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Chapter 3

Hemodynamic Monitoring in Neonates

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Additional information is available at the end of the chapter

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Abstract

Sick neonates are often hemodynamically unstable, hence their organs are inadequately supplied with oxygen. In order to maintain blood flow to vital organs, a number of compensatory mechanisms divert the blood flow away from the non-vital organs. If hemodynamic changes are detected early, the cardiovascular compromise can be recognized in compensated phase and thereby the escalation to decompensated phase of low cardiac output syndrome might be prevented. In the treatment of hemodynamically unstable neonate venous filling, contractility of the heart muscle, blood pressure in the aorta, systemic blood flow, and regional distribution of blood flow should be evaluated. There are many evaluation and measurement methods based on different physical basis, each of them having their advantages and disadvantages. For most of them, it has not been demonstrated that they improve outcomes of sick neonates. Using these methods, useful hemodynamic data for the treatment of sick neonates can be obtained. Using new techniques will clarify the pathophysiology of cardiovascular failure in sick neonates, assess the effects of drugs on blood pressure and perfusion of the heart and other organs.

Keywords: neonate, hemodynamics, oxygenation, perfusion, arterial blood pressure, cardiac output, peripheral vascular resistance

1. Introduction

In neonatal intensive care unit (NICU), hemodynamic instability is an important cause for admission and treatment after respiratory distress syndrome (RDS) and most common problems of prematurity [1]. Therefore, hemodynamic monitoring is important especially in transitional period to extrauterine life and during the next following days. Hemodynamic monitoring is also crucial in neonates with congenital heart defects (CHDs) and other complex surgical anomalies of neonates. During early transitional period, cardiac output (CO) is not dependent solely

on the performance of the neonate's left ventricle but also on pulsating blood flow through the umbilical vein. This pulsating blood flow is extremely important especially if newborn is under fetal distress, and it is usually prudent to postpone ligation of umbilicus for a short period of time to add additional pulsatile and volume support to neonate's CO [2, 3]. Even later in the life, neonate with RDS requires hemodynamic monitoring due to disturbances related to RDS or other common problems of prematurity or immaturity. Besides prematurity, immaturity of cardiovascular system in the first days and weeks of life and altered physiology of systemic and pulmonary circulation in neonates with CHD may need frequent hemodynamic monitoring, whether invasively or noninvasively.

2. Methods

We conducted electronic searches of articles on hemodynamic management and care of neonates, using key terms: neonate, hemodynamics, oxygenation, perfusion, arterial blood pressure, cardiac output, and peripheral vascular resistance in the PubMed data base from the years 2000 to 2017 and reported the most relevant ones. The article lists the methods for the evaluation of the venous filling, cardiac output, blood pressure, regional blood flow, and microcirculation, from the clinical methods to the noninvasive and invasive ones. Some methods for monitoring the cardiovascular status of neonates are mainly used for research purposes. This chapter includes the impact of optimal arterial blood pressure, tissue perfusion, and persistent ductus arteriosus on the hemodynamic management in neonates. Also, the short- and long-term outcomes in respect of hemodynamic management of neonates in the intensive care unit are addressed.

3. Physiology of hemodynamics

Hemodynamics describes the dynamics of blood flow in the body. Blood flows in the circulatory system, which is composed of the central pump—the heart—and the blood vessels, and is controlled by homeostatic mechanisms. The pulsatile rate of blood flow out of the heart is called the cardiac output. The main role of the cardio-circulatory system is to match the oxygen and nutrient needs of the organs and tissues and elimination of the metabolic wastes. The cardio-circulatory system should provide an appropriate blood flow to the organs and by that an appropriate tissue perfusion. In the physiologic conditions, the tissue oxygen and nutrient needs are matched by their supply. In cardiovascular compromise, the compensatory mechanisms allow the redistribution of blood flow to the vital organs—the brain, heart, and suprarenal gland in the neonate—at the expense of decreased blood flow to the non-vital organs.

