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Part 7.4: Monitoring and Medications

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Part 7.4: Monitoring and Medications

This section provides an overview of monitoring techniques and medications that may be useful during CPR and in the immediate prearrest and postarrest settings.

Monitoring Immediately Before, During, and After Arrest

Assessment During CPR

At present there are no reliable clinical criteria that clinicians can use to assess the efficacy of CPR. Although end-tidal CO_2 serves as an indicator of cardiac output produced by chest compressions and may indicate return of spontaneous circulation (ROSC),[1,2] there is little other technology available to provide real-time feedback on the effectiveness of CPR.

Assessment of Hemodynamics

Coronary Perfusion Pressure

Coronary perfusion pressure (CPP = aortic relaxation [diastolic] pressure minus right atrial relaxation phase blood pressure) during CPR correlates with both myocardial blood flow and ROSC (LOE 3).[3,4] A CPP of ≥15 mm Hg is predictive of ROSC. Increased CPP correlates with improved 24-hour survival rates in animal studies (LOE 6)[5] and is associated with improved myocardial blood flow and ROSC in animal studies of epinephrine, vasopressin, and angiotensin II (LOE 6).[5–7]

When intra-arterial monitoring is in place during the resuscitative effort (eg, in an intensive care setting), the clinician should try to maximize arterial diastolic pressures to achieve an optimal CPP. Assuming a right atrial diastolic pressure of 10 mm Hg means that the aortic diastolic pressure should ideally be at least 30 mm Hg to maintain a CPP of ≥20 mm Hg during CPR. Unfortunately such monitoring is rarely available outside the intensive care environment.

Pulses

Clinicians frequently try to palpate arterial pulses during chest compressions to assess the effectiveness of compressions. No studies have shown the validity or clinical utility of checking pulses during ongoing CPR. Because there are no valves in the inferior vena cava, retrograde blood flow into the venous system may produce femoral vein pulsations.[8] Thus palpation of a pulse in the femoral triangle may indicate venous rather than arterial blood flow. Carotid pulsations during CPR do not indicate the efficacy of coronary blood flow or myocardial or cerebral perfusion during CPR.

Assessment of Respiratory Gases

Arterial Blood Gases

Arterial blood gas monitoring during cardiac arrest is not a reliable indicator of the severity of tissue hypoxemia, hypercarbia (and therefore the adequacy of ventilation during CPR), or tissue acidosis. This conclusion is supported by 1 case series (LOE 5)[9] and 10 case reports[10–19] that showed that arterial blood gas values are an inaccurate indicator of the magnitude of tissue acidosis during cardiac arrest and CPR both in and out of hospital.

Oximetry

During cardiac arrest, pulse oximetry will not function because pulsatile blood flow is inadequate in peripheral tissue beds. But pulse oximetry is commonly used in emergency departments and critical care units for monitoring patients who are not in arrest because it provides a simple, continuous method of tracking oxyhemoglobin saturation. Normal pulse oximetry saturation, however, does not ensure adequate systemic oxygen delivery because it does not calculate the total oxygen content (O_2 bound to hemoglobin + dissolved O_2) and adequacy of blood flow (cardiac output).

Tissue oxygen tension is not commonly evaluated during CPR, but it may provide a mechanism to assess tissue perfusion because transconjunctival oxygen tension falls rapidly with cardiac arrest and returns to baseline when spontaneous circulation is restored.[20,21]

End-Tidal CO_2 Monitoring

End-tidal CO_2 monitoring is a safe and effective noninvasive indicator of cardiac output during CPR and may be an early indicator of ROSC in intubated patients. During cardiac arrest CO_2 continues to be generated throughout the body. The major determinant of CO_2 excretion is its rate of delivery from the peripheral production sites to the lungs. In the low-flow state during CPR, ventilation is relatively high compared with blood flow, so that the end-tidal CO_2 concentration is low. If ventilation is reasonably constant, then changes in end-tidal CO_2 concentration reflect changes in cardiac output.

Eight case series have shown that patients who were successfully resuscitated from cardiac arrest had significantly higher end-tidal CO_2 levels than patients who could not be resuscitated (LOE 5).[2,22–28] Capnometry can also be used as an early indicator of ROSC (LOE 5[29,30]; LOE 6[31]).

