Physiology and Pathophysiology of Shock (Paediatrics)

Vascular tone control

Vasomotor tone of vessels is affected by several mechanisms: nervous and humoral factors, composition of blood gases, local metabolic regulation, function of the endothelium and smooth muscles of the vascular media.

A mechanism that regulates vascular resistance in one region may be completely without effect in another region. E.g. in the context of hypovolemic shock , the perfusion of the heart and brain is preserved , and on the contrary, it is reduced in the muscles, skin and splanchnic.

Neuromodulation of vascular tone

Receptors to which noradrenaline , acetylcholine or neuropeptides bind are represented throughout the circulation. However, the distribution of receptors is organ-specific, allowing rapid and coordinated redistribution of blood flow in response to hypoxia , postural changes, and hemorrhage . In all organs, the nerve endings of efferent nerves also contain nonadrenergic and noncholinergic peptides, e.g. neuropeptide Y , VIP (vasoactive intestinal peptide), substance P, calcitonin gene-related peptide (CGRP). Most of these peptides, with the exception of neuropeptide Y, lead to vasodilation and help regulate regional perfusion

Humoral regulation of vascular tone

Humoral factors that regulate vascular tone include the renin-angiotensin-aldosterone system (RAAS), ADH , bradykinin , histamine , serotonin , thyroxine , natriuretic peptides, and a number of others. These factors affect vascular tone in a direct and indirect way. These factors tend to decrease in concentration during hypertension , congestive heart failure or shock , and their antagonists are often used in the therapy of these conditions. Certain factors such as histamine, serotonin, thyroxine probably affect vascular resistance only in pathological conditions and do not apply in physiological conditions.

Angiotensin plays a special role in blood pressure homeostasis . Hypovolemia leads to increased production of renin in the kidney, which converts angiotensinogen to angiotensin I. Angiotensin I is converted to active angiotensin II by angiotensin-converting enzyme (ACE) in the endothelium, especially in the pulmonary bed. However, angiotensin II can be produced directly from renin locally in the heart and vessel wall. Angiotensin II causes generalized vasoconstriction in the systemic and pulmonary circulation, but locally stimulates the release of vasodilating prostaglandins in the kidneys and lungs .

Aldosterone was primarily known for its effect on sodium and potassium balance . Its concentration increases with the release of renin. In patients with congestive heart failure, we find its high concentrations both due to dilutional hyponatremia and reduced degradation in the liver. High concentrations, which are a sign of the body's initially compensatory reaction overshooting, are harmful to the cardiovascular system. Inhibition of aldosterone by spironolactone appears to be of great benefit in the therapy of heart failure.

ADH (antidiuretic hormone, vasopressin) has an antidiuretic effect and at the same time causes vasoconstriction, low concentrations of ADH lead to vasodilation in the coronary, cerebral and pulmonary basins. The concentration of ADH decreases in septic shock, on the contrary, it increases in hypovolemia, congestive heart failure and liver cirrhosis . Selective ADH antagonists allow excretion of free water without ion excretion and are useful in the treatment of hypervolemia in patients with congestive heart failure, cirrhosis, or SIADH . Bradykinin **is a potent vasodilator in the pulmonary and systemic circulation. It is released locally from kallikrein by the action of proteolytic enzymes as a result of tissue damage**.

Histamine is also released from mast cells in response to tissue damage. It is a potent vasodilator in the systemic circulation, but leads to vasoconstriction in the pulmonary circulation. It also increases vascular permeability.

Natriuretic peptides are released from the heart as it distends in congestive failure. They cause vasodilation and increase natriuresis. ANP (atrial natriuretic peptide) is released especially in the atria, BNP (brain natriuretic peptide) from the ventricles and C-natriopeptide from the cardiac endothelium. Recombinant BNP (nesiritide) is more effective than dobutamine in the treatment of acute severe congestive heart failure.

Serotonin causes vasodilation or vasoconstriction depending on the type of serotonin receptor affected.

Effect of blood gases on vascular tone

The values of paO 2 and paCO 2 are dependent on the quality of tissue perfusion. Hypoxia and hypercapnia that accompany hypoperfusion are associated with a vasodilator effect.