3.1. Hemodynamic monitoring

Hemodynamic monitoring encompasses the observation and measurement of hemodynamic parameters over time. The ultimate goals of hemodynamic monitoring is to alert the

health-care team of impending cardiovascular crisis, to obtain information specific to the disease processes, which may facilitate diagnosis and treatment and allow one to monitor the response to therapy, and also to derive estimates of performances and physiological reserve that may in turn direct treatment [4]. The purpose of hemodynamic monitoring is to attain the optimal goals of cardiovascular therapy. Three functional-based questions should be addressed: (1) Will blood flow to the body increase (or decrease) if the neonates' intravascular volume is increased (or decreased), and if so, by how much? (2) Is the decrease in arterial blood pressure due to loss of vascular tone or merely due to inadequate blood flow? (3) Is the heart capable of maintaining an effective blood flow with an acceptable perfusion pressure without going into failure?

Physiologically, hemodynamic parameters can be divided into central or macro-hemodynamic parameters, which assess blood flow and pressure in the heart, vena cava, pulmonary artery, and the aorta, and the peripheral or micro-hemodynamic parameters, which assess the regional microvascular blood flow and tissue oxygenation (**Table 1**). The majority of existing hemodynamic monitoring assesses the central part of the cardio-circulatory system.

In the past, hemodynamic monitoring data were attained in neonates with CHD after heart surgery when the invasive and frequently inaccurate pulmonary artery catheters have been inserted [5]. Recently, efforts have been made to monitor the newborns as noninvasively

Hemodynamic parameter	Physiologic parameter	Clinical assessment	Noninvasive measurement	Invasive measurement
Central or macro	Preload—venous filling	Estimating jugular venous pressure, hand pressure on the liver, elevation of the legs	Inferior vena cava diameter and its collapsibility, lung ultrasonography	Central venous catheters*
	Cardiac output	Palpating peripheral pulses, heart rate*, capillary refill time, peripheral-core temperature difference	Echocardiography, cardiac magnetic resonance, electrical cardiometry*, arterial pulse waveform analysis*, electrocardiogram	Arterial catheters*
	Afterload—arterial blood pressure	Palpating peripheral pulses	Cuff oscillometry, Doppler ultrasound	Arterial catheters*
Peripheral or micro	Regional blood flow	Skin color, lactate	Perfusion index*, near-infrared spectroscopy*	
	Microcirculation		Laser-Doppler method, video microscopy, xenon clearance techniques	

*Continuous method, all others are intermittent.

Table 1. Physiologic hemodynamic parameters in neonates, assessed clinically, noninvasively, and invasively.

as possible and many new techniques have been applied in this vulnerable population to measure the central (arterial blood pressure and systemic blood flow) and peripheral hemodynamic parameters (peripheral vascular resistance). Arterial blood pressure is measured either noninvasively by sphygmomanometer or invasively through arterial catheters. Systemic blood flow is noninvasively assessed by echocardiography, cardiac magnetic resonance, electrical cardiometry, and arterial pulse waveform analysis. Invasive methods for measuring the systemic blood flow are applied through centrally inserted vascular catheters. It is not known whether laser-Doppler and spectroscopy in the near-infrared spectrum (near-infrared spectroscopy, NIRS) can reliably monitor peripheral vascular resistance (**Figure 1**) [6].