In case series totaling 744 intubated adults in cardiac arrest receiving CPR who had a *maximum* end-tidal CO_2 of <10 mm Hg, the prognosis was poor even if CPR was optimized (LOE 5).[1,2,24,25,32,33] But this prognostic indicator was unreliable immediately after starting CPR in 4 studies (LOE 5)[1,2,32,33] that showed no difference in rates of ROSC and survival in those with an *initial* end-tidal CO_2 of <10 mm Hg compared with higher end-tidal CO_2. Five patients achieved ROSC (one survived to discharge) despite an initial end-tidal CO_2 of <10 mm Hg.

In summary, end-tidal CO_2 monitoring during cardiac arrest can be useful as a noninvasive indicator of cardiac output generated during CPR (Class IIa). Further research is needed to define the capability of end-tidal CO_2 monitoring to

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guide more aggressive interventions or a decision to abandon resuscitative efforts.

In the patient with ROSC, continuous or intermittent monitoring of end-tidal CO_2 provides assurance that the endotracheal tube is maintained in the trachea. End-tidal CO_2 can guide ventilation, especially when correlated with the $PaCO_2$ from an arterial blood gas measurement.

Medications for Cardiovascular Support

Vasoactive drugs may be administered immediately before, during, and after an arrest to support cardiac output, especially blood flow to the heart and brain. Drugs may be selected to improve heart rate (chronotropic effects), myocardial contractility (inotropic effects), or arterial pressure (vasoconstrictive effects), or to reduce afterload (vasodilator effects). Unfortunately many adrenergic drugs are not selective and may increase or decrease heart rate and afterload, increase cardiac arrhythmias, and increase myocardial ischemia by creating a mismatch between myocardial oxygen demand and delivery. Myocardial ischemia, in turn, may decrease heart function. Moreover, some agents may also have metabolic effects that increase blood glucose, lactate, and metabolic rate.

Specific drug infusion rates cannot be recommended because of variations in pharmacokinetics (relation between drug dose and concentration) and pharmacodynamics (relation between drug concentration and effect) in critically ill patients,[34,35] so initial dose ranges are listed below. Vasoactive drugs must be titrated at the bedside to secure the intended effect while limiting side effects. Providers must also be aware of the concentrations delivered and compatibilities with previously and concurrently administered drugs.

In general, adrenergic drugs should not be mixed with sodium bicarbonate or other alkaline solutions in the intravenous (IV) line because there is evidence that adrenergic agents are inactivated in alkaline solutions.[36,37] Norepinephrine (levarterenol) and other catecholamines that activate α-adrenergic receptors may produce tissue necrosis if extravasation occurs. If extravasation develops, infiltrate 5 to 10 mg of phentolamine diluted in 10 to 15 mL of saline into the site of extravasation as soon as possible to prevent tissue death and sloughing.

Epinephrine

The use of epinephrine in cardiac arrest is discussed in Part 7.2: "Management of Cardiac Arrest." Epinephrine can also be used in patients who are not in cardiac arrest but who require inotropic or vasopressor support. For example, epinephrine is considered Class IIb for symptomatic bradycardia if atropine and transcutaneous pacing fail or pacing is not available (eg, in the out-of-hospital setting). It may also be used in cases of anaphylaxis associated with hemodynamic instability or respiratory distress.[38]

To create a continuous infusion of epinephrine hydrochloride for treatment of bradycardia or hypotension, add 1 mg (1 mL of a 1:1000 solution) to 500 mL of normal saline or D_5W. The initial dose for adults is 1 μg/min titrated to the desired hemodynamic response, which is typically achieved in doses of 2 to 10 μg/min. Note that this is the nonarrest infusion preparation and dose (ie, for bradycardia or hypotension).

