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DEPARTMENT OF CARDIO PULMONARY PERFUSION CARE
TECHNOLOGY

COURSE NAME : Pharmacology Pathology and Clinical Microbiology

II nd YEAR

TOPIC : INOTROPES



▶ INTRODUCTION

- ▶ An inotrope is an agent, which increases or decreases the force or energy of muscular contractions. & By enhancing myocardial contractility, cardiac output, the amount of blood ejected by the heart with each beat, will also increase.
- ▶ All inotropes are successful because they increase the myocardial contractility of the heart.
- ▶ As science advanced, other inotropes were developed which were more potent and have different chemical properties and physiological effects. used for CCF.





- ▶ The result of these direct and indirect effects are: -
- ▶ An increase in force and velocity of myocardial contractility (positive inotrope effect).
- ▶ Slowing of heart rate (negative chronographic effect).
- ▶ Decreased conduction velocity through the AV node.





- ▶ CLINICALLY APPROVED INOTROPES
- ▶ Cardiac Glycosides: - Digitalis Derivatives Digoxin →
- ▶ Sympathomimetics: - Epinephrine Dopamine (Intropin)
Dobutamine (dobutrex) Norepinephrine (levophed)
Isoproenol (isuprel)
- ▶ Phosphodiesterase Inhibitors: - Amrinone (Inocor)
Milirinone (Primacor)





- ▶ **CARDIAC GLYCOSIDES**
- ▶ An indirect effect on the cardiovascular system regulated by the autonomic nervous system which is responsible for the effect on the sino-atrial (SA) and atrioventricular (AV) nodes.
- ▶ A direct effect on cardiac muscle and the conduction system.
- ▶ Digitalis Glycosides have
- ▶ The first line of inotropes include all digitalis derivatives





▶ DIGOXIN LOADING DOSE

Loading doses of Digoxin range from 10 – 15mg/kg

Digoxin can be given orally, but with a slower onset of action and peak effect.

▶ DIGOXIN MAINTENANCE DOSE :- Initial therapy of Digoxin is usually started at 0.125 to 0.375mg/day.

▶ NOTE: DRAW A SERUM DIGOXIN LEVEL AT LEAST SIX HOURS AFTER THE LAST DOSE!

▶ .





- ▶ **SIDE EFFECTS ASSOCIATED WITH TOXICITY**
- ▶ **GASTROINTESTINAL:** Anorexia, nausea, vomiting, diarrhea Rare: abdominal pain, hemorrhagic necrosis of the intestines
- ▶ **CNS:** visual disturbances, (blurred or yellow vision), headache, weakness, dizziness, apathy and psychosis.
- ▶ **OTHER:** Skin rash, gynecomastia





- ▶ **SYMPATHOMIMETICS (ADRENERGIC)**
Sympathomemetic drugs exert potent inotropic effects by stimulating beta (B1 & B2), alpha(A1 & A2) and dopaminergic receptors in the myocardium, blood vessels, and sympathetic nervous system.





- ▶ DOPAMINE (INTROPIN) (200MG/5ML AMPULE).
- ▶ INTERMEDIATE DOSE 2 to 10 mcg/kg/minute
- ▶ LOW DOSE 0.5- 2mcg/kg/minute





- ▶ Indication:-
- ▶ Occlusive vascular disease.
- ▶ Tachyarrhythmias.
- ▶ Phaeochromocytoma.
- ▶ Pregnancy. Increases mesenteric flow in mesenteric ischaemia.
- ▶ Contraindication:
- ▶ Hypotention/haemodynamic compromise due to MI, trauma, sepsis, CCF. → Renal protection. →





- ▶ ADVERSE EFFECTS
- ▶ Hypotension when used concomitantly with dilantin
- ▶ Increased myocardial oxygen demand.
- ▶ Headache.
- ▶ Vomiting
- ▶ Nausea
- ▶ Pulmonary congestion
- ▶ Ventricular arrhythmias
- ▶ Supraventricular tachycardia
- ▶ Tachycardia