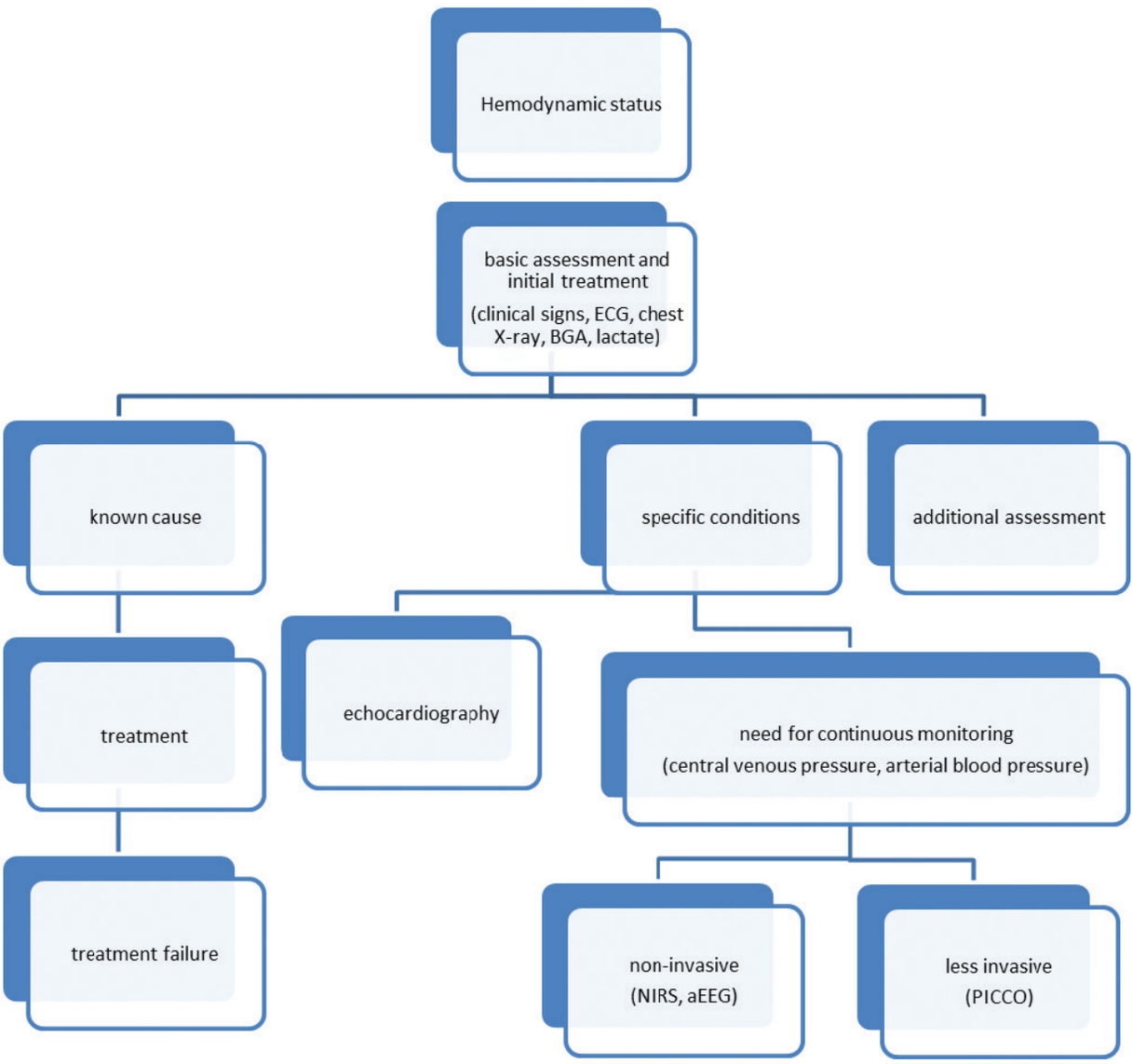

Figure 1. Assessment of hemodynamic status in neonatal intensive care unit. Adapted from Ref. [64]. aEEG, amplitude-integrated electroencephalogram; BGA, blood gas analysis; ECG, electrocardiogram; NIRS, near-infrared spectroscopy; PICCO, pulse-induced contour cardiac output.

4. The central hemodynamic monitoring

The central hemodynamic monitoring assesses the blood flow and the blood pressure in the heart and major vessels. The heart function and by that the stroke volume (SV) are determined by the preload—the venous filling, contractility of the heart muscle, and the afterload—which can be estimated only partially with the pressure in the aorta. The CO is the product of the SV and the heart rate (HR). Neonates increase their CO mainly by increasing the HR as they cannot sufficiently increase the SV. The HR is influenced by the body temperature, catecholamine secretion, and the autonomic nervous system.

4.1. The preload assessment

Clinically, the preload can be assessed visually assessing the jugular venous pressure, which is rarely possible in neonates with short neck. Using the hand pressure on the liver or elevation of the legs increases preload and is a simple method of assessing preload but less used in the NICU. The venous filling in neonates can be measured by inferior vena cava (IVC) diameter, and its collapsibility during respiration indicates volume responsiveness [7, 8]. IVC assessment is not an accurate marker of volume status and fluid responsiveness in cases of (1) increased right atrial pressure, (2) tricuspid or pulmonary valve regurgitation, (3) pulmonary hypertension, or (4) right ventricular dysfunction. Another method for assessing volume status of a neonate is lung ultrasonography (US) [9, 10]. Sonographic visualization of B-lines and measurement of extravascular lung water may aid diagnosing early volume overload in neonate. In a neonate with RDS after receiving surfactant, the B-lines are still visible [11].