Vasopressin

The use of vasopressin in cardiac arrest is discussed in Part 7.2. Like epinephrine, vasopressin may be used in prearrest and postarrest conditions. Vasopressin has been used for management of vasodilatory shock, such as septic shock and sepsis syndrome.[39,40] Standard therapy for vasodilatory septic shock includes antimicrobial agents, intravascular volume expansion, vasopressors, and inotropic agents that increase myocardial contractility. Inotropic agents and vasoconstrictor drugs that are commonly used in this setting, however, may have a diminished vasopressor action.[41] If conventional adrenergic vasopressor drugs are ineffective, a continuous infusion of vasopressin may be beneficial (Class IIb).[42]

Norepinephrine

Norepinephrine (levarterenol) is a naturally occurring potent vasoconstrictor and inotropic agent. Cardiac output may increase or decrease in response to norepinephrine, depending on vascular resistance, the functional state of the left ventricle, and reflex responses (eg, those mediated by carotid and aortic baroreceptors). Norepinephrine usually induces renal and mesenteric vasoconstriction; in sepsis, however, norepinephrine improves renal blood flow and urine output.[43,44] It may be effective for management of patients with severe hypotension (eg, systolic blood pressure $<$70 mm Hg) and a low total peripheral resistance who fail to respond to less potent adrenergic drugs such as dopamine, phenylephrine, or methoxamine.

Norepinephrine is relatively contraindicated in patients with hypovolemia. It may increase myocardial oxygen requirements, mandating cautious use in patients with ischemic heart disease. As noted above, extravasation may cause ischemic necrosis and sloughing of superficial tissues and must be treated promptly.

Norepinephrine is administered by adding 4 mg of norepinephrine or 8 mg of norepinephrine bitartrate (1 mg of norepinephrine is equivalent to 2 mg of norepinephrine bitartrate) to 250 mL of D_5W or 5% dextrose in normal saline (but not in normal saline alone), resulting in a concentration of 16 μg/mL of norepinephrine or 32 μg/mL of norepinephrine bitartrate. The initial dose of norepinephrine is 0.5 to 1 μg/min titrated to effect. It should not be administered in the same IV line as alkaline solutions, which may inactivate it.

Dopamine

Dopamine hydrochloride is a catecholamine-like agent and a chemical precursor of norepinephrine that stimulates both α- and β-adrenergic receptors. In addition, there are receptors specific for this compound (DA_1, DA_2 dopaminergic receptors). Physiologically dopamine stimulates the heart through both α- and β-receptors. Pharmacologically dopamine is both a potent adrenergic receptor agonist and a strong peripheral dopamine receptor agonist. These effects are dose dependent.

During resuscitation dopamine is often used to treat hypotension, especially if it is associated with symptomatic bradycardia or after ROSC. Dopamine in combination with other agents, including dobutamine, remains an option for

management of postresuscitation hypotension. If hypotension persists after filling pressure (ie, intravascular volume) is optimized, drugs with combined inotropic and vasopressor actions like epinephrine or norepinephrine may be used. Positive effects include increases in both cardiac output and arterial perfusion pressure. Although low-dose dopamine infusion has been frequently recommended to maintain renal blood flow or improve renal function, more recent data has failed to show a beneficial effect from such therapy.[45,46]

The usual dose of dopamine ranges from 2 to 20 μg/kg per minute. Doses >10 to 20 μg/kg per minute may be associated with systemic and splanchnic vasoconstriction. Higher doses of dopamine, like all adrenergic vasoconstrictor drugs, can be associated with adverse effects on splanchnic perfusion in some patients.

Dobutamine

Dobutamine hydrochloride is a synthetic catecholamine and potent inotropic agent useful for treatment of severe systolic heart failure. Dobutamine has complex pharmacology because of the effects of the different racemic components. The (+) isomer is a potent β-adrenergic agonist, whereas the (−) isomer is a potent α_1-agonist.[47] The vasodilating β_2-adrenergic effects of the (+) isomer counterbalance the vasoconstricting α-adrenergic effects, often leading to little change or a reduction in systemic vascular resistance. The beneficial effects of dobutamine may be associated with decreased left ventricular filling pressure. In addition to its direct inotropic effects, dobutamine may further increase stroke volume through reflex peripheral vasodilation (baroreceptor mediated), reducing ventricular afterload, so that arterial pressure is unchanged or may fall even though cardiac output increases. Hemodynamic end points rather than a specific dose should be used to optimize treatment with dobutamine.

