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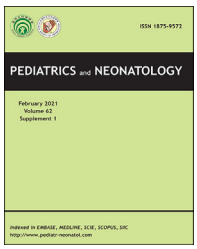

Mini Review Article

Recognition and management of neonatal hemodynamic compromise

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Hemodynamic compromise of the neonate can occur in various clinical situations, including but not limited to maladaptation during the early transitional period, sepsis, congenital heart anomalies, hemodynamically significant patent ductus arteriosus, persistent pulmonary hypertension of the newborn, systemic inflammatory diseases such as necrotizing enterocolitis, and dehydration. Despite the handful of advances in neonatal care through ground-breaking clinical trials, the management of neonatal shock is often dependent on the bedside clinician's experience and training without the aid of high-level evidence. However, the recognition for the importance of comprehensive and serial hemodynamic assessment is growing. There is now a wealth of literature investigating the use of functional echocardiography, near-infrared spectroscopy, and noninvasive impedance-based cardiometry to complement common bedside hemodynamic measures such as blood pressure and heart rate measurement. In this review article, the pathophysiology of neonatal hemodynamic compromise is outlined, and concomitant best-evidence management for hemodynamic compromise in the neonate is proposed.

1. Introduction

An intact circulatory system is crucial for adequate delivery of oxygen and nutrients to meet regional metabolic needs and remove carbon dioxide and metabolic waste from the tissue. Prolonged hypoperfusion or ischemia of the tissue can result in mitochondrial dysfunction, energy failure, and eventual cell death and organ failure. In preterm infants, hypotension is associated with complications such as

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intraventricular hemorrhage, white matter injury, cerebellar injury, and abnormal neurodevelopmental outcome.[1] Hypotension can lead to cerebral hypoperfusion. Although treating hypotension can improve cerebral blood flow (CBF), given the fact that critically ill and hypotensive preterm infants commonly have impaired CBF autoregulation, inappropriate choice or titration of vasopressor/inotrope can accentuate reperfusion injury. In addition, the underlying pathology leading to hypotension can have a direct negative impact on the brain. As hypotension is commonly treated and no data from randomized controlled trial (RCT) with a nontreatment arm are available, the extent of the individual contribution of hypotension, inappropriate treatment, and underlying etiology of hypotension to the observed brain injury is unknown. Given the paucity of RCTs or conclusive systematic review on the management of neonatal hypotension, strategies to reestablish adequacy of circulatory function by identifying the underlying pathophysiology and appropriately supporting the cardiovascular function seem prudent. Therefore, this review article will examine the determinants of a healthy circulatory system, discuss the pathophysiologic basis of neonatal hemodynamic compromise, and propose a pathophysiology-based management approach.

2. Definition and incidence of neonatal hypotension

Although there is a lack of consensus for "normal" blood pressure ranges in preterm infants, it is recognized that blood pressure increases with gestational age, birth weight, and postnatal age.[2] Hypotension is classically defined as abnormally low blood pressure, below a particular percentile mark for a given gestational age or birth weight. A more functional and theoretical definition for hypotension is based on the cerebral autoregulation curve. At the lower end of the curve or below the autoregulation plateau, CBF diminishes with lower blood pressure, also known as pressure passive CBF. Limited data suggest that a mean blood pressure of 28—30 mmHg is the critical lower limit at which pressure passive CBF occurs in preterm infants during the transitional period.[3] Unfortunately, little is known about the blood threshold below which organ function is impaired or tissue injury occurs. In particular, thresholds likely vary for different patients and even for the same patient under different clinical settings. Many neonatologists define lower limit of normal mean blood pressure in mmHg as equivalent to the infant's gestational age in weeks.[4] The definition of mean blood pressure limit based on gestational age likely prevails among the neonatologists secondary to its practicality and convenience. Interestingly, a recent population study (EPIPAGE 2) found that those who were treated for low blood pressure, defined as a mean blood pressure less than gestational age in weeks, had better short-term outcomes such as lower incidence of necrotizing enterocolitis and severe intracerebral abnormality, compared to a propensity-matched cohort that was not treated.[5]