4.2. Cardiac output

The measurement of CO is the most important parameter of the central hemodynamic monitoring, assessing the perfusion of organs. It is vital for the etiopathogenic diagnosis of low cardiac output syndrome, being due to either hypovolemia, myocardial dysfunction, vasodilatation, tamponade, pneumothorax, obstructive shock, pulmonary hypertension, or acute RDS. CO should be measured in the following clinical conditions: congenital and acquired heart diseases, shock, multiple organ failure, cardiopulmonary interactions during mechanical ventilation, clinical research, and assessment of new therapies [12]. The following three questions guide us in the interpretation of the adequacy of CO: (1) Is the delivery of oxygen adequate to meet the metabolic need of the patient? (2) Is oxygen delivery occurring with an adequate perfusion pressure? (3) Is the patient able to utilize the oxygen delivered, and if not, why so? [13]. Not only the measurement but also adequacy of CO and oxygen delivery is important, reflecting in clinical (capillary refill and core-peripheral temperature difference) and laboratory (lactic acid) parameters. But caveat is needed; normal values do not mean that regional perfusion is adequate, as well as abnormal values do not provide us with etiologic clue.

Clinically, CO with the systemic blood flow and perfusion can indirectly noninvasively be assessed by palpating the peripheral pulses and heart rate, capillary refill time, and measuring the peripheral-core temperature difference [14]. None of clinical methods for the evaluation

of CO is definitely reliable [15]. The HR in neonate is affected by many factors and so it is not necessarily a good indicator of hemodynamic status. In hypovolemic state, the immature heart muscle and the autonomic nervous system impact the cardiovascular response differently in neonates in comparison to adults. The capillary refill time is affected by the pressure technique, variability among investigators, ambient temperature, drugs, and maturity of neonatal skin. The capillary refill time of >3 s has 55% sensitivity and 81% specificity for the prediction of the low systemic blood flow [16].

Noninvasive methods that are used in clinical practice to assess neonatal CO are echocardiography, cardiac magnetic resonance, electrical cardiometry, and arterial pulse waveform analysis. Functional echocardiography (fECHO) enables visualization of the shape and size of the chambers of the heart, the heart valves, contractility, and relaxation of the heart muscle. Various forms of Doppler echocardiography, such as color, continuous and pulsed Doppler echocardiography, enable the determination of both the blood flow direction and velocity. By assessing the velocity of blood flow, two more parameters can be calculated: the difference in pressure above and below the narrowing with the modified Bernoulli's equation and the blood flow through the blood vessel diameter and a mean flow velocity of the blood [17].

fECHO is daily used in the neonatal intensive medicine and constitutes an important part of an integrated bedside hemodynamic monitoring of a neonate. An appropriate training and experience is necessary for performing fECHO; so the obtained measurements are accurate and reliable. It should be noted that fECHO is not a substitute for formal echocardiographic assessment of the neonate by a pediatric cardiologist, especially if the newborn is suspected to have CHD or the latter has already been diagnosed [18, 19]. fECHO enables discontinuous hemodynamic assessment of neonate in real time. With fECHO, we can estimate the central venous pressure, and thus the volume of blood, and the contractility and filling of the right and left cavities, pulmonary arterial pressure, and the SV of the both ventricles, thereby CO. With neonatal fECHO, we can assess the presence, direction, and measure the blood flow velocity through the shunts, such as persistent ductus arteriosus (PDA) and open foramen ovale, the pressure in the pulmonary artery and the superior vena cava (SVC) and thereby assess heart function. The drawback is the limited accuracy of the measurements (10% with a single investigator and 20% among various investigators). Acquired measurements also depend on the blood flow: from the transitional to neonatal, shunts through connections between the pulmonary and systemic blood flow and immaturity or lability of the lung vasculature, and thus the pressure in the pulmonary artery [20].

fECHO is helpful in the treatment of neonates with cardiovascular instability, PDA, persistent pulmonary hypertension, preterm premature rupture of membranes, perinatal asphyxia, sepsis, and general management in intensive care for a sick neonate. In the case of hemodynamically significant PDA, fECHO has significant limitations in measuring CO. Significant left-right shunting through PDA apparently increases SV of the left ventricle, which is a measure of pulmonary blood flow; outflow from the right ventricle is a measure of the systemic blood flow. Similarly, the measurement of flow from the right ventricle is affected by the presence of left-right atrial shunting which apparently increases SV and the outflow from the right ventricle. For this reason, the assessment of the systemic blood flow is made through the measurement

of the venous return to the heart through the SVC. The flow in the SVC is normally between 30 and 50% of the total systemic blood flow. Similarly, to assess the pulmonary blood flow, the blood flow velocity in the left pulmonary artery is measured [21].