- ▶ Nursing implication
- ▶ Monitor cardiac output, pulmonary artery pressure
ECG
- ▶ Monitor for hypertension, tachycardia, chest pain, and
premature ventricular contractions





- ▶ DOBUTAMINE (DOBUTREX) (250MG IN 20ML AMPULE)
- ▶ Usual dose: - 2.5 to 10 mcg/kg/minute.' Initial dose: - 2 to 3 mcg/kg/minute.'
- ▶ 2 Dobutamine administration concentrations: - Infusion pump: 500 mg per 250 cc normal saline Syringe pump: 250 mg (20cc) in total 50 cc normal saline (5 mg per cc)
- ▶ Maximum dose: - 20 mcg/kg/minute.



- ▶ Indication
 - ▶ Patient with atrial fibrillation should be digitalized before giving this drug to prevent ventricular tachycardia.
 - ▶ Correct hypovolemia before treating with this drug.'
- Contraindication:-
- ▶ Idiopathic hypertrophic subaortic stenosis.
 - ▶ Contraindication:- Idiopathic hypertrophic subaortic stenosis



- ▶ Adverse effects
- ▶ Hypokalemia
- ▶ Tremors
- ▶ Nausea
- ▶ Headache
- ▶ Myocardial ischemia
- ▶ Blood pressure fluctuation
- ▶ Arrhythmias
- ▶ Tachycardia





- ▶ Nursing implication
- ▶ Monitor cardiac output, pulmonary artery pressure
ECG
- ▶ Monitor for hypertension, tachycardia, chest pain, and premature ventricular contractions.





Adrenalin

Mechanism of action

- ❖ The action of adrenalin may vary by the type of tissue it act,
- ❖ It causes smooth muscle relaxation in the airway
- ❖ It causes smooth muscle contraction in the arterioles
- ❖ In cardiac muscles increase contractability





INDICATION:

- ▶ Anaphylaxis reaction
- ▶ Hypotension
- ▶ Bronchospasm
- ▶ Cardiac arrest
- ▶ Asystole





▶ DOSE:

For Infusion : 0.05 – 0.1 microgram/kg/minute

maximum dose: 1 – 1.5 microgram/kg/minute

For In arrest : 1 ml every 2 minutes





- ▶ Dilution
- ▶ 1 ampule = 1ml/1mg
- ▶ Preparation : 4ml of adrenalin + 46 ml NS = 50 ml
- ▶ Drug concentration = $4\text{mg}/50\text{ml} = 0.8\text{mg}$
- ▶ $0.8\text{mg} \times 1000 = 80 \text{ mcg/ml}$
- ▶ Rate of infusion : desired dose $\times 60 = \text{ml/hr}$

80 mcg

Example : $2 \text{ mcg} \times 60 \frac{\text{min}}{\text{hr}} = \frac{1.5}{80}$



Drug interaction

- ▶ Interacts with β -blocking agents, digitalis glycosides, antidepressants,





ADVERSE EFFECTS:

- ▶ Hypertension
- ▶ tachycardia
- ▶ Extravasations
- ▶ Anxiety, dysrhythmias
- ▶ dizziness
- ▶ pallor
- ▶ tremor,
- ▶ insomnia
- ▶ Headache, nausea
- ▶ palpitations





Nursing consideration:

- ▶ Inotropes must be administered in central line
- ▶ Do not cease infusion abruptly,
- ▶ Should be used with caution in patients with atherosclerosis, mesenteric and peripheral vascular thrombosis or other occlusive vascular diseases, metabolic acidosis, hypoxia or hyperthyroidism.
- ▶ It should be avoided in patients who are hypersensitive to the drug.
- ▶ discard diluted solutions after 24 hours Protect ampoules from light during storage and discard if discoloured





- ▶ Follow ten rights
- ▶ Monitor for adverse effect
- ▶ Continuous BP using invasive arterial BP monitor
- ▶ connect the patient with cardiac monitor and monitor ECG rythm
- ▶ Inotropes must be administered using infusion or syringe
- ▶ Should follow standard dilution
- ▶ The lable on loaded drug should contain drug concentration and dilution
- ▶ Monitor urine output