Local metabolic regulation of vascular tone

Local metabolic regulation of vasomotor tone represents an ideal homeostatic mechanism. With its help, the metabolic needs of tissues directly affect local perfusion. E.g. adenosine, which accumulates locally during high tissue metabolism and marginal tissue oxygenation, leads to vasodilation in the coronary basin, striated muscle, splanchnic, and cerebral circulation.

Regulation of vascular tone through the endothelium

The vascular endothelium plays a prominent role in the regulation of vascular tone. In addition to influencing vasoactive eicosanoids and their role in angiotensin metabolism, the endothelium produces a number of vasoactive substances. **Nitric oxide** (NO; a potent vasodilator) and **endothelins** are among the most important . Endothelins (ET-1, ET-2, ET-3) represent a family of vasoactive substances. ET-1 is a potent vasoconstrictor, otherwise the effect of endothelins depends on acting on two types of receptors: ET-A receptors located in vascular smooth muscle mediate vasoconstriction, ET-B on endothelial cells mediate vasodilation. Endothelin antagonists, such as bosentan, are beginning to be used therapeutically.

Regulation of vascular tone through smooth muscle of the vascular media

Changes in vascular smooth muscle tension are a response to distension or an increase in transmural pressure. An increase in vascular flow leads to local vasoconstriction. The opposite reaction is caused by a decrease in vascular flow.

Autoregulation

In all organs, if the perfusion pressure is suddenly increased or decreased while oxygen consumption is maintained constant, the flow rate will increase or decrease temporarily, but then return to the previous value. This phenomenon is called **autoregulation** .

The myogenic tonic response partially explains this phenomenon, but it is not the only mechanism. Some scientists believe that tissues have oxygen sensors that respond to transient increases or decreases in oxygen supply . Other researchers argue that the process of autoregulation is mediated by increased or decreased release of nitric oxide, which is transported to the tissues via hemoglobin as S-nitrosohemoglobin or by the release of ATP from erythrocytes .

Some autoregulatory mechanisms are specific to individual microcirculations (eg, renal). Self-regulatory mechanisms differ in individual organs.

Pulmonary circulation

In the fetus , the pulmonary circulation has the character of a systemic circulation, the pulmonary arteries have a strongly developed medial smooth muscle. This is the reason for the high pulmonary resistance in the fetus even early postnatally. After birth, within a few weeks, the musculature of the mediastinum involutes and progressively decreases the resistance of the pulmonary canal. During the first 24 hours after birth, the pulmonary arterial pressure drops to a value of approx. 50% of the mean arterial pressure , and the pulmonary circulation remains at low pressure with low vascular resistance. Due to the intimate relationship between small pulmonary vessels and alveoli, intra-alveolar pressure affects pulmonary flow, especially in patients with artificial pulmonary ventilation.

The most important factors that influence pulmonary vascular resistance in the postnatal period are the **oxygenation** rate and the **pH value** . When the oxygen tension in the alveoli decreases, hypoxic pulmonary vasoconstriction develops in a given lung segment. The goal is to redistribute blood flow to well-ventilated areas of the lung and thus maintain a favorable ventilation/perfusion (V/Q) ratio. This phenomenon is highly specific to the pulmonary circulation, as the blood vessels of other organs (including the CNS) respond to hypoxia by vasodilation. Acidosis potentiates hypoxic pulmonary vasoconstriction, alkalosis reduces it. The actual mechanism of the pH-mediated response of the pulmonary vascular bed is not fully understood, but it appears independent of pCO 2. The mechanism of alveolar hyperoxia and alkalosis is often used to induce pulmonary vasodilation in patients with pulmonary hypertension. Hypocapnia and RAL in turn lead to vasoconstriction in the systemic circulation, which may have adverse consequences in CNS and cardiac perfusion.

Selective pulmonary vasodilators are oxygen and inhaled nitric oxide (iNO).