Measuring the ejection fraction (EF) and fractional shortening (FS) in hemodynamic monitoring of the newborn is not very useful measurement, except in the case of severe myocardial dysfunction, when measurements are not really necessary, since the poor contractility of the heart muscle is obvious. We calculate them on the basis of measurement differences in dimensions of left ventricle in the long axis between diastole and systole. The problem of measurement in neonates is that the anterior wall of the ventricle is relatively stiff in comparison to the posterior and lateral wall of the left ventricle. To avoid this, they proposed measuring the dimensions of the left ventricle in short axis [22]. Two new US methods for assessing cardiac function are the measurement of diastolic function and tissue Doppler US. Diminished diastolic relaxation effects systolic function of the heart muscle, and thus the SV and CO. We may assess the diastolic function from the shape of Doppler wave of the inflow of blood into the ventricle. The filling of the ventricle has two phases: early ventricular filling during relaxation (E wave) and late active ventricular filling due to atrial systole (A wave). In a healthy neonate, 80% of the blood fills the left ventricle early in diastole, so the predominance of A wave indicates impaired diastolic function [23]. But when assessing impaired diastolic function, we have to be aware that diastolic function in premature and mature infants is already impaired because of immature contractile system of cardiac muscles [22]. The method of tissue Doppler echocardiography detects low frequency of high energy resulting from the movement of the ventricular wall which cannot be assessed by the standard Doppler investigation. In the four-chamber view of the heart in the longitudinal axis, we observe three different variables of ventricular wall motion: velocity, acceleration, and displacement [24]. Even if the method is advantageously used in adult patients, their clinical utility in the treatment of sick newborns is not yet fully understood [25].

Cardiovascular magnetic resonance (CMR) imaging is a method of nuclear magnetic resonance based on the spinning of hydrogen nuclei in a magnetic field, which are most numerous in the human body. CMR is the gold standard for the assessment of CO. Special expensive equipment, trained personnel, sedation, and transportation of a neonate are needed to perform CMR. In adults, CMR is used to assess the function of the ventricles, in complex congenital heart disease and cardiomyopathy. Compared with adults, it is necessary to increase the image resolution in neonates, both spatially (because of the size of the heart), as well as the time (due to the relatively high heart rate of newborn). The essential advantages of this method are detailed assessment of CO, cardiovascular anatomy, and good repeatability. CMR cannot measure the oxygen need and consumption [26]. Images obtained by CMR in real time have lower quality. Kino CMR enables improved anatomy imaging and the ventricular wall motion, by which the heart is imaged at specific phases of the cardiac cycle, depending on the electrocardiographic (ECG) recording. This creates a series of images that can be played as a movie (kino). End-diastolic and end-systolic endocardial and epicardial borders are followed and we reconstruct three-dimensional models of ventricles: end-systolic and end-diastolic volume, ejection fraction, and SV. CMR with a phase contrast allows the measurement of blood flow to the heart throughout the cardiac cycle [27]. This method quantifies the flow in IVC and descendent aorta,

which indicates the systemic perfusion in the premature neonate. Similarly, we can measure the flow in the internal carotid and basilar arteries and thus the blood flow in the brain [28].

Electrical impedance cardiometry is the only available method that enables continuous noninvasive monitoring of SV and CO in a neonate [29, 30]. The method is based on a model of the electrical velocimetry, using four-surface ECG electrodes attached to the left side of the neck (two electrodes), and to the chest (two electrodes). Alternating electric current (AC) of constant amplitude flows through the pair of external electrodes toward the direction of the aorta. The ratio of the current and measured voltage is equal to the conductivity (or bioimpedance). Each tissue in the chest has its bioimpedance: that of the blood is very low, whole bone and lungs, filled with air, have high bioimpedance. Moreover, bioimpedance of bone is static, and bioimpedance of the lungs, which are filled and emptied of air, and of the heart and large blood vessels, which are filled with blood, is dynamic, in accordance with the respiratory or cardiac cycle. In case of sudden acceleration of blood flow into the aorta in systole, the conductivity dramatically increases. Electrical bioimpedance of the chest is strongly increased with every heartbeat. The neonate's movement causes artifacts in measuring the electrical impedance [31, 32].