Devoid of a clear definition of neonatal hypotension, its true incidence is unclear. Perhaps we could appreciate the incidence of this clinical entity by examining the frequency of vasopressor-inotrope use in the neonatal intensive care unit. Based on data from 6 units in a regional observational study, the incidence of vasopressor-inotrope use within the first 24 h ranged from 4% to 39% in very low birth weight infants.[6] In 34 hospitals analyzing a resource utilization national database, the incidence of using dopamine or dobutamine in preterm or low birth weight infants was 4.4%—38%.[7] In a prospective observational study within a research network, 55% of infants born at 23 to 26 6/7 weeks gestational age received anti-hypotensive therapy.[8] The results of these studies indicate that the treatment threshold varies greatly among units and practitioners.

3. Fluid dynamics and blood pressure

Through Ohm's law of electricity and fluid dynamics, we can better understand the relationship between blood pressure and blood flow:

$$\Delta P\ (\text{Pressure}) = Q(\text{flow}) \times R(\text{resistance}).$$

When applied to cardiovascular physiology:

$$\begin{aligned}\text{Mean blood pressure} \\ -\text{Right atrial pressure} &= \text{Cardiac output}(CO) \\ &\times \text{Systemic vascular resistance}(SVR).\end{aligned}$$

Based on the above equation, we can better appreciate that blood pressure is a dependent hemodynamic variable. Two major determinants of blood pressure, CO and SVR, are not routinely nor continuously measured in the neonatal intensive care setting. This shortcoming in conventional hemodynamic assessment is the reason that circulatory compromise or shock may exist (and be subclinical or compensated) despite having "normal" blood pressure. One variable may offset the deficit in the other and result in normal blood pressure. Indeed, the correlation between CO and blood pressure is poor ($r = 0.38$), especially in preterm infants during the transitional period.[9] As mentioned earlier, the lower limit of "normal" blood pressure may vary between individuals and even within the same individual experiencing different pathological states. Despite these limitations, monitoring blood pressure does provide us with valuable information on the hemodynamic status of the patient. At extreme value, low mean blood pressure can be used as a marker of circulatory function inadequacy. Low systolic and diastolic blood pressure is suggestive of low CO and SVR, respectively.

4. Cardiac output

CO, described as the blood volume ejected out of the left ventricle within a time frame (milliliters per minute), is an important hemodynamic parameter that is not routinely measured or monitored in the neonatal intensive care setting. For practical purposes, normal CO is estimated to be approximately 150—300 mL/kg/min. Noninvasive bedside CO measurement or trend is possible with echocardiography and impedance cardiometry.[10] CO is the product of stroke volume (SV) and heart rate. Understanding the determinants of SV (preload, contractility, and

afterload) is important in elucidating the etiology of low CO state and administering appropriate treatment (Fig. 1).[11] However, it is essential to note that "normal" CO values do not necessarily translate to adequate systemic blood flow. These are two different entities, especially in the neonatal population, due to physiological shunts. For example, in infants with aorto-pulmonary shunts, such as patent ductus arteriosus, or aortic regurgitation, the CO will overestimate systemic blood flow as ejected blood is returned to pulmonary circulation or the left ventricle, respectively. We will now focus on the determinants of CO and SVR and their respective disturbances that can lead to hemodynamic compromise (Fig. 2) as well as pathophysiology-based management. Echocardiographic parameters that can help the clinician pinpoint the perturbed determinant(s) of CO or SVR are beyond the scope of this review.