Nor adrenalin

Mechanism of action

- ❖ The action of Inotropes may vary by the type of tissue it act,
- ❖ It causes smooth muscle relaxation in the airway
- ❖ It causes smooth muscle contraction in the arterioles
- ❖ In cardiac muscles increase contractability





INDICATION:

- ▶ Anaphylaxis reaction
- ▶ Hypotension
- ▶ Bronchospasm
- ▶ Cardiac arrest
- ▶ Asystole





Formula for rate of infusion of inotropes

▶ Rate of infusion : $\frac{\text{desired dose} \times \text{weight} \times 60}{\text{drug concentration}} = \text{ml/hr}$

drug concentration





- ▶ Dilution for adrenalin/nor-adrenalin
- ▶ 1 ampoule adrenalin = 1ml/1mg
- ▶ 1 ampoule nor-adrenalin = 2ml/2mg
- ▶ Preparation : 4ml of adrenalin + 46 ml NS = 50 ml
- ▶ Drug concentration = 4mg/50ml = 0.8mg
- ▶ $0.8\text{mg} \times 1000 = 80 \text{ mcg/ml}$
- ▶ Rate of infusion : desired dose x 60 = ml/hr

drug concentration

Example : 2 mcg x 60 min

$$\frac{\text{-----}}{80 \text{ mcg}} = 1.5$$



- ▶ Dilution for dopamine an
- ▶ In this we have calculate the patient weight
- ▶ 1 ampule dopa=250 mg ,
- ▶ Each ml dopa-50 mg,
- ▶ Prepration : 5+ 45 ml NS =50 ml
- ▶ Drug concentration = 250/50ml =5
- ▶ 5 x 1000 = 5000 mcg/ml
- ▶ Rate of infusion:desired dose x weight x60 =ml/hr

$$\frac{\text{Example : } 2 \text{ mcg} \times 60 \text{ min} \times 60 \text{ kg}}{5000} = 1.44 \text{ ml/hr}$$

drug concentration



- ▶ Dilution for dobutamine
- ▶ In this we have calculate the patient weight
- ▶ 1 ampule dopa=200 mg ,
- ▶ Each ml dopa-40 mg,
- ▶ Prepration : 5+ 45 ml NS =50 ml
- ▶ Drug concentration = 200/50ml =4
- ▶ 4x 1000 = 4000 mcg/ml
- ▶ Rate of infusion: desired dose x weight x60 =ml/hr

drug concentration

Example : 2 mcg x 60 minx60kg

----- =1.8ml/hr

4000



- ▶ Dilution for NTG
- ▶ 1 ampule = 5ml/25mg
- ▶ Preparation : 5ml of NTG + 45 ml NS = 50 ml
- ▶ Drug concentration = $25\text{mg}/50\text{ml} = 0.5\text{mg}$
- ▶ $0.5\text{mg} \times 500 = 250 \text{ mcg/ml}$
- ▶ Rate of infusion : $\frac{\text{desired dose} \times 60}{\text{drug concentration}} = \text{ml/hr}$

Example : $2.5 \text{ mcg} \times 60 \text{ min} = 0.6$
 250 mcg



Drug interaction

- ▶ Interacts with β -blocking agents, digitalis glycosides, tricyclic antidepressants, mono-amine oxidase inhibitors, cocaine .





ADVERSE EFFECTS:

- ▶ Hypertension
- ▶ bradycardia
- ▶ Extravasations
- ▶ Anxiety, dysrhythmias
- ▶ dizziness
- ▶ pallor
- ▶ tremor
- ▶ insomnia
- ▶ Headache, nausea
- ▶ palpitations





Nursing consideration:

- ▶ Inotropes must be administered in central line
- ▶ Do not cease infusion abruptly,
- ▶ Should be used with caution in patients with atherosclerosis, mesentric and peripheral vascular thrombosis or other occlusive vascular diseases, metabolic acidosis, hypoxia or hyperthyroidism.
- ▶ It should be avoided in patients who are hypersensitive to sodium metabisulfite (which is the preservative in the solution).
- ▶ discard diluted solutions after 24 hours Protect ampoules from light during storage and discard if discoloured



