ICU
MANAGEMENT & PRACTICE

Vasopressor Therapy and Intensive Care Patient Management

Vasopressors are commonly used in critically ill patients to increase vascular tone in cases of severe hypotension with signs of altered tissue perfusion, such as poor skin perfusion, altered mental status, or decreased urine output—indicative of shock. Shock is associated with elevated lactate levels (>2 mmol/L) and can be classified into four types: hypovolaemic, cardiogenic, obstructive, and distributive. In the first three, cardiac output is insufficient to maintain blood pressure, whereas distributive shock involves normal or high cardiac output with reduced vascular tone. Since arterial pressure depends on both cardiac output and vascular tone, treating hypotension must not compromise cardiac output or oxygen delivery to tissues.

Adrenergic agents are the first-line vasopressors for severe hypotension due to their well-documented effects and short half-life. These agents act on alpha and beta-adrenoceptors, influencing vascular tone and cardiac output.

- **Norepinephrine** is the preferred vasopressor, as it provides vasoconstriction with mild inotropic effects, helping to maintain cardiac output. A meta-analysis suggests it has a lower risk of arrhythmias compared to other agents.
- **Epinephrine**, a strong alpha- and beta-agonist, can increase arterial pressure and cardiac output but may reduce regional blood flow, induce arrhythmias, and increase metabolism. It is typically used in life-threatening hypotension, including cardiac arrest.
- **Dopamine** was historically used for its potential renal protective effects but has since been shown to offer no survival benefits over norepinephrine and is no longer recommended.
- **Phenylephrine**, a selective alpha-agonist, is effective in acute severe hypotension, such as during surgery, but can reduce cardiac output and should be reserved for emergencies.

Overall, norepinephrine ± dobutamine is the preferred approach in most cases, allowing for independent control of vasopressor and inotropic effects.

Studies suggest vasopressin may reduce the need for renal replacement therapy (RRT) and improve survival, especially when used early in septic shock before severe deterioration. The recommended dose is 0.03–0.05 units/min, as higher doses can harm peripheral circulation. A 1-unit bolus may help assess blood pressure responsiveness before continuous infusion.

Terlipressin, a vasopressin analogue, has stronger V1a receptor affinity and fewer hormonal side effects. It is useful for hepato-renal syndrome but is less favoured in intensive care due to its long half-life.

Angiotensin II (Ang II) is a potent vasopressor initially studied in the 1960s but largely unused due to its strong vasoconstrictive effects. Interest resurfaced with the **ATHOS-3 trial,** which showed its efficacy in vasodilatory shock, leading to FDA approval. However, its high cost (~EUR 1000/day) requires evidence of superiority over adrenergic agents. Currently, Ang II may be useful as part of a multimodal vasopressor strategy to optimise benefits while minimising toxicity from high doses of a single agent.

Nitric Oxide (NO) plays a crucial role in the vasodilation seen in septic shock, but its effects are complex and not always harmful. Several strategies have been explored to target the NO pathway:

- NOS Inhibition: Blocking NO synthase (NOS) with 546C88 produced a vasopressor effect but increased mortality, making this strategy unsuitable.
- Methylene Blue (MB): An inhibitor of soluble guanylate cyclase, MB has shown faster vasopressor discontinuation in a small trial. However, its use remains experimental due to potential splanchnic ischaemia risks.
- NO Scavenging: A novel approach using hydrophobic phospholipid nanoparticles (VBI-S), which absorb NO, has shown promising vasopressor effects and reduced vasopressor requirements.

While targeting NO remains an area of interest, current evidence is insufficient for routine clinical use, and further trials are needed.

Other Vasopressors include metaraminol, once widely used but now mostly abandoned due to risks of excessive vasoconstriction. Still used in some institutions, particularly in Australasia; mephentermine increases norepinephrine release, but it is no longer widely available; hydroxocobalamin (Vitamin B12) inhibits NO-mediated vasodilation, offering potential vasoconstrictive effects; however, its benefits remain unproven. These agents have largely been replaced by more effective and safer alternatives.

With respect to blood pressure targets in septic shock, no single optimal MAP target is defined. Clinical trials show varying outcomes, emphasising the need for individualised targets. The SEPSISPAM trial compared 80–85 mmHg vs. 65–70 mmHg MAP targets. No difference in overall outcomes was observed, but higher MAP improved renal function in hypertensive patients. MAP should be titrated based on perfusion rather than a fixed number to optimise outcomes.

Vasopressors should be used carefully, with close monitoring of cardiac output and tissue perfusion, to avoid harmful vasoconstriction. Vasopressors restore tissue perfusion, but blood pressure alone is not enough—blood flow must also be considered. The optimal arterial pressure varies by patient, depending on comorbidities and disease factors. Vasopressor therapy must be tailored to the patient, balancing blood pressure with adequate blood flow and tissue perfusion.

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