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Intraventricular Hemorrhage in Preterm Infants, Review Article

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Abstract

Intraventricular hemorrhage (IVH) or germinal matrix (GM) in other words, is a condition that can occur in premature births and can lead to long-term medical and developmental effects. While GM/IVH can happen in full-term infants, the hemorrhage in this group of infants is different from periventricular hemorrhage (PVH)/IVH in premature infants. Family members and caregivers of preterm infants and those at risk of preterm birth are confronted with two significant uncertainties concerning these newborns: Is the survival of this child likely? Will the child experience long-term sequelae, particularly developmental sequelae, if they survive? The significance of these questions lies in their potential to impact future medical decisions, including the level of intensity in the care provided. Infants born prematurely can suffer from various acquired lesions in the central nervous system (CNS), leading to long-term disability. These lesions include GM/IVH, periventricular white matter injury, hemorrhage, and diffuse injury to the developing brain. GM/IVH continues to be a major contributor to both illness and

death in premature newborns. GM/IVH is primarily diagnosed by brain imaging techniques, typically cranial ultrasonography, as depicted below. Screening and serial examinations are essential for diagnosing GM/IVH, as it can occur without any noticeable clinical indications.

Keywords: IVH, preterm, infant, newborn, ventricles, hemorrhage.

Introduction:

Premature babies frequently have intraventricular hemorrhage (IVH), which carries a significant risk of morbidity and permanent impairment. IVH is the most common and serious neurological consequence of preterm birth which can happen about 20% to 40% of all newborns born around the world weighing less than 1500 grams. Although survival has improved, death still ranges from 30% to 60%, and those who survive run the danger of seizures, hydrocephalus, and cerebral palsy, as well as intellectual impairment [1]. IVH typically begins in the germinal matrix, a densely vascularized assemblage of neuronal-glial precursor cells in the developing brain. The intrinsic fragility of the germinal matrix vasculature and the disruption in cerebral blood flow (CBF) are the two main causes of the complex etiology of IVH [2]. Premature and critically unwell infants are surviving beyond the neonatal period thanks to advancements in neonatal medicine over the past few decades. Due to their survival at lower birth weights and earlier gestational ages, these babies are more susceptible to intraventricular hemorrhages (IVHs). Many seemingly benign care tasks have been connected to changes in cerebral blood flow patterns, which may contribute to IVHs even though alterations in cerebral perfusion have been linked to the development of severe brain bleeds [3].

One of the main risk factors for neurodevelopmental problems in preterm newborns is IVH. Few research, have looked into the connection between IVH and pregnancy problems that result in preterm delivery [4]. Germinal matrix hemorrhage (GMH) and IVH are the most prevalent neurological conditions affecting preterm infants, affecting over 12,000 babies annually in the United States. The three main neurodevelopmental aftereffects of IVH are hydrocephalus, cognitive impairments, and cerebral palsy [2]. The severity of the IVH clinical spectrum is divided into four grades by one of the most widely used classification systems: IVH grades 1 and 2 deal with minor bleeding that frequently stops on its own, IVH grades 3 and 4 deals with moderate to severe bleeding.

In Europe study have done approved that, the percentage of extremely preterm babies that experienced IVH grade 3-4 varied from 5% in 99 cases of babies delivered at less than 28 weeks' gestational age at the University Hospital of Antwerp, Belgium, to 52% in 247 cases of babies born between 25 and 28 weeks' gestational age in three Romanian hospitals between 2007 and 2010. However, a further research showed that children born between 2011 and 2014 had a significantly decreased prevalence of IVH grade 3–4 by 12% in the three Romanian hospitals. In population-based studies, the percentage of extremely preterm newborns with IVH grade 3–4 ranged from 6–8% of babies delivered at 24–27 weeks' gestational age from the Swiss Neonatal Network to 17% of babies with a birth weight of less than 1,000 g (58% born at 22–26 weeks' gestational age) in Finland. In the largest population-based investigation, among 599–1,498 children born at 23–28 weeks' gestational age in France, the incidence of IVH grade 3–4 was 11–17% [5].