- ▶ Follow ten rights
- ▶ Monitor for adverse effect
- ▶ Continuous BP using invasive arterial BP monitor
- ▶ connect the patient with cardiac monitor and monitor ECG rythm
- ▶ Inotropes must be administered using infusion or syringe
- ▶ Should follow standard dilution
- ▶ The lable on loaded drug should contain drug concentration and dilution
- ▶ Monitor urine output





- ▶ ISOPROTERENOL (ISUPREL)
- ▶ Has nearly pure beta-adrenergic receptor activity.
- ▶ Increase heart rate and contractility and cause peripheral vasodilation.
- ▶ Used for temporary control of symptomatic bradycardia.
- ▶ Initial drug of choice for heart transplant.
- ▶ Increases myocardial oxygen requirements and the possibility of inducing or exacerbating myocardial ischemia is present.
- ▶ The risk of arrhythmias is also increased.
- ▶ It is not the first treatment of choice for bradycardias.
- ▶ Atropine, epinephrine or pacing should be initiated first.





DOSE: - □ Initial dose of 2 mcg/minute □ Titrate dose to a maximum of 10 mcg/min. or heart rate is 60 or greater. □ Decrease the rate if blood pressure is >120/60 □ Decrease rate if PVC's or Ventricular tachycardia is noted. Isoporterenol administration concentration: - □ 1 mg in 250 cc crystalloid (4 mcg/cc).





- ▶ Adverse effects: -
- ▶ Arrhythmias.
- ▶ Ventricular tachycardia.
- ▶ Ventricular fibrillation. Warning:-
- ▶ May exacerbate tachyarrhythmias due to digitalis toxicity.
- ▶ May precipitate hypokalemia.





- ▶ **PHOSPHODIESTERASE INHIBITORS** Powerful positive inotropic agents. The action is not fully understood.
- ▶ Inhibits phosphodiesterase, an enzyme that degrades (CAMP)
 - ▶ Cyclic Adenosine Monophosphate.
 - ▶ There is no effect on alpha or beta-receptors.
 - ▶ Increase contractile force and velocity of relaxation of cardiac muscle.
 - ▶ Increasing cardiac output without increasing myocardial oxygen consumption.
 - ▶ They cause vasodilation and a decrease in SVR (systemic vascular resistance) and PVR (Pulmonary vascular resistance & in afterload (resistance to ventricular ejection)





- ▶ AMRINONE (INOCOR)
- ▶ Has a hemodynamic effect similar to Dobutamine.
- ▶ Increase cardiac output and decrease pulmonary vascular resistance.
- ▶ It should be used with caution in patients with ischemic heart disease because it can exacerbate ischemia.
- ▶ It should be considered for use in patients with severe congestive heart disease, which is no longer responsive to other inotropes, diuretics, and vasodilators.
- ▶ It is also used after aorto-coronary bypass surgery.
- ▶ It is recommended that the lowest dose that produce the desired hemodynamic effect to be used.



- ▶ **LOADING DOSE:**
- ▶ 0.5 TO 0.75 mg/kg given over 2-3 min.
- ▶ **IV DO NOT EXCEED 1 mg/kg.**
- ▶ Maintenance dose: 5 to 10 mcg/kg/min Maximum dose: 10mg/kg/24hours.
- ▶ Doses higher than 15 mcg/kg/minute can produce tachycardia
- ▶ **NEVER DILUTE WITH DEXTROSE!**
- ▶ (Chemical reaction occurs) Syringe pump: Use Straight Solution Concentration 5 mg/cc Adverse reaction: -
Thrombocytopenia occurs in 10% of all patients seen 48 – 72 hours after infusion and resolves when drug is discontinued. Gastrointestinal upset Myalgia Fever Hepatic dysfunction Ventricular irritability



