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Review Article

Role of inotropes and vasopressors therapy in the intensive care unit

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ABSTRACT

Vasopressors and inotropes are often administered to critically ill patients in intensive care unit for the management and treatment of haemodynamic impairment, heart failure, septic and cardiogenic shock, trauma among certain other diseases. In patients with shock, vasopressors and inotropes are used to induce vasoconstriction or enhance cardiac contractility. Vasopressors induces vasoconstriction, which causes systemic vascular resistance, leading to increase in mean arterial pressure and elevates organ perfusion. While inotropes raise cardiac output, which helps maintain mean arterial pressure and body perfusion. Due to a decreased risk of side effects compared to other catecholamine vasopressors, norepinephrine is considered a first-line vasopressor titrated to attain an optimal arterial pressure. An inotrope such as dobutamine may be given to raise cardiac output to a sufficient level to fulfil tissue demand if tissue and organ perfusion still is not enough. Due to their strengthening effect on cardiac contractility, inotropes have been utilized in the care of patients with heart failure for decades, particularly for patients with systolic dysfunction, or heart failure with reduced ejection fraction. Along with their beneficial inotropic impact, they also have chronotropic and peripheral vascular effects. For patients with severely reduced cardiac output and peripheral organ hypoperfusion, they are most frequently employed in intensive care unit. Along with their benefits they are also associated with certain considerate side-effects. The purpose of this research is to review the available information about role of inotropes and vasopressors therapy in the intensive care unit.

Keywords: Inotropes, Vasopressors, Intensive, Care

INTRODUCTION

The cornerstone of hemodynamic management of critically ill patients is prompt introduction of vasoactive medicines and adequate fluid resuscitation. As opposed to vasopressors, which cause vasoconstriction and hence raise mean arterial pressure, inotropes are used to promote myocardial contractility and cardiac output. There are various recommendations for the use of

inotropic and vasopressor medications for various forms of shock. These vasoactive medications are used on a regular basis in clinical practice, despite conflicting recommendations and dearth of evidence. Despite the fact that these drugs significantly enhance haemodynamic parameters, they are also linked to significant side effects such as elevated myocardial oxygen consumption, myocardial ischaemia, and arrhythmias. There is mounting proof that too much adrenergic stimulation can be harmful when someone is critically ill.[1] Clinicians need to be confident in using vasopressors and inotropes to address an aging and more complex patient population. These drugs are employed to improve the cardiovascular health of seriously ill patients. Different hemodynamic effects are produced by different drug classes. Vasopressors cause peripheral vasoconstriction, which raises mean arterial pressure and systemic vascular resistance. By strengthening heart contraction, inotropes raise mean arterial pressure and cardiac output. While some agents only result in one of these behaviours, others have a variety of outcomes. These medications are specifically utilized by clinicians to maintain the perfusion of essential organs during acute and serious disease.[2]

To maintain stable circulation and maximize oxygen delivery, intensive care patients frequently need inotropic assistance. The catecholamines norepinephrine, epinephrine, dopamine, and dobutamine are still the cornerstones of treatment in this situation. They offer a range of adrenoceptor-mediated activities, including vasoconstriction and vasodilatation, to varying degrees. They also enhance inotropy and heart rate, which increases cardiac output. Their excellent pharmacokinetic profile makes it simple to manage their effects. Various catecholamines can be combined with one another, or with other medications like phosphodiestaerase inhibitors or nitrates, to provide a wide range of potential hemodynamic effects. However, adverse effects including tachycardia, hypertension, and problems with organ perfusion caused by vasoconstriction limit the usage of catecholamines. Additionally, long-term therapy causes receptor downregulation, which reduces the effectiveness of catecholamine therapy.[3]

Vasopressors are a diverse group of potent medications used to raise blood pressure when hypotension is an emergency. The purpose of therapy is to raise blood pressure and keep perfusion levels adequate so that nutrients and oxygen reach important organs. There are five different commonly used vasopressors norepinephrine, phenylephrine, dopamine, epinephrine, and vasopressin.[4] Vasopressors are frequently used in anaesthesiology and critical care medicine to treat both life-threatening and non-life-threatening disorders such as anaesthesia-induced hypotension. Some vasopressors used in medicine resemble naturally occurring chemicals, such as norepinephrine, whereas others are manufactured synthetically including phenylephrine. Except for vasoconstriction alone, the majority of the drugs employed in diverse clinical circumstances have varied effects. Therefore, before using a chemical in practice, it is crucial to have a complete understanding of its pharmacology and clinical profile. Furthermore, in order to deliver vasopressor-based therapy safely, the foundations of vascular physiology and vasotonic control must be understood.[5] The purpose of this research is to review the available information about role of inotropes and vasopressors therapy in the intensive care unit.