5. Preload

Preload is best described as the extent of cardiac muscle fiber stretch before myocardial contraction occurs. Based on the description of the length—tension relationship by the Frank—Starling Law, optimal stretching of muscle fibers increases actin-myosin cross bridges and improves SV. The ventricular myocardial fiber is stretched by volume and distending pressure before the contraction. Factors affecting preload include, but are not limited to blood volume, venous return, intrathoracic pressure, and the heart's systolic and diastolic functions. In preterm neonates during the early transitional period, immediate cord clamping may reduce venous return, decrease ventricular preload, and decrease CO.[12] Extracardiac effects from increased intrathoracic pressure secondary to high mean airway pressure on mechanical ventilation or tension pneumothorax, and pericardial tamponade can also impede venous return. However, absolute hypovolemia from acute hemorrhage and increased gastrointestinal or renal losses are less common causes of decreased preload in the neonate. Lastly, cardiac myopathies with a small ventricular cavity, such as infants of diabetic mothers with hypertrophic cardiomyopathy, can have diastolic dysfunction and reduced heart filling.

5.1. Management of Low preload

In the setting where inadequate preload or ventricular stretch is suspected clinically or suggested on echocardiography with a small ventricular cavity or decreased left ventricular internal diameter at end-diastole, factors that impede venous return as described above needs to be managed accordingly. Echocardiographic markers for hypovolemia in newborns are not well validated. Fluid boluses should be administered judiciously. Generally, a 10—20 mL/kg fluid bolus is well tolerated. However, when there is evidence of poor myocardial contractility and ventricular dilatation, a rapid fluid bolus can worsen myocardial function and clinical status. The choice of volume replacement is important. Table 1 compares electrolyte content, pH, and osmolarity of various fluid replacement options. Whenever clinically indicated, fresh frozen plasma (for coagulopathy), packed red blood cell (for anemia), or 5% albumin (for significant hypoalbuminemia) can address specific deficiency and provide volume replacement at the same time. Otherwise, although not adequately studied in neonates, crystalloids are preferable to colloids.[13,14] Normal saline (0.9% NaCl) is the most commonly used crystalloid.[15] The high chloride content of normal saline (Table 1) can lead to hyperchloremic acidosis, and therefore, the acid-base status should be closely monitored when fluid bolus exceeds 20—30 mL/kg. Lactated Ringer has lower chloride content but is not adequately studied in the neonatal population. The similarity between Plasma-Lyte A and plasma in terms of electrolyte content, pH, and osmolarity makes this solution appealing; however, there is no published study on plasma-

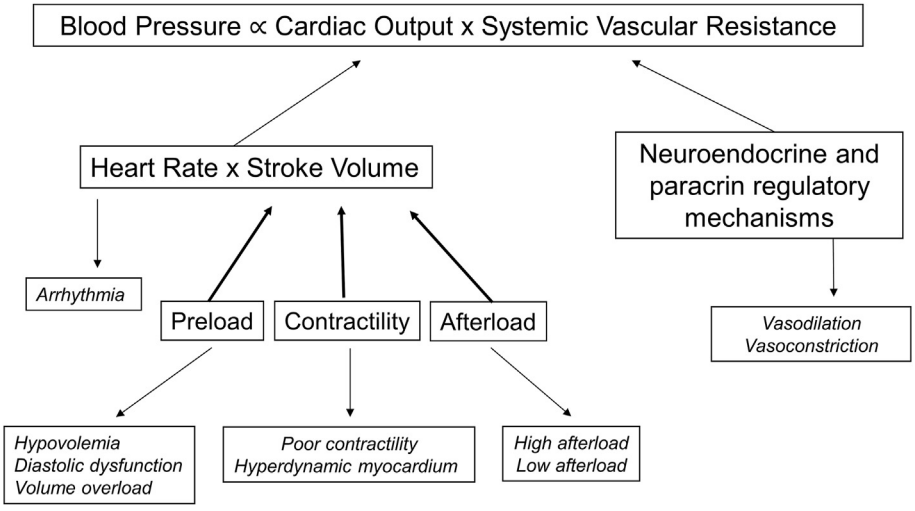

Figure 1 Pathophysiology of circulatory compromise. By understanding the underlying pathophysiology, we can individualize the treatment approach. We need to determine whether the circulatory compromise is due to dysregulation of vascular tone or inadequate cardiac output. If the cardiac output is compromised, whether it is due to rhythm, preload, contractility, or afterload issues.

