Review Article

The Relationship Between Inotrope Use and Intraventricular Hemorrhage in Preterm Neonates

Abstract

In preterm newborns, intraventricular haemorrhage (IVH) may be preceded by erroneous hemodynamic alterations in cerebral circulation. Neonatal hypotension requiring use of inotropes was found to be the significantly risk factors in IVH. Reduced use of inotropic medications (such dopamine or epinephrine), which have been linked to the development of IVH, and a reduced incidence of hypotension, may be linked to the increased intravascular volume.

Keywords: Inotrope, Intraventricular Hemorrhage, Preterm Neonates

Introduction

IVH is the most prevalent and serious neurological disorder linked to prematurity, impacting 20–40% of all infants born globally who weigh less than 1500 g. It is believed that neonatal IVH occurs due to the interplay between delicate germinal matrix vessels and the swift hemodynamic fluctuations that premature infants are susceptible to. Newborns may undergo ischemia as a result of decreased heart rate, which is subsequently followed by reperfusion as ventricular function starts to recover during the initial days of life [1].

These abrupt instances of ischemia-reperfusion can place stress on the vessels of the germinal matrix, resulting in IVH [22,23]. It is believed that this phenomenon happens in premature infants because of an immature germinal matrix, developing brain autoregulatory mechanisms, and heightened hemodynamic variations linked to underdeveloped cardiopulmonary systems [1].

Factors such as the underdevelopment of autoregulatory mechanisms predispose premature infants, leading to decreased cerebral blood flow as a result of variations in MAP and carbon dioxide partial pressure [2].

Inotropes are drugs that alter the contractile force of the heart muscle. Contractility is increased by positive inotropes and decreased by negative inotropes. These chemicals affect smooth muscle in both excitatory and inhibitory waysof the heart and blood vessels, as well as important effects on metabolism, the presynaptic autonomic nervous system and the central nervous system [20,21,24,25]. They are frequently used to increase vascular tone (RVS) or cardiac output (CO) in order to enhance haemodynamics.to provide oxygen to sustain important organs while the fundamental illness is being addressed [3].

Intraventricular hemorrhage

Premature babies are susceptible to periventricular-intraventricular haemorrhage (PIVH). When the arteries in the periventricular region's germinal matrix burst, haemorrhage occurs, which may proceed into the ventricles as intraventricular haemorrhage (IVH). In extreme cases, the bleeding will expand inhabit a sizable section of the ventricle and extend into the intraparenchymal region. Due to the fact that the germinal matrix begins to involute during 33 weeks gestation, infants born before this time are the most vulnerable [4]

The global prevalence of peripheral viral hepatitis ranges from 3.70% to 44.68%. Studies have revealed a 36.2% overall incidence, with 7% of cases exhibiting severe grades (III, IV). The overall prevalence of class I, II, III, and IV PIVH in preterm infants is 17.0%, 12.1%, 3.3%, and 3.8%, respectively, with 1% of cases [5].

Risk factors

Germinal matrix-IVH is mostly caused by extremely low gestational age. Pregnant women who give birth before 32 weeks are considered high-risk. Asphyxia, respiratory distress, pneumothorax, pulmonary haemorrhage, choroid amnionitis, mechanical ventilation, sepsis, patent ductus arteriosus, and variations in cerebral blood flow [6]

It was shown that elevations in arterial blood pressure and the incidence of IVH were strongly correlated with changes in cerebral blood flow. Reduced haematocrit levels, hypercarbia, fast volume replacements, hypoglycemia, and disruption of cerebral autoregulation are the primary reasons for the increase in cerebral blood flow. In premature newborns with abnormally low birth weights, hypernatraemia was found to be an independent risk factor for IVH (Dalton et al.).

Cerebral blood flow fluctuation

Cerebrovascular autoregulation (CAR) is crucial for ensuring consistent and sufficient cerebral blood flow during hypotension, hypoperfusion, or hypertension [7]

- **Hypotension and Hypertension**

Irregular hemodynamic fluctuations in cerebral circulation may occur before IVH in preterm infants [8].

Preterm infants with hypotension underwent notably extended durations of cerebral hypoxia and had impaired CAR, with these traits linked to early IVH or mortality [9].

The incidence of IVH was shown to be higher in critically sick preterm newborns with pressure-passive circulation than in neonates with good autoregulation. This implies that preterm newborns are more negatively impacted by high blood pressure. A considerably higher frequency of severe IVH was linked to extreme mean arterial blood pressure (MABP) values (i.e., <23 and >46 mmHg) in preterm infants born at a gestational age of less than 30 weeks [10].

Inotropes

An inotrope, or inotropic agent, refers to a drug or substance that modifies the strength or energy of muscle contractions. Negatively inotropic agents reduce the strength of muscle contractions. Agents that are positively inotropic enhance the force of muscular contractions [11].

- **Mechanism of action**

Drugs known as vasopressors and inotropes cause vasoconstriction or enhance cardiac contractility in shock patientsor any other condition that results in abnormally low blood pressure. One of the main features of shock is a decreased blood flow to essential organs, whichcan result in multiple organ failure and eventually death [12].

Vasopressors increase contractility and heart rate, which in turn causes peripheral vasoconstriction, which raises systemic vascular resistance (SVR) and CO. Raising the SVR leads to increased organ perfusion and mean arterial pressure (MAP) [13]. By enhancing cardiac contractility, inotropes raise cardiac output (CO), supporting body perfusion and MAP.

The relationship between the two is expressed by the equation MAP = CO x SVR [14].

- Inotrope associated with intraventricular hemorrhage

Prophylactic indomethacin usage [15], limiting the number of intubation attempts for extremely preterm newborns [16], and reducing the use of inotropes are some of the strategies used to lower the incidence of severe IVH [17].

The elevated intravascular volume might correlate with a lower occurrence reduction in the use of inotropic medications (such as dopamine or epinephrine) and hypotension, both of which have been linked to the development of IVH [18].

Early inotrope use was independently linked to mortalityand/or severe brain injury in preterm children delivered before 29 weeks of gestation, and a greater prevalence of both severe and any IVH in infants born between 24 and 27 weeks was associated with the requirement for inotropic treatment within 72 hours of birth.

Conclusion

Various investigations have shown the independent effect of vasopressors on interrupting cerebral autoregulation, inotropes may be a useful predictor of how serious a patient's condition is [19]. After adjusting for confounding variables, recent research shown that using inotropes was linked to a higher risk of severe IVH rather than hypotension in and of itself [18].

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