LITERATURE SEARCH

This study is based on a comprehensive literature search conducted on December 7, 2022, in the Medline and Cochrane databases, utilizing the medical topic headings (MeSH) and a combination of all available related terms, according to the database. To prevent missing any possible research, a manual search for publications was conducted through Google Scholar, using the reference lists of the previously listed papers as a starting point. We looked for valuable information in papers that discussed the information about role of inotropes and vasopressors therapy in the intensive care unit. There were no restrictions on date, language, participant age, or type of publication.

DISCUSSION

Although vasopressors and inotropes have been used since 1940s, evidence-based data available is often insufficient to support their usage in critically ill patients. Few clinical trials that studied various vasoactive medications have shown that their use is in fact linked to better patient outcomes. These drugs are frequently prescribed in therapeutic settings based on the opinions of experts, the clinicians' own experiences, molecular knowledge of the drugs, mechanisms of action, and available evidence studies. Strong evidence backing the use of additional vasopressors and inotropic medications in septic and cardiogenic shock is absent, with the exception of norepinephrine as the first line vasopressor in shock. In refractory vasodilatory shock, angiotensin II has lately been advocated as a second-line vasopressor based on clinical trial involving a relatively limited number of patients. In order to better understand the usage of vasoactive/inotropic medicines in critically ill patients, extensive clinical trials are required. It is challenging to apply the findings from major clinical trials to clinical practice, especially when the available evidence is sparse, as is the case in many other areas of critical care medicine due to the high degree of heterogeneity among patients who require vasopressors and inotropes. Many specialists have argued in favour of employing a tailored approach that takes into account the characteristics of patients and the pathophysiological factors.[6]

Use of inotropes and vasopressors in commonly reported diseases in intensive care unit is briefly explained below.

Heart failure and shock

Hemodynamic assistance is needed for patients who are frequently in shock when they are admitted to the cardiac intensive care unit. The cornerstone of supportive medical therapy for shock is fluid resuscitation, when necessary, along with vasopressors and inotropes. Patients with shock must promptly begin receiving the best vasopressor and inotrope therapy in order to restore efficient tissue perfusion and restore normal cellular metabolism. When deciding on therapeutic measures, the use of vasoactive drugs for hemodynamic support of patients with shock should take into account both arterial pressure and tissue perfusion. Norepinephrine is an appropriate choice as a first-line vasopressor titrated to produce a sufficient arterial pressure for the majority of patients with shock, including cardiogenic or septic shock, because it has a reduced risk of side effects in comparison to the other catecholamine vasopressors.[7]

Sheeren et al demonstrated in their study that norepinephrine, while predominantly a vasopressor, was regarded as the best catecholamine for the treatment of circulatory shock when combined with dobutamine. Norepinephrine's classification as a pure vasoconstrictor or as a substance with simultaneous vasopressor and inotropic actions is controversial, even among professionals. Norepinephrine has been demonstrated to raise blood pressure, preload, and systemic and microcirculatory blood flow in septic shock patients by stimulation of beta-1 adrenergic receptors. Due to their most prominent physiological effect, norepinephrine and epinephrine may be perceived as pure vasopressors by some clinicians, whereas other clinicians may view it as a vasopressor with clinically significant inotropic effects that may be sufficient to support contractility as a single agent.[8] Levy, Buzzon and Kimmoun stated that norepinephrine is a viable first-line treatment when blood pressure has to be raised. While levosimendan may be used as second-line drug or as a preference in patients who have already received beta-blocker treatment.[9]

Shankar et al demonstrated in their study that to maintain tissue perfusion and improve volume status in cardiogenic shock, vasopressors and inotropes are viable alternatives as the initial medical management of the condition. However, safety concerns and the risk profile suggest that these drugs should only be used occasionally and at the lowest possible doses. Based on the hemodynamic and clinical profile, a tailored patient strategy should be modified to choose the vasoactive drugs. Cardiogenic shock outcomes have been shown to improve with pharmacologic management and early use of mechanical circulatory devices in a shock team approach, but further research into the precise incorporation of vasoactive and inotropic agents in the context of cardiogenic shock teams and protocols is required. Despite being a staple of the pharmacologic therapy of cardiogenic shock, research studies on vasopressors and inotropes are quite few.[10]