Arterial pulse waveform analysis is a relatively good method for monitoring the dynamics of arterial blood pressure and assessment of CO. It is based on the analysis of the curve of arterial pulse waveform derived from arterial catheter and on the fact that the pulse pressure is proportional to SV [33]. The arterial pulse waveform changes in the case of arrhythmia, shock, or hypothermia, when it comes to peripheral vasoconstriction. Typically, the devices for calculating the SV and CO are based on the analysis of arterial pulse waveform, and require periodic, and in advance calibrations. An additional limitation of the method is that it assumes a constant rate of systemic vascular resistance [34]. So far, the methods of arterial pulse wave analysis have not been studied in neonates.

Invasive methods for assessing the CO have been developed in adults, and then applied in sick neonates, where their use is limited. Limitations of these methods are the invasiveness, complexity, and relatively long process (need for central vascular approach and taking sequential blood samples for laboratory analysis), for which reason they are seldom used in practice. Invasive methods for estimating average CO over time are based on a few physical principles. Fick's law is the law of mass/mass flow conservation. The amount of oxygen in the pulmonary artery and the amount of oxygen in the capillaries, flowing from the alveoli, is equal to the concentration of oxygen in the pulmonary vein [35].

Clinically, the O_2 consumption can be measured by measuring the concentration of oxygen in the inhaled and exhaled air and pulmonary ventilation. Consumption is estimated as the difference between the amount of oxygen in the inhaled and exhaled air. The concentration of oxygen in the peripheral arteries is the same as in the pulmonary veins. Pulmonary arteries have mixed venous blood. Samples for the analysis of O_2 are obtained from the pulmonary artery or the right ventricle through the cardiac catheter. Thus, we can calculate the CO (CO = O_2 consumption/AVΔO_2). Neonates compensate the reduced release of oxygen from fetal hemoglobin in tissues with higher hemoglobin concentrations, a larger volume of blood per unit of body weight, and increased CO. Instead of measuring O_2 consumption, we can measure the formation of CO_2 using capnography and assume that it is equal to the exchange of CO_2 in

the lungs [36]. In neonates with a healthy alveolar-capillary membrane, the partial pressure of CO_2 in arterial blood is equal to the partial concentration of CO_2 in the exhaled air [37].

Stewart principle is a method of dilution of the indicator and provides calculation of the CO on the basis of change in the concentration of the dye (lithium-based dilution devices) or a change in the temperature of the solution (thermodilution-based devices). We inject a known amount/temperature of a substance proximally and measure its concentration/temperature distally. We calculate the total flow rate ($Q = m/\int cdt$) from the time profile (integral) curve and a known quantity of the injected substance [38]. Clinically, a known amount of dye or isotope is injected rapidly into a large central vein, or the right side of the heart. We measure the concentration of dye or isotope in arterial blood: the larger the CO the greater the dilution. The most common indicator is a small volume of cold saline; we calculate flow from the temperature change. The average blood flow through an organ can also be calculated from the change in the volume of the hollow body in time: dV/dt (volume of a cavity is imaged within a specified time sequence: by ultrasound, magnetic resonance, X-ray).

4.3. Arterial blood pressure

Arterial blood pressure in the newborn can be measured noninvasively using appropriate cuffs or through the invasive arterial catheters. In principle, the matching of both methods is good [39]. We currently do not know what the normal arterial blood pressure is for a given gestational and postnatal age. Also, we do not know what the value of blood pressure is when the blood flow to vital organs is diminished and the auto-regulatory mechanisms in the brain fail. Thus, neonatal hypotension is not precisely defined. In addition, there is currently no evidence that the treatment of hypotension has significant impact on the clinical outcome in neonates [40–42].

Global perfusion pressure is measured via invasive arterial blood pressure monitoring. However, "adequate" blood pressure does not signify an "adequate" CO; therefore, an increase in blood pressure does not necessary mean an increment of CO. However, without measuring CO we can only assume that adequate mean blood pressure means also adequate CO, which is not always true. Second, the increase in blood pressure does not always mean the elevation of CO (failing myocardium poorly responds to a high vascular resistance). In neonates, the threshold heart rates and perfusion pressure are different depending on gestational and post-menstrual age of premature neonates [42, 43].