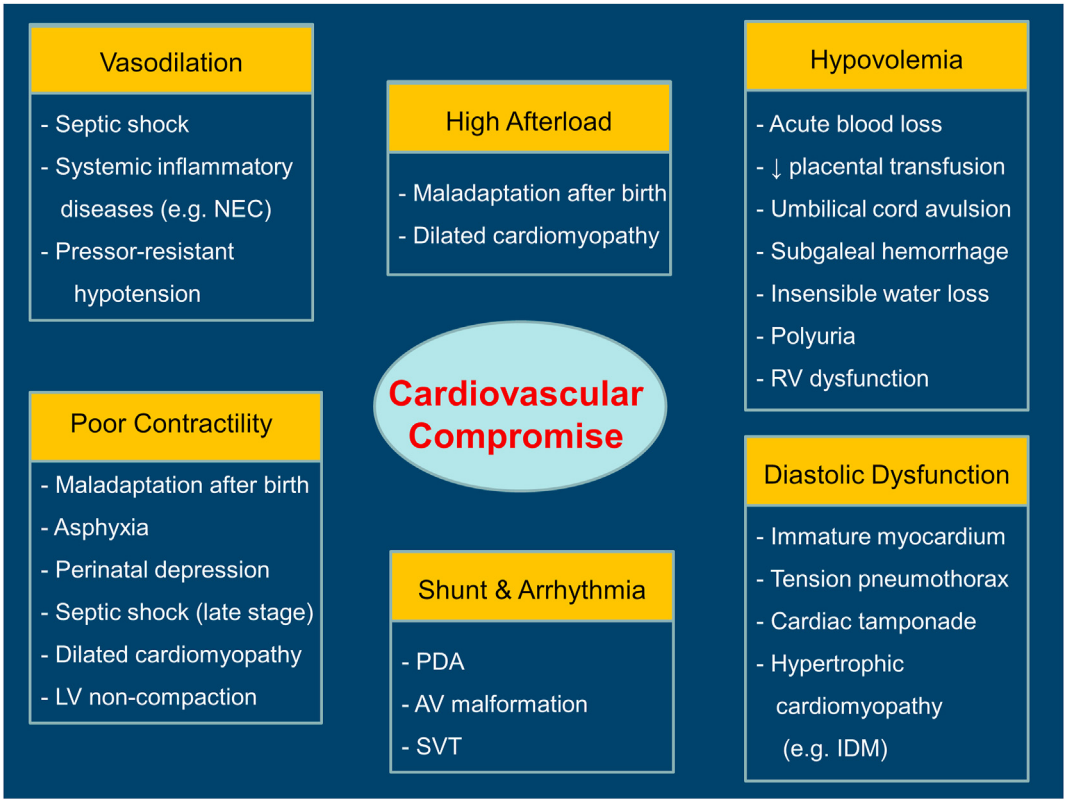

Figure 2 Causes of cardiovascular compromise in neonates. Review of history, physical exam, and diagnostic tests can identify the primary underlying pathophysiology and categorize the cause of cardiovascular compromise in an individual patient, which could aid in selecting an appropriate management strategy. AV, arteriovenous; IDM, infant of diabetic mother; LV, left ventricle; NEC, necrotizing enterocolitis; PDA, patent ductus arteriosus; RV, right ventricle; SVT, supraventricular tachycardia.

Table 1 Electrolyte content, pH, and osmolarity of various fluid replacement options.