The usual dose of dobutamine ranges from 2 to 20 μg/kg per minute; however, there is a wide variation in individual response to the drug in critically ill patients. Elderly patients may have a significantly decreased response to dobutamine. At doses >20 μg/kg per minute, increases in heart rate of >10% may induce or exacerbate myocardial ischemia. Doses of dobutamine as high as 40 μg/kg per minute have been used, but such doses may greatly increase adverse effects, especially tachycardia and hypotension.

Inodilators (Inamrinone and Milrinone)

Inamrinone (formerly amrinone) and milrinone are phosphodiesterase III inhibitors that have inotropic and vasodilatory properties. Phosphodiesterase inhibitors are often used in conjunction with catecholamines for severe heart failure, cardiogenic shock, and other forms of shock unresponsive to catecholamine therapy alone. Optimal use requires hemodynamic monitoring. These drugs are contraindicated in patients with heart valve stenosis that limits cardiac output.

Inamrinone is administered as a loading dose of 0.75 mg/kg over 10 to 15 minutes (may give over 2 to 3 minutes if no left ventricular dysfunction) followed by an infusion of 5 to 15 μg/kg per minute, titrated to clinical effect. An additional bolus may be given in 30 minutes.

Milrinone is more often used today because it has a shorter half-life than inamrinone and is less likely to cause thrombocytopenia.[48,49] Milrinone is renally excreted with a half-life of around 1½ to 2 hours, so it requires 4½ to 6 hours to achieve near–steady state concentrations if given without a loading dose. A slow milrinone IV loading dose (50 μg/kg over 10 minutes) is followed by an IV infusion at a rate of 0.375 to 0.75 μg/kg per minute (375 to 750 ng/kg per minute) for 2 to 3 days. In renal failure the dose should be reduced. Adverse effects include nausea, vomiting, and hypotension.

Calcium

Although calcium ions play a critical role in myocardial contractile performance and impulse formation, retrospective and prospective studies in the cardiac arrest setting have shown no benefit from calcium administration.[50,51] Furthermore, high serum calcium levels induced by calcium administration may be detrimental. For this reason, calcium should not be used routinely to support circulation in the setting of cardiac arrest. When hyperkalemia, ionized hypocalcemia (eg, after multiple blood transfusions), or calcium channel blocker toxicity is present, use of calcium is probably helpful.[52] Ideally, ionized calcium concentration should be measured because total calcium concentration does not correlate well with ionized concentration in critically ill patients.[53,54]

When necessary, a 10% solution (100 mg/mL) of calcium chloride can be given in a dose of 8 to 16 mg/kg of the salt (usually 5 to 10 mL) and repeated as necessary. (The 10% solution contains 1.36 mEq of calcium or 27.2 mg elemental calcium per milliliter.)

Digitalis

Digitalis preparations have limited use as inotropic agents in emergency cardiovascular care. Digitalis decreases the ventricular rate in some patients with atrial flutter or fibrillation by slowing atrioventricular nodal conduction. The toxic to therapeutic ratio is narrow, especially when potassium depletion is present. Digitalis toxicity may cause serious ventricular arrhythmias and precipitate cardiac arrest. Digoxin-specific antibody is available for the treatment of serious toxicity (Digibind, Digitalis Antidote BM).

Nitroglycerin

Nitrates are used for their ability to relax vascular smooth muscle. Nitroglycerin is the initial treatment of choice for suspected ischemic-type pain or discomfort (see Part 8: "Stabilization of the Patient With Acute Coronary Syndromes").

IV nitroglycerin is also an effective adjunct in the treatment of congestive heart failure from any cause,[55] and it may be useful in hypertensive emergencies, particularly if related to volume overload. The action of nitroglycerin is mediated through local endothelial production of nitric oxide, particularly in the venous capacitance system. Nitroglycerin is most effective in patients with increased intravascular volume. Hypovolemia blunts the beneficial hemodynamic effects of nitroglycerin and increases the risk of hypotension; nitrate-induced hypotension typically responds well to fluid replacement therapy. Other potential complications of use of IV

nitroglycerin are tachycardia, paradoxical bradycardia, hypoxemia caused by increased pulmonary ventilation-perfusion mismatch, and headache. Nitroglycerin should be avoided with bradycardia and extreme tachycardia or within 24 to 48 hours of the use of phosphodiesterase inhibitors to treat erectile dysfunction.