Patients with severe heart failure are the most difficult to treat of all patient groups who need inotropic treatment. In most circumstances, inotropes are only appropriate as a temporary treatment to keep patients stable until more permanent, frequently surgical, procedures may be planned. The use of levosimendan in patients with severe heart failure and cardiogenic shock has garnered a lot of interest. Early research suggests that levosimendan therapy in these situations may enhance heart function with little to no increase in myocardial effort. However, when it comes to treating heart failure, neither dobutamine nor milrinone have been shown to be more effective than the other. In addition, treatment with milrinone is linked to higher-than-expected mortality rates in those with heart failure although it is it is unclear why this is the case.[11] Inotropes are recommended for heart failure patients with marginal or even normal blood pressure who exhibit signs of hypoperfusion, in addition to individuals in overt cardiogenic shock. This proof consists of both clinical and analytical results. An inotrope or an inodilator is typically part of these patients' treatment plans in an effort to rectify the hypoperfusion. The choice of which specific agent to provide to each patient is based on their unique haemodynamic characteristics. When compared to other inotropic drugs, inodilators milrinone and levosimendan have some special qualities that make them a better therapeutic choice for specific patient populations. Inotropic substances have long been linked to unfavourable complications in terms of mortality, including arrhythmogenesis. Due to the lack of other effective medicinal or interventional methods, they continue to be a vital tool in the toolbox of clinicians.[12]

Results of meta-analysis showed that there was no change in mortality between the therapy group and control group after undergoing treatment with adrenaline, noradrenaline, vasopressin, milrinone, levosimendan, dobutamine, or dopamine. Although, levosimendan showed a trend toward a superior result when compared to the control. There was insufficient evidence to support the claim that patients with acute myocardial infarction related to cardiogenic shock who regularly take vasopressors and inotropes have lower mortality rates.[13] Gao and Zhang reported in their findings that because inotropes may be linked to an increased risk of death in cardiogenic shock patients, they should be taken with caution. When high-dose inotropes are delivered, supporting therapies should be taken into account as they may reduce the risk of hospital mortality in these patients receiving low doses of norepinephrine and milrinone.[14]

Sepsis

Almost 10% of admissions to intensive care units are due to sepsis. The death rate from sepsis remains between 20% to 30%, despite improvements in critical care, early diagnosis and prompt management of septic patients. In order to improve perfusion to distant organs while minimizing adverse effects, the optimal vasopressor for

the treatment of septic shock would boost mean arterial pressure and venous return and increase preload via venous constriction. In septic shock, norepinephrine is advised as the first-line vasopressor since it is linked to decreased death and dysrhythmia rates. Epinephrine and vasopressin can be administered as second-line medications, either to boost norepinephrine and necessitate lower doses or to try to satisfy mean arterial pressure targets and distal perfusion. Patients with bradycardia or those who are at low risk of tachyarrhythmias may benefit from dopamine. Uncertainty surrounds the appropriate second agent, which must be adapted to the physiology of the patient. Patients with baseline cardiac dysfunction or septic myocardial dysfunction may benefit from inotropes.[15] Vasoactive medications should be used in cases with fluid refractory shock. Dopamine is the preferred option. Nor-epinephrine is a vasopressor, whereas dobutamine and low dosage epinephrine are recommended inotropic medications recommended for the management of septic shock.[16]

Results of a meta-analysis showed that norepinephrine was linked to lower all-cause mortality when compared to dopamine, with an absolute risk reduction of 11% and a number needed to treat of 9. Compared to dopamine, norepinephrine was associated with a decreased risk of serious adverse events including cardiac arrhythmias. The comparisons of norepinephrine to epinephrine, phenylephrine, and vasopressin/terlipressin did not reveal any further mortality benefits. The different vasopressors had similar hemodynamic data, with norepinephrine having a little advantage in central venous pressure, urine output, and blood lactate levels. There is evidence that norepinephrine has advantages over dopamine in terms of survival, a better hemodynamic profile, and a lower rate of adverse events. When treating septic shock, norepinephrine ought to be thought of as the first line vasopressor.[17]

For patients with sepsis-related hypotension, norepinephrine is recommended as the first-line vasopressor. Dobutamine is regarded as the first-line inotrope in sepsis and need to be taken into consideration for individuals who exhibit persistent symptoms of hypoperfusion or myocardial dysfunction. Clinicians should take into account the physiology and data from clinical trials because vasopressor and inotrope therapy have complicated effects that are frequently challenging to predict. It is crucial to regularly re-evaluate the patient to ascertain whether the chosen treatment is producing the desired results.[18] Sato et al reported that although recommendations state that inotropes should be used in cases of cardiac dysfunction, it is yet unknown how inotropes like epinephrine, dobutamine, and milrinone affect in-hospital mortality in septic shock patients. Dobutamine and epinephrine use was linked to noticeably higher in-hospital mortality in septic shock patients. Both time and dose were factors that affected these effects. Milrinone use, on the other hand, was not linked to a rise in in-hospital mortality.[19] Literature strongly advocates the need for further research especially clinical trials to elaborately study the role and efficacy of inotropes and vasopressors among critically ill patients in intensive care unit as available studies are quite scarce and limited, only further research can aid in improvising patient outcomes further.

CONCLUSION

Although inotropes and vasopressors are considered the arsenal of clinicians for management of critically ill patients in intensive care unit, they are associated with significant adverse events because of which they require continuous monitoring and time and dose adjustments as per patients' needs and additionally are administered for brief time.

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