Fluid Type	Na	K	Cl	Mg	Ca	Acetate	Gluconate	Lactate	pH	Osmolarity
	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L		mOsmol/L
Plasma-Lyte A	140	5	98	1.5		27	23		7.4	294
0.9% NaCl	154		154						5.5	308
Lactaed Ringer's	130	4	110		1.5			28	6.2	275
5% albumin*	145±15	<2							6.4-7.4	

Plasma-Lyte A (Baxter), 0.9% NaCl (Baxter), Lactated Ringer's (B. Braun Medical Inc.), 5% albumin (Flexbumin 5%, Takeda Pharmaceutical Company)
*No data avaiable on osmolarity or electrolyte content other than Sodium and potassium

like isotonic solution as a fluid bolus in the neonate. A recent RCT of Plasma-Lyte A *versus* moderately hypotonic solution as a maintenance/replacement fluid in acutely ill children (6 months—12 years old) found a 6.7-fold greater risk of developing electrolyte disorder in the Plasma-Lyte A group.[16] In adults, Lactated Ringer's solution is associated with a better outcome in septic shock. A recent secondary analysis of a cluster-randomized trial of balanced crystalloids (either Lactated Ringer or Plasma-Lyte A) *versus* normal saline found a lower 30-day in-hospital mortality in the balanced crystalloid group in critically ill adults with sepsis.[17] Other than administering crystalloids and colloids, vasopressors can increase the preload by increasing the tone of the venous capacitance vessels. Similarly, medications or physiologic changes that reduce pulmonary vascular resistance in patients with severe pulmonary hypertension improve left ventricular preload.

6. Contractility

Contractility or cardiac inotropy is an isometric measure of intrinsic contractile strength in the form of myocardial fiber shortening. However, physiologically, both preload and afterload affect contractility, and cardiac function is often evaluated in its entirety in the clinical setting using conventional echocardiography. Cardiovascular developmental immaturity such as higher water content in the

Table 2 Estimated relative cardiovascular receptor stimulatory effects of inotropes, lusitropes, and vasopressors. Amrinone and milrinone are the PDE-III inhibitors used in neonates. Sildenafil is the PDE-V inhibitor used in neonates. V1a, vasopressin receptor expressed in the vasculature. α1/α2/β1/β2, subtypes of alpha- and beta-adrenoreceptors; DA, dopamine; DOB, dobutamine; PDE, phosphodiesterase enzyme.

	Adrenergic, Dopaminergic and Vasopressin Receptors					
	α1/α2	β2	α1	β1/β2	DA1/DA2	V1a
	Vascular	Vascular	Cardiac	Cardiac	Vascular/Cardiac	Vascular
Phenylephrine	++++	0	+	0	0	0
Norepinephrine	++++	+/0	++	++++	0	0
Epinephrine	++++	++	++	++++	0	0
Dopamine	++++	++	++	+++	++++	0
Dobutamine	+/0	++	++	++++	0	0
Isoprenaline	0	+++	+++	++++	0	0
Vasopressin	0	0	0	0	0	++++
PDE-III Inhibitors	0	0	0	0	0	0
PDE-V Inhibitors	0	0	0	0	0	0

myocardium, decreased calcium reserve in myocardium due to lack of sarcoplasmic reticulum, lesser contractile elements, and relative adrenal insufficiency predispose preterm and term infants to myocardial dysfunction. Infants with perinatal asphyxia are also a high-risk group who may have myocardial injury and transient cardiac dysfunction requiring inotropic support.[18] In a retrospective cohort study, 62% of infants with hypoxic-ischemic encephalopathy required inotropic support for more than 24 h for hypotension.[19] Accordingly, it is recommended to obtain an echocardiography study for infants born with low APGAR score and/or perinatal depression.[20]