- ▶ Nursing implication: -
- ▶ Monitor for arrhythmias, hypotension, thrombocytopenia & hepatotoxicity.
- ▶ Monitor cardiac output, pulmonary artery pressure and heart rate.
- ▶ Effects last for 2 hours after drip is discontinued.
- ▶ The loading dose may be given over 2 to 5 minutes, but to prevent Hypotension it is recommended the loading dose be given over 10 to 15 minutes.
- ▶ MILRINONE (Primacor)
- ▶ Milrinone is about 10 fold more potent than Amrinone.
- ▶ A positive inotropic agent that increases cardiac output and decreases systemic vascular resistance.
- ▶ Because of its vasodilating effect, Milrinone is not generally associated with an increase in myocardial oxygen demand.
- ▶ Milrinone can be diluted in dextrose or saline solution.





- ▶ **LOADING DOSE:-** 50 mcg/kg given IV over 10 minutes
- ▶ **MAINTENANCE DOSE:-** 0.375 to 0.75 mcg/kg/minute
- ▶ **Warning; -**
- ▶ **DOSES TOO HIGH CAN CAUSE HYPOTENSION AND TACHYCARDIA.**
- ▶ **MILRINONE IS INCOMPATIBLE WITH L ASIX!**
- ▶ **ADVERSE EFFECTS:**
 - ▶ Supraventricular tachycardia
 - ▶ Ventricular arrhythmias
 - ▶ Ventricular ectopy
 - ▶ Increased ventricular rate in atrial fibrillation/flutter
 - ▶ Headache
 - ▶ Hypokalemia
 - ▶ Tremors
 - ▶ Thrombocytopenia





- ▶ **EASY FORMULAS FOR DRUG CALCULATIONS FOR INFUSION PUMP TO DETERMINE DESIRED RATE:-** (Remember 1 mg = 1000 mcg) (Desired mcg) X kg. X 60 ÷ mcg/cc (in solution)
- ▶ **Example:-** Give Dopamine 5 mcg/kg/min to a patient who weights 65 kg. $5 \times 65 \times 60 \div (800 \text{ mg in } 500 \text{ cc})$ (5 mcg) X (65 kg) X 60 ÷ (800 mg ÷ 500 cc = 1.6 mg. X 1000) = 1600 mcg $19500 \div 1600 = 12.18 \text{ cc}$
- ▶ **Example:** Give Dopamine 2.5 mcg/kg/min to a patient who weight 55 KG. $2.5 \times 55 \times 60 \div 1600$ (2.5 mcg) X (55 kg) X 60 ÷ 1600 = 5.15 cc



- ▶ TO DETERMINE MCG/KG/CC INFUSING:
- ▶ Example: You have a patient that weighs 85 kg who has a dopamine drip infusion at 8cc per hour and you want to determine how many mcg/kg/min the patient is receiving.
- ▶ The dopamine is mixed at 1600 mcg per cc. $MCG/CC \times RATE \div 60 \div KG$ $1600 \times 8 \div 60 \div 85 = 2.5$ mcg/kg/minute
- ▶ Example: You have a patient that weighs 102 kg who has a Dobutamine drip infusing at 12 cc per hour and you want to determine how many mcg/kg/min the patient is receiving.
- ▶ The Dobutamine is mixed at 500 mg in 250 cc = 2000 mcg per cc. $(500 \text{ mg} \div 250 = 2 \times 1000 = 2000)$ $2000 \times 12 \div 60 \div 102 = 3.92$ mcg/kg/min.



- ▶ **CONCLUSION**
- ▶ Inotropes are very effective drugs when administered properly.
- ▶ Patients receiving inotropes should be monitored closely including blood pressure, cardiac monitoring, intake and output, and laboratory tests that have been ordered by the physician.
- ▶ Knowledge of desired effects and side effects is critical to the administration of inotropes.
- ▶ **CONCLUSION CONT...**
- ▶ A thorough grasp of the pharmacology of inotropes is crucial to understand the rationale for drug therapy of heart failure.
- ▶ Inotropes continue to improve through scientific research.
- ▶ Oral forms of inotropes are now being investigated to manage congestive heart failure at home.



THANK YOU