DRUGS WHICH PULL PEOPLE TO VARIOUS CARDIAC DISEASES ARE:

Arthritis pain drug diclofenac leads to adverse heart effects.

Researchers are calling for the removal of a widely used pain medication from worldwide markets due to a high risk of heart attack and other adverse cardiovascular events associated with the drug.

Diclofenac, a non-steroidal anti-inflammatory drug, or NSAID, is often prescribed for relieving the pain and inflammation of arthritis. But the researchers say diclofenac, which is sold under a variety of brand names, including Voltaren in Canada, carries an almost identical risk of serious cardiovascular side-effects as Vioxx. Vioxx was a highly touted and highly promoted NSAID that ended up being pulled from the market by its maker. After a patient trial showed it was linked to an increased rate of heart attacks and strokes. This drug increases the risk of heart attack by about the same degree as Vioxx did. And Vioxx was withdrawn from world markets in 2004 by the manufacturer because of that risk, who has a background in clinical pharmacology and has studied NSAIDs for about two decades. So this drug is still there, very widely used, and internationally the most popular drug despite having an almost identical cardiovascular risk profile to a drug that was taken off the market eight years ago.In Canada, the diclofenac makes up 17 per cent of all NSAIDs sold. People taking diclofenac have a 40 per cent higher risk of having a heart attack than those taking naproxen, considered the safest NSAID choice for minimizing cardiovascular risk. For people with underlying heart disease, taking diclofenac significantly raises the risk of heart attack, said Henry. While diclofenac makes up a respectable proportion of NSAIDs sold in Canada, the U.K. and Australia, the researchers' biggest concern is about low- and middle-income countries in Asia and South Asia, where the drug commands a huge market share. The researchers have been raising a red flag about diclofenac in medical journal studies for several years, but regulatory agencies in countries around the world have been slow to label the drug as being high-risk.

In fact, many countries continue to keep it on their essential medicines lists, which encourages doctors to continue prescribing the drug despite evidence of its risks to heart health.

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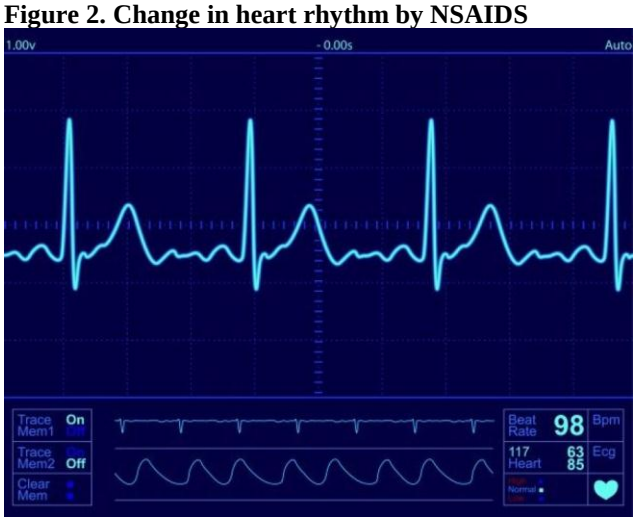
High doses of common pain drugs NSAIDs can cause heart attack!

Taking prescription-strength doses of non-steroidal anti-inflammatory drugs can lead to heart attack and stroke. NSAIDs are also found in over-the counter meds like Advil and Voltaren**.**

Figure 2. Change in heart rhythm by NSAIDS



High doses of some commonly used pain drugs like ibuprofen can increase heart attacks, strokes and related deaths. The drugs, known as non-steroidal anti-inflammatory drugs (NSAIDs), are widely used to manage pain caused by inflammatory disorders.

NSAIDs are very commonly used for both acute and chronic pain. Over-the-counter doses are lower and generally recommended for short periods for acute painful conditions. Chronic use of more than about a week or 10 days can be prescribed for back, knee, hip or neck pain, or chronic headaches.

Earlier research had linked the drugs' use to a risk of serious gastrointestinal problems. This led to a new generation of NSAIDs called coxibs that were designed to reduce these complications, but instead came under scrutiny for increasing the risk of heart attacks. The new study, published in The Lancet, found that high doses of not only coxibs but also older-generation NSAIDs like ibuprofen (Advil) or diclofenac (Voltaren) were associated with heart disease risk. For every 1,000 individuals with a moderate risk of heart disease allocated to one year of treatment with high-dose diclofenac or ibuprofen, about three would experience an avoidable heart attack of which one would be fatal. In addition, all NSAIDs double the risk of heart failure and produce a 2-4 times increased risk of serious upper gastrointestinal complications such as bleeding ulcers. A high dose of diclofenac is indicated as 150 milligrammes per day and of ibuprofen about 2,400 milligrams per day.