6.1. Management of poor contractility

Several pharmacological agents have inotropic properties (Table 2), and among the most commonly used in neonates are dopamine, dobutamine, and epinephrine.[21] In a meta-analysis comparing the effects of dopamine *versus* dobutamine in preterm infants, dopamine was more effective in improving systemic hypotension, whereas dobutamine improved CO and SVC flow,[22] with no differences in outcomes such as intraventricular hemorrhage, periventricular leukomalacia, or death. The differing effects on blood pressure and systemic blood flow are likely secondary to the vasopressor property of dopamine (increasing vascular tone via alpha-adrenergic receptor) as opposed to the possible vasodilator property of dobutamine (acting on both alpha-adrenergic and beta-adrenergic receptors) and the difference in inotropic potency (dobutamine > dopamine); Table 3[23]. Therefore, in the presence of systolic myocardial dysfunction without vasodilation, dobutamine may be preferable.[24] However, when systolic myocardial dysfunction and peripheral vasodilation are present concomitantly, for example, in a subset of patients with septic shock, a medication with both inotropic and vasopressor effects such as dopamine or epinephrine is more appropriate (see the Management of Low SVR section).

7. Afterload

Afterload is the force that the myocardial fibers overcome prior to the ejection of blood out of the ventricles during systole. This "load" is quantified as left ventricular wall stress and follows the Law of Laplace ($P \propto \text{Thickness} \times \text{Tension}/\text{Radius}$), which describes the relationship of pressure, radius, and tension within a sphere. Applying this law and rearranging the equation to derive wall stress result in as follows:

$$\text{Wall Stress} \propto \text{Pressure} \times \text{Radius}/\text{wall thickness}$$

Hence, afterload is increased with higher ventricular pressure, greater radius, and a thinner ventricular wall. For

Table 3 Mechanisms of action of dobutamine enantiomers and metabolites. Adrenergic receptor stimulatory and inhibitory effects of the left (−) and right (+) rotating enantiomers of dobutamine and its major metabolite [(1)-3-O-methyl-dobutamine] are shown. The form of dobutamine used in clinical practice is depicted as (±) dobutamine. The relative effect is indicated by the number of symbols. α1/α2/β1/β2, subtypes of alpha- and beta-adrenoreceptors; ↑, ↓, 0, increase, decrease, or no effect on myocardial function or vascular tone.

Enantiomers, Metabolites	Pharmacologic Activity		Heart		Vasculature
	Agonist	Antagonist	Force	Rate	Tone
(−) Dobutamine	α1		↑		↑
(+) Dobutamine	β1/β2		↑	↑	↓
(+)-3-O-methy-Dobutamine		α1	↓		↓
(±) Dobutamine	α1/β1/β2		↑↑	↑	0/↓

example, in dilated cardiomyopathy, the ventricles are dilated with thin walls (↑radius; ↓wall thickness) and, therefore, subjected to high afterload/wall stress.

Similarly, high afterload could have a clinical significance in newborns delivered after severe chronic anemia and evidence of hydrops fetalis. The dilated ventricles secondary to congestive heart failure in these patients make them especially sensitive to volume administration. As such, the correction of anemia would be better tolerated using an isovolumetric exchange transfusion where simultaneous blood withdrawal and packed red blood cell transfusion occurs. Another clinical scenario where high afterload may lead to circulatory compromise is myocardial maladaptation during the early postnatal transitional period. Although not a consistent finding,[25] in a subset of extremely preterm infants, the myocardium may not be able to adapt to the increase in afterload after removal of low resistance placental circulation, and as a result, low systemic flow may ensue.[26] Finally, high right ventricular afterload, for example, in cases with increased pulmonary vascular resistance, can lead to systemic hypoperfusion via ventricular interdependence, as discussed earlier. It is important to note that SVR is not synonymous with afterload. From the equation above, SVR is one of the determinants of blood pressure and contributes to LV cavity pressure. Other determinants, such as radius and wall thickness, are equally important. SVR is explained in more detail below.