5. The peripheral hemodynamic monitoring

Hemodynamic failure results in low cardiac output syndrome with inadequacy of oxygen and nutrients delivered to peripheral tissues and cells. Clinically, peripheral perfusion of organs can be assessed by observing the skin color of a neonate. The method is vastly subjective. A laboratory method of defining the peripheral perfusion is the measurement of the concentration of lactic acid in the peripheral blood. In case of lowered peripheral perfusion tissue hypoxia occurs, which leads to anaerobic metabolism and lactic acid formation. Lactic acid is present in the less perfused tissues and therefore it is primarily not present centrally

in systemic circulation; therefore, lactic acidosis (>2.5 mmol/L) is a late sign of low cardiac output syndrome. Consequently, the concentration of lactic acid in the systemic blood rises after the reanimation. Moreover, the production of lactic acid is increased in the case of adrenaline treatment, which increases glycogenolysis and glycolysis in the liver [44]. The plasma concentration of the lactic acid is associated with the stage of the disease and a higher mortality in neonates [45].

Noninvasively, the peripheral perfusion may be assessed by the perfusion index [46]. It is based on an analysis of the pulse oximetry signal. The perfusion index is the ratio between pulsatile and non-pulsatile pulse oximetry signal (AC/DC × 100). It reflects the difference between the amount of blood in the tissue between systole and diastole. The perfusion index correlates well with the capillary refill time, the surface-core body temperature difference [47], and also the severity of the disease in neonates [48].

Assessing the function of peripheral organs is another way of assessing the peripheral hemodynamics. Using amplitude-integrated electroencephalogram (aEEG), we assess the brain function. Observing respiratory rate and pattern indicates the lung function and myocardial contractility indicates the heart function. By measuring the urine output and cleared substances, we assess the renal function. Measurement of diuresis in the neonate for hemodynamic monitoring has many caveats, especially in premature neonates, since immature renal tubules are not able to concentrate the urine. Moreover, the accurate monitoring of diuresis is an invasive method. Laboratory measurements of liver enzymes, clotting factors, and ammonia concentration assess liver function, and measurements of muscle enzyme assess the muscle function [49].

The peripheral monitors enable measuring the micro-vascular blood flow to the peripheral organs by perfusion index and laser-Doppler method and regional tissue oxygenation by NIRS.

5.1. The regional blood flow monitoring in the peripheral organs in the neonate

Regional blood flow is a complex and dynamic variable that changes depending on the functional activity of the body. In pathological conditions, like, for example, a sudden change in blood pressure or hypoxia, blood flow through the body can change very quickly. Like CO also the regional blood flow is measured in mL/min and expressed either normalized by body weight either by 100 g of tissue, or as a percentage of the CO. Assessing and measuring the blood flow is not a part of the permanent clinical practice in neonatal intensive care units, because the methods are generally complicated, inaccurate, invasive, and expensive, and currently their use is not showing clinical welfare for sick newborns.

With the help of the abovementioned physical principles and listed methods for CO monitoring, it is also possible to estimate the regional blood flow in peripheral organs. Using Fick's law, we can calculate blood flow through the peripheral organ, knowing its oxygen consumption. By applying this principle, several methods for the evaluation of blood flow in the brain—through the inhalation of 15% nitrous oxide [50] and the clearance of a radioactive

isotope of xenon [51]—have been developed. Regional blood flow to peripheral organs can be measured using Doppler ultrasound [52]. The method is based on measuring the blood flow velocity through the blood vessel. The product of the flow rate and maximum vessel diameter allows us to evaluate blood flow in the vessel, and if the vessel supplies the oxygen and nutrients to the organ we can estimate the blood flow to the organ. Blood flow to the brain can also be measured using magnetic resonance imaging (MRI) techniques. Blood flow to the brain is supplied by four arteries in the neck; hence, it can be evaluated using a scan through the arteries: the cross section of the vessels is multiplied by the blood flow velocity. The blood flow velocity is measured by the loss of magnetization caused by the fresh blood flowing into the plane of imaging (imaging with phase contrast) [28]. For quantitative measurement of the flow, a contrast agent containing gadolinium can be used [53]. The blood flow in each blood vessel can be measured with an electromagnetic flowmeter: the moving particles-ions are deflected to right angles to the direction of movement in an electric field and by that deflection the electric current is measured. Blood flow can also be measured by thermodilution method: the faster the blood flow, the cooler the tip of the heated sensor. Using the plethysmography, the displaced blood volume from the vessels is measured [38].