Coronary circulation

The right and left coronary arteries arise from the sinus of Valsalva and run along the surface of the heart . Perfusion of the heart takes place during diastole. In tachycardia , diastole shortens, myocardial perfusion decreases and ischemia may occur . Under normal circumstances, right ventricular perfusion takes place even during systole due to the low pressures. The coronary circulation also exhibits autoregulation. An increase in pressure causes vasoconstriction, a decrease in pressure leads to vasodilation. When the pressure drops below 40 torr, the autoregulation mechanism is no longer effective and ischemia develops.

Renal circulation

Approximately 20% of cardiac output flows through the kidneys , although the weight of the kidneys represents approximately 0.5% of the total body weight. The reason is to promote sufficient glomerular filtration to maintain water and solute homeostasis. At the end of the arterial river we find afferent arterioles, which open into the capillary network within the glomerulus. Glomerular capillaries form in the outflow part into an efferent arteriole,

which subsequently creates a secondary capillary system (peritubular capillaries). The increased hydrostatic pressure inside the glomerular capillaries promotes filtration, while the much lower pressure inside the peritubular capillaries aids reabsorption. Changes in the resistance of afferent and efferent arterioles allow for dynamic changes in renal function in response to fluid and solute needs.

Renal flow is determined by the difference between renal arterial pressure (corresponding to systemic arterial pressure) and renal venous pressure. Renal vasomotility is influenced by both external factors (sympathoadrenal system , natriuretic peptides , RAAS) and internal factors that are responsible for autoregulation of renal flow in response to changes in renal perfusion pressure (RPP). **Glomerular filtration** is given by glomerular filtration pressure (glomerular filtration pressure, GFP). GFP depends on RPP and the balance between arterial tone of afferent and efferent arterioles. Specifically, vasoconstriction of the vas efferens increases glomerular filtration, vasoconstriction of the vas afferens decreases glomerular filtration.

Endothelial function

The endothelium performs a number of functions:

- Endothelial cells play an important role in the body's defenses - they enable the adhesion and subsequent extravasation of leukocytes through molecules - selectins, adherins, integrins.
- The endothelium is intimately linked to the function of the coagulation system . It has the ability to produce procoagulant factors (platelet activating factor = PAF, von Willebrand factor , fibronectin, ff. V and X) and anticoagulant factors (heparan, dermatan sulfate, thrombomodulin) and by producing NO and PGI2 it inhibits platelet aggregation and degranulation .
- The endothelium regulates capillary permeability by producing endothelin 1 (ET-1), which increases permeability, and by producing PGE1, which decreases permeability.

Relationship between flow, pressure and vascular resistance

From the point of view of the diagnosis of the shock state syndrome, the parameter of perfusion efficiency with subsequent manifestations of organ dysfunction is absolutely essential.

Organ perfusion (flow) is determined by the pressure of flowing blood and vascular resistance. Under normal circumstances, a sufficient pressure gradient is present and vasomotor control regulates individual organ perfusion according to metabolic need. Under resting conditions, only part of the vascular system is open. In most cases, the onset of shock syndrome is linked to a drop in pressure and subsequent failure of organ perfusion. However, the level of blood pressure is not the only determinant of perfusion. With high blood pressure, but at the same time high vascular resistance, tissue perfusion is also not sufficient.

Thus, the severity of the shock state is primarily determined by the depth of the tissue perfusion disorder. Good tissue perfusion ensures an adequate supply of nutrients and oxygen at the cellular level. However, we must always relate tissue perfusion to the current needs of the organism. In conditions with hyperkinetic circulation (thyrotoxicosis , high flow phase of sepsis , liver failure), even "normal" perfusion may be insufficient, as the tissues show a higher need for oxygen and energy substrates than the organism is able to provide at the given moment. Simply put, demand for O2 exceeds supply. **The parameters of adequate oxygen supply** are:

- absence of hypotension ,
- warm periphery with good capillary return,
- diuresis > 1 ml/kg/hour,
- normal consciousness _
- lactate < 2 mmol/l,
- With vc O 2 > 70%.

The decisive parameter determining the regional perfusion Q is the blood flow generating the dynamic blood pressure. According to **Poiseuille's law** :

Q = (P in - P out) / R

where Q is tissue flow, P in is input pressure, P out is output pressure, R is resistance. In the case of a simple tube, this is determined by the diameter of the tube, its length, it is inversely proportional to the fourth power of the radius and directly proportional to the value of the viscosity of the flowing fluid.

