Regulation of vasculature diameter by endothelium

Medical physiology department

ILOs

1. **Identify mechanisms that control of arteriolar diameter**
2. Describe Endothelium-derived relaxing factors and Endothelium-derived constricting factors.
2. Describe other factors affecting vascular tone.

The Control of arteriolar diameter Consists of
2 major mechanisms (methods):

❶ **Central Mechanisms**

❷ **Local mechanism**

Aim: Of central regulation is to regulate **the total peripheral resistance** (TPR) to maintain a constant ABP to ensure adequate blood supply to vital organs (heart & brain)

Central mechanisms includes (consists of) 2 types

① Neural mechanism

Consists of 2 types of fibers:
VC fibers VD fibers

② Vasoactive substances

Consists of : **Circulating VD substances & VC substances**

① Neural mechanism

1- Vasoconstrictor fibers (VC)

- sympathetic VC fibers to arterioles are
- Through α-adrenergic receptors
- To all arterioles except heart+ brain

2- Vasodilator fibers (VD):

❶ Sympathetic VD fibers

- Skeletal muscles through **cholinergic** receptors
- Coronary vessels through **B1 adrenergic** receptors

❷ Parasympathetic VD fibers

VD of parasympathetic is secondary to increase metabolic activity except genital tract

❸ Antidromic VD impulses

Stimulation of skin pain receptors

②Vasoactive substances:

2 types: VD &VC substances

Circulating VD substances

❶ Kinins:

1. Relaxes smooth ms of Bl. Vessels→ VD & decrease ABP.
2. Contracts smooth ms of viscera.
3. Increase capillary permeability.

❷ANP

"Atrial Naturetic Peptide“

1. Naturesis is increase Na^+ excretion, which is accompanied by Cl loss & H_2O loss (Diuresis)

3. Decrease the response of Blood vessels to VC substances
4. Decrease formation of renin
5. Decrease secretion - Vasopressin &Aldosterone

❸ Histamine

VD in allergic and inflammatory conditions

Circulating VC substances

❶ Catecholamine

① Adrenaline

② Noradrenaline (most potent VC)

❷ Angiotensin II

a) Powerful VC: In seconds (rapid)

b) Salt & water retention:

❸ Vasopressin = ADH "Antidiuretic Hormone"

1- Water reabsorption

2- Vasoconstriction

NB:

Noradrenaline has a stronger VC effect than adrenaline

Adrenaline causes VD in liver & skeletal muscle

❷ Local Mechanism

- It regulates blood flow according to the local metabolic needs of tissues
- Local mechanisms include (consists of) 2 mechanisms:

① Auto regulation

Definition: It is the ability of a tissue to regulate its own blood flow

Theories:

1. Myogenic theory:

- It is Bayliss response (intrinsic response)
- Stretch of smooth muscle → contraction

2-Metabolic theory:

- On increase tissue activity or decrease blood flow, vasodilator metabolites accumulate → VD → Increase blood flow

- **VD metabolites are:**

1. Low O_2 & Low pH in most tissues
2. Increase CO_2 in brain, skin
3. K+ in skeletal muscle
4. Adenosine in cardiac muscle
5. Lactate + Increase temperature of tissue activity
6. Histamine in inflammation

Endothelial derived substances

Substances secreted by Endothelium

vasodilators

1. Bradykinin.
2. Endothelium derived relaxing factor (EDRF): now known as Nitric oxide **(NO).**
3. Prostacyclin **(PGI2).**

vasoconstrictors

1. Endothelin-1.
2. Thromboxane A_2 (TXA2).
3. Prostaglandin.

What is Endothelium?

- **Endothelium**: is the single layer of cells lining the inner surface of the blood vessels.
- It shares in regulation of BV diameter by secreting dilator or constricting factors when stimulated by:

1. Substances present in blood.
2. Shear stress.

Substances secreted by Endothelium

1) Prostacyclin:

- **Chemical nature:** Is derived from arachidonic acid via cyclooxygenase enzyme (COX)
- **Formed by**: Endothelial cells
- **Functions:** 1. Decrease platelets aggregation
  2. VD

2) Endothelium derived relaxing factor: (EDRF) (Nitric Oxide "NO"):

- **Chemical nature**:
  - It Is Nitric Oxide (NO)
  - Synthesized from Arginine by the action of NO synthetase.
- **Mechanism of action**: It activates Guanylate cyclase enzyme producing cGMP which relaxes the smooth muscles

1. The most important vasodilator substance
2. Its tonic release is necessary for normal ABP
3. Its deficiency causes hypertension

3) Endothelins: Most potent VC produced by endothelium

4 types: E1, E2, E3 & VIC

1. Contracts vascular smooth muscle, veins > arteries.
2. VC of coronaries (intense VC).
3. VC of renal vessels → Increase resistance.
4. Decrease renal blood flow → decrease GFR (glomerular filtrate rate).
5. +ve inotropic and +ve chronotropic effects.
6. Increase catecholamine, renin, aldosterone & ANP.

Endothelin-1

- Its synthesis is stimulated by presence of vasoconstrictor substances in the blood as angiotensin, vasopressin, thrombin, epinephrine

Endothelium in CVS diseases

- Dysfunction of endothelium contributes to the early stages of atherosclerosis.
- Damage of endothelium is a crucial factor leading to thrombus formation due to lack of prostacyclin.


Thank
you!