High doses are generally doses available only with a prescription. Increased heart attack risk from NSAIDs rose in proportion to a patient's underlying risk, so it was highest in those with a previous history of heart disease, high blood pressure or cholesterol. The reason for the heart attack link was not clear, but likely because they increase likelihood of clotting. These drugs also increase blood pressure. Alternative medicines include acetaminophens (Tylenol) or opioids. Powerful drugs may have serious harmful effects. It is therefore important for prescribers to take into account these risks and ensure patients are fully informed about the medicines they are taking. But it was also important to note that, it is not sure whether the risks would persist in longer-term treatment or on lower doses.

Commonly Prescribed Diabetes Drugs May Cause Heart Failure And Fluid Buildup

Two diabetes medications taken by more than 6 million Americans may lead to serious side effects, including the onset of congestive heart failure and pulmonary edema, according to researchers at UT South-western Medical Center at Dallas. The researchers report that the oral drugs pioglitazone and rosiglitazone can cause or exacerbate heart failure and pulmonary edema and should be avoided in patients with left ventricular dysfunction (impaired pumping ability of the heart) or chronic renal insufficiency. Both medications – among a class of drugs known as thiazolidinediones – are used for the treatment of non-insulin dependent (type 2) diabetes mellitus.

Many physicians are prescribing these drugs in patients with chronic renal insufficiency because a first-line diabetes drug, metformin, is not recommended for them. These new data suggest that such patients may be at particularly high risk of developing heart failure. These are newer agents, and we need to become more familiar with their side effects so that we can use them judiciously. Congestive heart failure, which affects 3 million Americans, is an imbalance in pump function in which the heart fails to maintain adequate circulation of blood. The most severe manifestation of congestive heart failure is pulmonary edema, or fluid in the lungs. Patients with coexisting type 2 diabetes have an increased mortality rate. The researchers reviewed the records of six patients with type 2 diabetes who were treated at the VA emergency room after experiencing shortness of breath, weight gain and swelling of the feet – all signs and symptoms of congestive heart failure and pulmonary edema. These symptoms developed after one to 16 months of therapy with pioglitazone or rosiglitazone. In three patients, doses of these medications were increased three weeks to three months prior to the onset of congestive heart failure. The researchers provided follow-up care to the patients during clinic visits. After discontinuing the medications and administering diuretics, the patients no longer exhibited the signs and symptoms of congestive heart failure and pulmonary edema. The Food and Drug Administration approved rosiglitazone and pioglitazone in 1999.

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The prescribing information indicates that the drugs should not be used by individuals with New York Heart Association (NYHA) Class III and IV status, particularly in combination with insulin. Patients with NYHA Class I or II cardiac status may also be at risk of thiazolidinedione-associated cardiac failure.

The New York Heart Association functional classification for patients with heart failure is used to characterize patients' limitation from left ventricular failure. Class I represents no limitation of physical activity; Class II, slight limitation of physical activity; Class III, marked limitation of physical activity; and Class IV, unable to carry on any physical activity without symptoms.

Actos -Severe and Life-Threatening Side Effects

Actos is used for the treatment of type 2 diabetes. Clinical studies have shown that patients can develop severe and life-threatening Actos side effects, such as bladder cancer, congestive heart failure, bone fractures and lactic acidosis.Actos side effects can also worsen pre-existing medical conditions. Patients with pre-existing congestive heart failure (NYHA Class I or II) should start Actos at lower dosages. It is recommended that heart patients be monitored closely when taking Actos for symptoms of congestive heart failure, including weight gain and edema. Bladder cancer is another life-threatening Actos side effect, and users with a history of cancer, bladder tumors or bladder problems in general should only use the drug as a last resort medication. Actos carries a black-box warning, the toughest warning given by the FDA, for its heart risks.

The drug is linked to an increase in heart failure in patients with or without pre-existing heart problems. Actos has long been shown to increase the risk of heart failure, a condition that develops over time and is characterized by the heart's inability to properly pump blood; it is different from a heart attack.

Two Actos side effects, severe weight gain and water retention (edema) are both known to contribute to heart problems.

Actos + Heart Disease = heart failure

Actos + Edema = heart failure

Erythromycin, QTc interval

Prolongation,and torsade de pointes.