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Thus, regional perfusion is determined by blood pressure and regional resistance. The resistance of various areas of the systemic circulation and the cardiac output determine the value of the systemic arterial pressure. Local factors controlling regional perfusion may have different effects than control mechanisms regulating systemic arterial pressure. For example, hypoxia leads to vasoconstriction by activating central baroreceptors, but vasodilation occurs in the periphery. If we take into account the whole body perfusion Q co and neglect P out (the venous pressure is small compared to the value of the arterial pressure), we get the equation:

Pa = Q co x R vol

where P a is arterial pressure, Q is cardiac output, Rsv is systemic vascular resistance. For a more accurate determination of tissue perfusion, however, we take venous pressure into account (P out = CVP) in a situation where we want to define the perfusion pressure parameter = perfusion pressure PerP. This corresponds to the difference between mean arterial pressure MAP and central venous pressure CVP. So:

erP = MAP - CVP

Limit values of perfusion pressure in cm H 2 O (mm Hg - rounded values)

Children's age	Perfusion pressure in cm H 2 O (mm Hg)
newborns	55 (40)
infants	60 (45)
toddlers	65 (50)
preschoolers	65 (50)
school children	65 (50)

However, perfusion pressure is not the only important parameter, it is necessary to simultaneously maintain S vc O 2 > 70% with the help of transfusion or inotropic support, lactate level < 2 mmol/l, good peripheral perfusion, diuresis > 1 ml/kg/h.

In conditions with **intra-abdominal hypertension** (ascites , ileus) the perfusion pressure is equal to the difference MAP - IAP (intra-abdominal pressure). The relationship between flow, pressure and resistance can also be applied to individual organs. In the kidneys, for example, renal flow Q = (mean renal arterial pressure - mean renal venous pressure) / renal vascular resistance.

Some organs, as already mentioned above, have the ability of **vasomotor autoregulation** , which maintains blood flow even at low blood pressure. This works up to a certain critical point where the perfusion pressure is reduced below a value where sufficient flow can still be maintained in the organ. The purpose of shock treatment is to maintain the perfusion pressure above a given critical point (but be careful - the critical point is not a fixed value, it is strictly individual).

The kidneys are a textbook example: the kidneys need the second highest blood flow. At the same time, accurate determination of diuresis and creatinine clearance is very easy and enables the quality of renal perfusion to be assessed. And it is the quality of renal perfusion that provides a picture of perfusion in other visceral organs as well. The kidneys thus represent a kind of "window" into organ perfusion. Therefore, an accurate assessment of diuresis in every critically ill patient is absolutely essential!

If hypotension occurs, it is the result of low cardiac output or low vascular resistance. From this point of view, it is possible to divide shock states into only two basic categories - **shock with low cardiac output** and **shock with low systemic vascular resistance .**

Age-Specific Vital Signs and Laboratory Values (Pediatric Critical Care 2005)

Age	Heart rate (beats per minute)	Respiratory rate (breaths per minute)	Leukocytes (leu x 10/3 in ml)	Systolic BP (mm Hg)
0 days - 1 week	> 180 x < 100	> 50	> 34	< 65
1 week – 1 month	> 180 x < 90	> 40	> 19.5 x < 5	< 75
1 month – 1 year	> 180 x < 90	> 35	> 17.5 x < 5	< 100
25 years	> 140	> 22	> 15.5 x < 6	< 94
6 – 12 years	> 130	> 18	> 13.5 x < 4.5	< 105
13 – 18 years	>110	> 14	> 11 x < 4.5	< 117

Note: the values shown represent the 5th or 95th percentile for the given age group. Any shock state can result in a systemic inflammatory response (SIRS). Unattenuated cascades of cytokines, complement and coagulation lead to a violation of the integrity of the vascular wall and an increase in the adhesiveness of the endothelium. The result is then extravasation, vasodilatation, thrombosis , tissue hypoxia. Lactic acidosis is an expression of mitochondrial hypoxia.

Links

Source

- HAVRÁNEK, Jiří: *Shock* . (edited)

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