Nitroglycerin is administered by continuous infusion (nitroglycerin 50 or 100 mg in 250 mL of D_5W or 0.9% sodium chloride) at 10 to 20 μg/min and increased by 5 to 10 μg/min every 5 to 10 minutes until the desired hemodynamic or clinical response occurs. Low doses (30 to 40 μg/min) predominantly produce venodilatation; high doses ($\geq$150 μg/min) provide arteriolar dilatation. Uninterrupted administration of nitroglycerin (>24 hours) produces tolerance.[56]

Sodium Nitroprusside

Sodium nitroprusside is a potent, rapid-acting, direct peripheral vasodilator useful in the treatment of severe heart failure and hypertensive emergencies.[57] Its direct venodilatory effects decrease right and left ventricular filling pressure by increasing venous compliance. The net effect on venous return (preload) depends on the intravascular volume. In many patients cardiac output improves secondary to the afterload-reducing effects of nitroprusside, meaning that venous return must also increase, but the latter occurs at a lower end-diastolic pressure, resulting in relief of pulmonary congestion and reduced left ventricular volume and pressure. Arteriolar relaxation causes decreases in peripheral arterial resistance (afterload), resulting in enhanced systolic emptying with reduced left ventricular volume and wall stress and reduced myocardial oxygen consumption. In the presence of hypovolemia, nitroprusside can cause hypotension with reflex tachycardia. Invasive hemodynamic monitoring is useful during nitroprusside therapy.

Although nitroprusside may be useful for the treatment of pulmonary artery hypertension, it reverses hypoxic pulmonary vasoconstriction in patients with pulmonary disease (eg, pneumonia, adult respiratory distress syndrome). The latter effect may exacerbate intrapulmonary shunting, resulting in worse hypoxemia. The major complication of nitroprusside is hypotension. Patients may also complain of headaches, nausea, vomiting, and abdominal cramps.

Nitroprusside is rapidly metabolized by nonenzymatic means to cyanide, which is then detoxified in the liver and kidney to thiocyanate. Cyanide is also metabolized by forming a complex with vitamin B_{12}.[58] Thiocyanate undergoes renal elimination. Patients with hepatic or renal insufficiency and patients requiring >3 μg/kg per minute for more than 72 hours may accumulate cyanide or thiocyanate, and they should be monitored for signs of cyanide or thiocyanate intoxication, such as metabolic acidosis.[59] When thiocyanate concentrations exceed 12 mg/dL, toxicity is manifested as confusion, hyperreflexia, and ultimately convulsions. Treatment of elevated cyanide or thiocyanate levels includes immediate discontinuation of the infusion. If the patient is experiencing signs and symptoms of cyanide toxicity, sodium nitrite and sodium thiosulfate should be administered.

Sodium nitroprusside is prepared by adding 50 or 100 mg to 250 mL of D_5W. The solution and tubing should be wrapped in opaque material because nitroprusside deteriorates when exposed to light. The recommended dosing range for sodium nitroprusside is 0.1 to 5 μg/kg per minute, but higher doses (up to 10 μg/kg per minute) may be needed.

IV Fluid Administration

Limited evidence is available to guide therapy. Volume loading during cardiac arrest causes an increase in right atrial pressure relative to aortic pressure,[60] which can have the detrimental effect of decreasing CPP. The increase in CPP produced by epinephrine during CPR is not augmented by either an IV or intra-aortic fluid bolus in experimental CPR in dogs.[61]

If cardiac arrest is associated with extreme volume losses, hypovolemic arrest should be suspected. These patients present with signs of circulatory shock advancing to pulseless electrical activity (PEA). In these settings intravascular volume should be promptly restored. In the absence of human studies the treatment of PEA arrest with volume repletion is based on evidence from animal studies.[60–63] Current evidence in patients presenting with ventricular fibrillation (VF) neither supports nor refutes the use of routine IV fluids (Class Indeterminate).