Erythromycin is a macrolide antibiotic that is widely used for various infections of the upper respiratory tract, skin, and soft tissue. Erythromycin is linked to sudden cardiac Death (SCD).Slow IV infusion of erythromycinlactobionate was associated with significant QTc interval prolongation and torsade depointes (TdP) arrhythmia. .Erythromycin is an effective and widely used antibiotic and QT interval prolongation and cardiac arrhythmia is a rare side effect. Analysis show marked QTc prolongation and TdP in adults receiving the drug occur predominantly, although not exclusively, in middle-aged and older adults. Major identified risk factors are female sex, old age, and presence of heart disease.

Other risks include concomitant administration of drugs that impair erythromycin Metabolism or that are associated with QTc prolongation in their own right. Co administration of erythromycin with such agents should be avoided. Patients will become were severely ill. It is therefore reasonable to suggest that erythromycin should be administered with great caution to severely ill patients with concomitant risk factors for QTc prolongation, particularly elderly females and those with heart disease. For severely ill patients in a hospital setting, it would certainly be advisable to take a baseline ECG prior to considering administration of erythromycin, to correct any modifiable risk factors such as electrolyte abnormalities and to repeat ECG monitoring during erythromycin administration, should it be given. The Administration of alternative antibiotics free of QTc prolonging effects may be worth considering for severely ill individuals.

Table 1. Drugs Withdrawn From Market due to Adverse Cardiac Effects

Name of Drug	Use	Side Effects to Heart
1. Darvon & Darvocet (Propoxyphene)	Opioid pain reliever	Serious toxicity to the heart; between 1981 and 1999 there were over 2,110 deaths reported.
2. Bextra (Valdecoxib)	NSAID (pain relief)	serious cardiovascular adverse events (like death, MI, stroke
3. Hismanal (Astemizole)	Antipsychotic	slowed potassium channels in the heart that could cause torsade de pointes (TdP; a heart condition marked by a rotation of the heart's electrical axis) or long QT syndrome (LQTS; prolonged QT intervals)
4. Meridia (Sibutramine)	Appetite Suppressant	increased cardiovascular and risk
5. Micturin (Terodiline)	Bladder incontinence	QT prolongation and potential for cardio toxicity
6. Permax (Pergolide)	Parkinson's disease	valve regurgitation (a condition that causes the valves to not close tightly, which allows blood to flow backward over the valve) in the mitral,

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		tricuspid, and aortic heart valves, which can result in shortness of breath, fatigue, and heart palpitations
7. Pondimin (Fenfluramine)	Appetite suppressant	30% of patients prescribed the drug had abnormal echocardiograms; 33 cases of rare valvular disease in women; 66 additional reports of heart valve disease
8. Propulsid (Cisapride)	**:** Severe nighttime heartburn associated with gastroesophageal reflux disease (GERD)	more than 270 cases of serious cardiac arrythmias (including ventricular tachycardia, ventricular fibrillation, torsades de pointes, and QT prolongation)
9. Raxar (Grepafloxacin)	Antibiotic for bacterial infections	cardiac repolarization; QT interval prolongation; ventricular arrhythmia (torsade de pointes)
10. Redux (Dexfenfluramine)	Appetite suppressant	30% of patients prescribed the drug had abnormal echocardiograms; 33 cases of rare valvular disease in women; 66 additional reports of heart valve disease
11. Seldane (Terfenadine)	Antihistamine	life-threatening heart problems when taken in combination with other drugs (specifically erthromycin (an antibiotic) and ketoconazole (an antifungal)
12. Trasylol (Aprotinin)	antifibrinolytic to reduce blood loss during surgery	Increased chance of death,congestive heart failure, and strokes.
13. Vioxx (Rofecoxib)	NSAID (pain relief)	increased risk of heart attack and stroke; linked to about 27,785 heart attacks or sudden cardiac deaths
14. Zelnorm (Tegaserod maleate)	irritable bowel syndrome with constipation (IBS-C) and chronic idiopathic constipation (CIC) in women younger than 55	higher chance of heart attack, stroke, and unstable angina (heart/chest pain

CONCLUSION

The use of recreational drugs has reached epidemic proportions in many countries and threatens to overwhelm economic, social, and health care systems. It is estimated that almost 1 in 4 people in developed countries have used recreational drugs at some time during their life. It is therefore inevitable that many doctors will have to manage and treat the ill effects associated with the abuse of these drugs.

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CONFLICT OF INTEREST:

The authors declare that they have no conflict of interest.

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