7.1. Management of high afterload

Management of circulatory failure due to high afterload depends on the underlying cause of the high afterload. Management discussion of dilated cardiomyopathy (such as diuretics and angiotensin-converting enzyme inhibitors) and increased pulmonary vascular resistance (such as inhaled nitric oxide and sildenafil) is beyond the scope of this review. Here we will focus on the management of postnatal myocardial maladaptation to increased afterload. Two approaches have been tested: the first one focused on improving lusitropy and reducing afterload and the second on improving contractility. Lusitropes are medications that increase the rate of myocardial relaxation. Milrinone has a lusitropic property and, at least in more mature infants, also increases myocardial contractility. In addition, milrinone can cause vasodilation. This unique pharmacodynamic profile makes milrinone a good candidate for managing postnatal myocardial maladaptation. However, an RCT evaluating milrinone *versus* placebo effects in preventing low SVC flow in the extremely preterm infants found no beneficial effects.[27] Similarly, neither dopamine nor dobutamine was effective in increasing SVC flow in preterm infants with low SVC flow in an RCT, although dobutamine produced a greater increase in systemic blood flow.[28] In a more recent RCT of dobutamine *versus* placebo, there was no difference in achieving normal SVC flow (>41 mL/kg/min).[29] Although the investigators meticulously selected patients with low SVC flow and titrated dobutamine to the desired effect, there were some limitations to the study. The authors assumed that contractility caused low SVC flow, hence, the choice of dobutamine for treatment. Unfortunately, myocardial contractility, volume status, and SVR were not evaluated, and therefore, the lack of response to dobutamine may be due to heterogeneous causes of low SVC flow in the population under study.

8. Systemic vascular resistance

The vascular system in general and arterioles, in particular, generate resistance to flow. Through hormonal, neuronal, and local factors, the vascular tone of arterioles is modulated to regulate blood flow to various tissue beds. These changes in arteriolar vascular tone determine SVR. SVR cannot be measured, but with the knowledge of CO and blood pressure, it can be calculated by rearranging the Ohm's Law: SVR = (mean arterial blood pressure—right atrial pressure)/CO. In addition, the assessment of peripheral microcirculation with a more comprehensive hemodynamic monitoring technology such as near-infrared or visible light spectroscopy and laser tissue Doppler can shed light on the SVR status. SVR is a measure of resistance in the entire circulatory system, which is a culmination of varying degrees of vascular tone within different organs. When systemic blood flow is low, selective vasoconstriction in the non-vital organs allows for preferential blood flow to vital organs such as the brain, adrenal glands, and heart. The overall increase in SVR may be adequate in maintaining organ perfusion pressure despite a compromised CO. The compensated shock can be overlooked clinically as blood pressure remains in the perceived normal range. Low SVR secondary to peripheral vasodilation is a leading cause of hypotension and circulatory compromise in newborns. Septic shock most commonly presents as a vasodilatory shock in the neonatal period, although cold shock can also occur.[30,31] The prevalence of myocardial dysfunction in neonatal septic shock is unknown. In older children, about 50% of patients with sepsis and 75% of patients with fluid and pressor-resistant septic shock have some degree of systolic and/or diastolic myocardial dysfunction.[32,33] Systemic inflammatory diseases such as necrotizing enterocolitis are often associated with dysregulation of peripheral vascular tone; therefore, low SVR should always be considered as a pathophysiology of circulatory compromise in such a setting.

