



# **DIRECTLY ACTING DRUGS**

**PAVAN  
GOUD**

# VASODILATORS

- Dilate blood vessels.
- By relaxation of the vascular smooth muscle.
- Decrease peripheral vascular resistance and blood pressure.

# CLASSIFICATION OF DIRECTLY ACTING DRUGS

## ARTERIORLAR

- HYDRALAZINE
- MINOXIDIL
- DIAZOXIDE

## ARTERIORLAR+VENO US

- SODIUM  
NITROPRUSSIDE

## VENOUS

- NITROGLYCERINE

# HYDRALAZINE

- first orally acting antihypertensive drug to be marketed in US.
- used infrequently because of tachycardia and tachyphylaxis.

## MECHANISM OF ACTION:

Opens K<sup>+</sup> channels and relaxes the smooth muscles of arterioles

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graph TD; A[Opens K+ channels and relaxes the smooth muscles of arterioles] --> B[decrease in peripheral vascular resistance]; B --> C[Decrease in arteriolar blood pressure];
```

decrease in peripheral vascular resistance

Decrease in arteriolar blood pressure

# Hydralazine - Compensatory Response

- It causes reflex stimulation of sympathetic system. This leads to
  - ❖ increased heart rate
  - ❖ Increased myocardial contractility
  - ❖ Increased cardiac output
  - ❖ Increased plasma renin activity
  - ❖ Increased fluid retention
- This leads to increased arterial pressure and their antagonizes its antihypertensive action.
- It is thus given with
  - A beta blocker
  - A diuretic

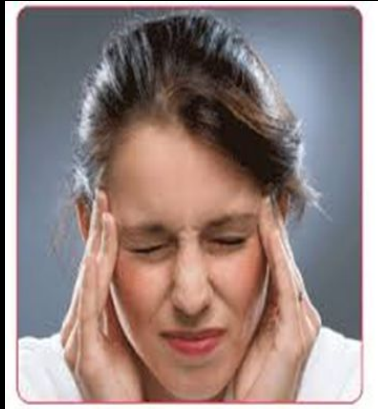
# Hydralazine: ABSORPTION, METABOLISM AND EXCRETION:

- Well absorbed in GIT
- Metabolized by liver
- Excreted in urine
  
- **DOSE:** 40mg/day to 200mg/day

# Hydralazine: THERAPEUTIC USES:

- no longer a first line drug on account of its unfavourable adverse effects.
- a combination pill containing of isosorbide dinitrate that is used for the treatment of heart failure.
- useful in the treatment of hypertensive emergencies in pregnant women

# ADVERSE EFFECTS OF HYDRALAZINE:PHARMACOLOGICAL



## CNS:

Headache,  
dizziness,  
peripheral  
neuropathy

GIT:  
Anorexia, nausea



## CVS:

Palpitations,  
flushing, reflex  
tachycardia,  
angina.

SKIN:  
Sweating, lupus  
erythematosus like  
syndrome characterized  
by arthralgia, myalgia,  
skin rashes and fever





# **HYDRALAZINE: IMMUNOLOGICAL REACTIONS**

- Drug induced lupus syndrome
- Serum sickness
- Vasculitis

## **CONTRAINDICATIONS:**

used with great caution in elderly patients and in hypertensive patients with coronary artery disease because of the possibility of myocardial ischaemia.

# LUPUS ERYTHEMATOSUS



# HYDRALAZINE



# ARTERIOLEAR+VENOUS VASODILATORS: SODIUM NITROPRUSSIDE



- rapidly and consistently acting vasodilator

## MECHANISM OF ACTION:

- nitrovasodilator that acts by releasing NO.
- NO activates guanylyl cyclase-cyclic GMP-PKG pathway leading to vasodilation mimicking the production of NO by vascular endothelial cells.

# Nitroprusside:

## PHARMACOLOGICAL EFFECTS

- dilates both arterioles and venules.
- in subjects with normal left ventricular function, venous pooling leads to reduced cardiac output.
- in patients with severely impaired left ventricular function and diastolic ventricular distention, the reduction of arterial impedance leads to increased cardiac output.

# Sodium nitroprusside: ABSORPTION, METABOLISM AND EXCRETION:

- unstable molecule that decomposes under strongly alkaline conditions or when exposed to light.
- It is further metabolized by liver.
- excreted in urine.
  
- DOSE: 0.25-1.5  $\mu\text{g}/\text{kg}/\text{min}$

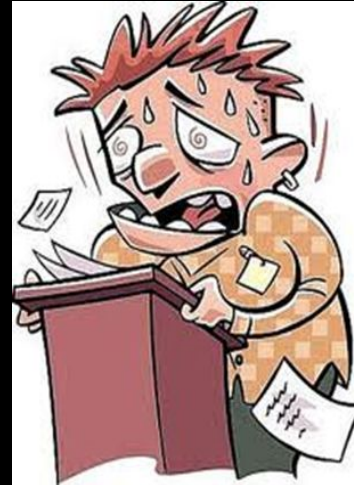
# Sodium nitroprusside:

## THERAPEUTIC USES:

- **hypertensive emergencies**
- acute aortic dissection
- to improve cardiac output in congestive heart failure, especially in hypertensive patients with pulmonary oedema.
- to induce hypotension during anesthesia to reduce bleeding during surgical procedures.

# ADVERSE EFFECTS

- Palpitation
- Nervousness
- Vomiting
- Perspiration
- Pain in abdomen
- Weakness
- Disorientation
- lactic acidosis







# VENOUS DILATOR NITROGLYCERINE



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- used medically as a potent vasodilator to treat heart conditions, such as angina pectoris and chronic heart failure.

## MECHANISM OF ACTION:

GTN forms free radical NO which activates guanylate cyclase resulting in an increase of cyclic GMP in smooth muscle and other tissues. This regulates the contraction of smooth muscle and results in vasodilatation.

# Nitroglycerine: ABSORPTION , METABOLISM AND EXCRETION:

- rapidly absorbed following sublingual administration.
- metabolized by liver.
- metabolism is the primary route of excretion.

# DOSE AND ROUTES OF ADMINISTRATION

- 0.5 mg sublingually
- 0.4-0.8mg spray
- 5-15mg orally
- One patch 14-16hr/day
- 5-20 $\mu$ g/min Intra-venously
- Ointment- cutaneously

# Nitroglycerine - THERAPEUTIC USES

- effective in treatment of angina. For terminating an attack, sublingual GTN tablet or spray is used.
- to prevent further coronary occlusion, increased coronary blood flow and decrease myocardial stress.
- treatment of biliary colic
- to relieve pain in oesophageal spasm.

# ADVERSE EFFECTS

- Headache , Vertigo, dizziness, weakness, palpitation, postural hypotension particularly in erect, immobile patients.
- Flushing, drug rash, and exfoliative dermatitis have been reported in patients receiving nitrate therapy.



Vertigo



Exfoliative dermatitis



Face rash

# NTG -CONTRAINDICATIONS

- patients with early myocardial infarction, severe anemia, increased intracranial pressure, and those with a known hypersensitivity to nitroglycerine.
- who are allergic to it.





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Thank  
you