A study done in USA approved that, about 12,000 preterm newborns experience IVH annually. In very low birth weight (VLBW) newborns less than 1500 gram, the incidence of IVH decreased from 40 to 50% in the early 1980s to 20% in the late 1980s Nonetheless, the incidence of IVH has not changed during the past 20 years. About 45% of neonates with extremely preterm birth weights of 500–750 gram have IVH. Thus, IVH remains a significant issue for premature infants in contemporary neonatal intensive care units (NICUs) across the globe [6].

A study done in USA between 2001 and 2007 (approved by the Institutional review Board at the University of Michigan) to identify infants with severe IVH grade three and grade four, on infants with very low birth weight >1500 gram, admitted in neonatal intensive care, found that 59% of very low birth weight infant saving during first 3 days infected by severe IVH during the first seven to ten years of life, 28% in grade three, 31% in grade four, infants with severe IVH did not exhibit complicated heart defects or a recognized brain abnormality [7].

In 2010 study done in Saudi Arabia on 35,000 preterm infant, 8% death rate was recorded related to preterm birth problems, the prevalence of IVH in premature babies born in Saudi Arabia varies from 13% to 27%. Preterm newborns risk of IVH has been demonstrated to be decreased by antenatal steroids. There are regional variations in the reported rates of prenatal steroid injection around the globe, the incidence of IVH remains high in Saudi Arabia, despite the fact that 62% to 79% of women get prenatal steroids. So it's critical to find more IVH risk factors in preterm newborns and create efficient preventative measures [8].

Pathophysiology:

The periventricular germinal matrix is where IVH typically begins. The highly vascularized collection of glial and neuronal precursor cells known as the germinal matrix is situated beneath the ventricular ependyma and on top of the caudate nucleus. In premature neonates, this periventricular area is primarily susceptible to bleeding during the first 48 hours of life. The ependyma ruptures and the cerebral ventricle fills with blood when there is a significant amount of bleeding in the germinal matrix. As a result, IVH usually follows germinal matrix hemorrhage in progression [2].

In both neonatal and adult populations, IVH is a major source of morbidity and mortality. Through mass effect and increased intracranial pressure, IVH not only immediately damages surrounding structures, but the inflammation that follows results in further brain damage and edema. Twenty to thirty percent of infants with severe IVH will go on to develop post-hemorrhagic hydrocephalus (PHH). PHH increases the risk of white matter damage, seizures, and even mortality in both newborns and adults [9]. a significant consequence of preterm birth is IVH, and a significant percentage of impairment results from massive hemorrhages or hemorrhages connected to parenchymal brain damage. If a newborn survives, massive IVH may cause hypovolemia and mortality, and huge hemorrhages may cause hydrocephalus in the survivors. The subependymal germinal matrix's capillaries, not an artery, are the source of IVH in premature newborns. Premature infants are particularly vulnerable, which is thought to be caused by: 1-a subependymal germinal matrix rich in immature vessels that are poorly supported by connective tissue; 2- significant variations in cerebral blood flow; and 3- severe respiratory issues that cause significant swings in intrathoracic and venous pressure, which are then transmitted to the fragile germinal matrix [10].

IVH Diagnosis:

In order to diagnose newborns with IVH and hydrocephalus defined as ventricular enlargement with index greater than the 97th percentile, real-time ultrasound (RT-US) has gained widespread acceptance as a dependable technique. Due to the lack of information on the ventricular system's dimensions in preterm newborns, Levene conducted a study in which he used RT-US to create reference ranges for ventricular index based on gestational age from week 26 to week 42. From the falx to the lateral wall of the lateral ventricle's body, the ventricular index is calculated. It is generally agreed upon that the “action line” to begin interventions is an index 4 mm above the 97th centile (p97+4) [11].