8.1. Management of Low SVR

Vasopressors are the drug of choice to support circulatory function when peripheral vasodilation is the only underlying pathophysiology of circulatory compromise in addition to treating the pathology causing vasodilation. A vasopressor is a synthetic or endogenous substance that acts on various receptors (e.g., alpha-adrenergic and V1a) on vascular smooth muscle cells to initiate a cascade of events, leading to increased intracellular calcium levels, which in turn increase vascular tone. The most commonly used medications in the NICU (dopamine and epinephrine) have both vasopressor and inotropic properties, albeit to a different degree. Dopamine has a vasopressor effect at low to moderate doses and a mild inotropic effect at moderate to high doses.[34] Dopamine has consistently been shown to improve blood pressure in hypotensive neonates. At low doses (<0.1 mcg/kg/min), epinephrine is primarily an inotrope. With an increase in the dose, the vascular alpha-1

receptor is progressively stimulated, and epinephrine becomes a potent vasoconstrictor. The high potency as a vasopressor is one of the reasons that it is uncommonly used as first-line therapy for hypotension for a concern over excessive vasoconstriction. The transient increase in serum lactate and hyperglycemia via its beta-receptor stimulation in the liver, muscle, and pancreas are other concerns.[35] Indeed, the rise of the lactate levels can be challenging to differentiate from the consequence of excessive vasoconstriction. However, when carefully titrated, both dopamine and epinephrine can improve blood pressure and increase CBF in hypotensive preterm infants.[36] Similarly, both medications appear to be comparable in treating septic shock in neonates.[37]

Norepinephrine has both vasopressor and inotropic properties but is considered to have a more potent vasopressor effect than epinephrine. Although norepinephrine is the drug of choice in treating septic shock in adults, it is not adequately studied in neonates.[38] A retrospective study showed improvement in blood pressure, urine output, and oxygen requirement 8 h after initiation of norepinephrine treatment in a cohort of preterm infants with septic shock and hypotension unresponsive to standard therapy, including dopamine and epinephrine[39] On the other hand, another retrospective study of preterm infants with cardiovascular compromise unresponsive to inotropes showed no improvement in pH, lactate level, or urine output after initiation of norepinephrine despite an improvement in blood pressure.[40] Furthermore, almost half of the 48 patients in the study died.

Vasopressin is a vasopressor without any inotropic effect. It exerts its systemic vascular effect via the V1a receptor. In physiologic doses, vasopressin has minimal effect on systemic vascular tone, but it is quite potent in pharmacological doses. The medication also acts on the pulmonary vasculature and causes pulmonary vasodilation in adults. There are limited data regarding its use in neonates. A pilot RCT in hypotensive extremely low birth weight infants found that vasopressin is comparable with dopamine in improving blood pressure.[41] The vasopressin group had less tachycardia and no other significant side effects. As hypotensive neonates could have different causes for circulatory compromise besides vasodilation, the use of vasopressin as a first-line treatment without assessment of underlying etiology is not recommended. However, vasopressin could be considered for selected populations such as vasodilatory septic shock, refractory hypotension with pulmonary hypertension, and hypertrophic cardiomyopathy unresponsive to volume.[42,43]

Corticosteroids are effective in treating hypotension, but due to their side effects, they are not recommended as a first-line medication. However, low-dose hydrocortisone should be considered in cases of refractory hypotension. A comprehensive review of corticosteroids for treating circulatory failure is beyond the scope of this article, and readers are referred to a recent review of the subject.[44]

9. Conclusion

There are significant gaps in our knowledge about early diagnosis and management of cardiovascular insufficiency in neonates, especially in preterm infants. Because of challenges in conducting RCTs, management of hypotension and circulatory compromise remains controversial. Blood pressure is a valuable but imperfect maker of circulatory function. Blood pressure should be monitored and interpreted along with other markers of the adequacy of circulatory function. Point-of-care echocardiography and other monitoring technologies such as near-infrared spectroscopy can provide valuable information to guide the management of cardiovascular insufficiency.

Hemodynamic management of critically ill neonates requires knowledge of developmental physiology, hemodynamics, and pharmacokinetics and pharmacodynamics of the cardiovascular medications. History and physical exam can point to the likely pathophysiology of circulatory compromise and aid in selecting an appropriate intervention. Point-of-care echocardiography can be used to confirm or refute the proposed underlying pathophysiology, select the medication with the best profile for the condition, and monitor response to treatment.

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Declaration of competing interest

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