Animal studies suggest that hypertonic saline may improve survival from VF when compared with normal saline.[64,65] Human studies are needed, however, before the use of hypertonic saline can be recommended. If fluids are administered during an arrest, solutions containing dextrose should be avoided unless there is evidence of hypoglycemia.

Sodium Bicarbonate

Tissue acidosis and resulting acidemia during cardiac arrest and resuscitation are dynamic processes resulting from no blood flow during arrest and low blood flow during CPR. These processes are affected by the duration of cardiac arrest, the level of blood flow, and the arterial oxygen content during CPR. Restoration of oxygen content with appropriate ventilation with oxygen, support of some tissue perfusion and some cardiac output with good chest compressions, then rapid ROSC are the mainstays of restoring acid-base balance during cardiac arrest.

Little data supports therapy with buffers during cardiac arrest. There is no evidence that bicarbonate improves likelihood of defibrillation or survival rates in animals with VF cardiac arrest. A wide variety of adverse effects have been linked to bicarbonate administration during cardiac arrest. Bicarbonate compromises CPP by reducing systemic vascular resistance.[66] It can create extracellular alkalosis that will shift the oxyhemoglobin saturation curve and inhibits oxygen release. It can produce hypernatremia and therefore hyperosmolarity. It produces excess carbon dioxide, which freely diffuses into myocardial and cerebral cells and may paradoxically contribute to intracellular acidosis.[67] It can exacerbate central venous acidosis and may inactivate simultaneously administered catecholamines.

In some special resuscitation situations, such as preexisting metabolic acidosis, hyperkalemia, or tricyclic antidepressant overdose, bicarbonate can be beneficial (see Part 10: “Special Resuscitation Situations”).

Sodium bicarbonate is not considered a first-line agent for the patient in cardiac arrest. When bicarbonate is used for special situations, an initial dose of 1 mEq/kg is typical. Whenever possible, bicarbonate therapy should be guided by the bicarbonate concentration or calculated base deficit obtained from blood gas analysis or laboratory measurement. To minimize the risk of iatrogenically induced alkalosis, providers should not attempt complete correction of the calculated base deficit. Other non–CO_2-generating buffers such as Carbicarb, Tham, or Tribonat have shown potential for minimizing some adverse effects of sodium bicarbonate, including CO_2 generation, hyperosmolarity, hypernatremia, hypoglycemia, intracellular acidosis, myocardial acidosis, and "overshoot" alkalosis.[68–70] But clinical experience is greatly limited and outcome studies are lacking.

Diuretics

Furosemide is a potent diuretic agent that inhibits reabsorption of sodium in the proximal and distal renal tubule and the loop of Henle. Furosemide has little or no direct vascular effect, but it reduces venous and pulmonary vascular resistance through stimulation of local prostaglandin production[71] and therefore may be very useful in the treatment of pulmonary edema. The vascular effects occur within 5 minutes, whereas diuresis is delayed. Although often used in acute renal failure to stimulate increased urine output, there is no data to support this indication, and some data suggests an association with increased mortality.[72] The initial dose of furosemide is 0.5 to 1 mg/kg IV injected slowly.

Newer "loop" diuretics that have an action similar to that of furosemide and a similar profile of side effects include torsemide and bumetanide. In patients who do not respond to high doses of loop diuretics alone, a combination of such agents together with the administration of "proximal tubule"–acting thiazide diuretics (such as chlorothiazide or metolazone) may be effective. Such combinations require close observation with serial measurement of serum electrolytes to avoid profound potassium depletion from their use.

Summary

Maintenance of adequate CPP is linked with survival following CPR. Rescuers can support adequate CPP by providing compressions of adequate rate and depth, allowing full chest recoil after each compression, avoiding overventilation, and minimizing interruptions in chest compressions (see Part 4: "Adult Basic Life Support"). Exhaled CO_2 can be a useful indicator of cardiac output produced by chest compressions. Pulse oximetry is not helpful during arrest, but it should be monitored in high-risk patients to ensure adequate oxygenation. No medications have been shown to improve neurologically intact survival from cardiac arrest. Better tools are needed to monitor effectiveness of CPR.

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