Frequently used noninvasive and continuous method for the indirect assessment of blood flow in various organs is the spectroscopy in the near-infrared spectrum [54–56]. The method is based on the principle of different absorption patterns of oxyhemoglobin and deoxyhemoglobin. It measures the index of tissue oxygenation and enables the calculation of the extraction of oxygen of the tissues in the target organ. If we assume that changes in the regional tissue oxygenation are not accompanied by changes in the arterial blood oxygen saturation (SaO_2), oxygen consumption, the amount of blood in the arteries and veins, and hemoglobin concentration, then the measured tissue oxygenation can be used to assess organ perfusion. NIRS optodes can be placed practically anywhere on the surface of the body, they measure tissue oxygenation approximately 4 cm below the surface (in the brain, kidneys, intestines, liver, and muscle) [57].

5.2. Microcirculation monitoring in the neonate

Microcirculation encompasses arterioles, capillaries, arteriolar-venous connections, venules, and lymphatic vessels. It supplies the target organs with oxygen and nutrients. Capillary filling or opening depends on the tone of arterioles and precapillary sphincters, whose diameter changes in parallel to the contractions/relaxations of smooth muscle in the vessel wall. The humoral factors, endothelial vasodilators (NO, CO, and H_2S), vasoconstrictors (epinephrine, norepinephrine, and endothelin-1), myogenic mechanism, local metabolites, and the parasympathetic nervous system affect the tone of smooth muscles. Blood flow in the microcirculation reflects the function of the central elements of the blood flow and is thus the ultimate indicator of cardiovascular efficiency. Microcirculation in individual organs also operates globally and represents one of the largest virtual organs in the body. In adults, it is estimated that 5% of the total blood volume is located in the capillaries, which may increase its capacity to fourfold [58].

Microcirculation in the newborn can be assessed using a variety of methods, the most commonly used is the evaluation of flow by laser-Doppler method, video microscopy (dynamic capillaroscopy), and xenon clearance techniques [59]. Flow measurement by laser-Doppler method is based on the fact that the frequency of the light beam, which passes through the tissue, changes as a result of reflection from the moving parts—red blood cells (the Doppler effect). The flow is proportional to the concentration and speed of moving red blood cells in the microcirculation. Since the flow in microcirculation is highly variable, we usually assess microcirculatory response to some of the challenge tests and monitor the dynamics of change. The most commonly used provocation methods are the postocclusive reactive hyperemia (hyperemia after a transitional cuffing of the proximal artery), thermal methods (local heating or cooling), and iontophoresis of vasoactive substances [60, 61]. In the first days after birth, the blood flow is very fragile and the peripheral blood flow in the microcirculation is unstable. The myogenic and nervous controls of skin blood flow enable thermoregulation. The blood flow to the skin in the first days after birth is reduced. The blood flow is related to gestational and postnatal age and the incidence of morbidity and cardiovascular function [62]. The deterioration of peripheral blood flow regulation in microcirculation causes vasodilation and decreased peripheral vascular resistance and contributes to the vulnerability of blood flow. The peripheral blood flow in the first days after birth differs in boys and girls; boys have stronger vasodilation; the mechanism is possibly associated with an increased incidence of hypotension in newborn males [63].

6. Limitations

The described methods for hemodynamic monitoring of neonates have many limitations. The clinical ones are vastly subjective and do not correlate well with the laboratory methods. The continuous bedside noninvasive methods are less accurate and sometimes demand complex deducement to what is happening. There are no trials on resuscitation using the noninvasive methods. The more sophisticated noninvasive methods require expensive equipment and are time consuming, measuring the parameters in the moment of measurement and not continuously.

7. Conclusion

Hemodynamic monitoring, which was for a long time not available in neonates and prematures, is becoming an indispensable tool for understanding how cardiovascular system adapts to extrauterine life. This is especially important when treating the smallest premature with peculiar and very vulnerable hemodynamics. This article adds some of the latest information on hemodynamic monitoring in neonates with specific emphasis on the methods which are available, cost-effective, noninvasive, and easy to manage and understand.

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