During the first week of life, a subependymal hyperechoic globular thickening is typically found on cranial ultrasound when bleeding is restricted to the germinal matrix (GMH). This thickening typically lasts for a few weeks. Before a diagnosis of GMH is made, both coronal and parasagittal scans should be carefully inspected, as in some situations, it may be challenging to differentiate a small subependymal GMH from the surrounding hyperechoic choroid plexus. The choroid plexus is thin in the most anterior region, filling the foramen of Monro at the level of the caudo-thalamic groove; in the posterior region, the plexus thickens and frequently exhibits pulsations. It is not visible in the lateral ventricle's frontal and occipital horns, and in coronal sections, it creates a nearly symmetrical image. The most typical site for GMH, the caudo-thalamic groove in coronal planes, has asymmetric hyperechoic thickening during the early postnatal days, which clearly implies unilateral GMH. Of course, bilateral GMH is also possible .on the other hand, hyperechoic germinolysis rather than late GMH should be suggested by an echogenicity that develops at the groove in the late neonatal era [12].

Anemia is linked to a greater death rate in intensive care units and is common in neuro-critical illnesses, manage by blood transfusion. After a week, the baby's clinical condition has improved, and a transcranial ultrasonography revealed grade I. both periventricular leukomalacia (PVL) and Post hemorrhagic hydrocephalus (PHH) are two important IVH squeals. PHH patients typically exhibit rapidly growing head

circumferences and enlarged ventricles on radiologic examinations. analysis and indications of elevated cerebral pressure, however the symptoms and Hydrocephalus symptoms might not be noticeable for a few weeks following the bleeding due to the newborn brain's cooperation [13].

RT-US is still the preferred diagnostic technique, Because of its sensitivity and specificity in identifying this pathology as well as the advantages of being a bedside examination, This approach has the drawbacks of being operator dependent and not providing continuous monitoring [11].

IVH Management:

By 10 weeks of gestation, the fetus starts to produce the coagulation proteins on its own, and as the gestational age increases, so does their concentration. Only after six months of life can the vitamin K-dependent proteins attain adult levels. It has been demonstrated that thrombin generation is lower in newborns than in older kids or adults, and that clot formation usually gets better with age. In order to lower the risk of hemorrhagic illness in neonates, vitamin K is administered as part of the current standard therapy on the first day of life, IVH of preterm remains a significant treatment problem, nonetheless. An intriguing study that bolsters our theory demonstrates that healthy preterm and small-for-date newborns do not have an increased rise in coagulation factor activity following the injection of 1 mg of vitamin K [14].

Medical intervention in the acute bleeding may involve lowering intracranial pressure (ICP) and maintaining cerebral perfusion by lowering PaCO2 and maybe utilizing medication. Nevertheless, a sizable multicenter randomized study revealed that the treatment arm's outcome was worse when acetazolamide and furosemide were used to reduce cerebrospinal fluid (CSF) production. Drainage, irrigation, and fibrinolytic therapy (DRIFT), based on the theory that lowering blood pressure, free iron, and proinflammatory and profibrotic cytokines may lower the risk of mortality and severe disability [15].

Preeclampsia (PE), also known as early-onset PE, is a dangerous pregnancy condition that is most common in the second trimester. The only curative treatment available at this time is delivery, which commonly results in very preterm (VPT) delivery for moms with early-onset PE. Finding the right balance between carrying out a pregnancy to the end, with its hazards for the health of both mother and fetus, and giving birth in the second trimester, which avoid IVH in infant with very low birth weight. It is commonly known that PE affects fetal growth and fetoplacental blood circulation. When a fetus is short for gestational age (SGA), abnormal patterns of umbilical artery blood flow velocity suggest intrauterine growth restriction brought on by placental insufficiency. Precautions should be taken into consideration during childbirth, age at delivery, parity, obstetric complications (preterm prelabor rupture of the membranes, placental abruption, placenta previa, and clinical chorioamnionitis), mode of delivery, and fetal or maternal indications for cesarean section (CS) (abnormal fetal heart rate tracing, abnormal fetal Doppler velocimetry, and breech presentation). For the PE group, the number of days that elapsed between the first AST dose and delivery was noted. Pregnancy-related diagnoses of hypertension and antihypertensive therapy (β- and calcium channel blockers or magnesium sulfate [MgSO4]) [16].

Risk factors of IVH in preterm infant:

We discovered that hypoxia is one of the elements that raise the possibility of severe IVH. Hypercapnea and an oxygen shortage are caused by irregular gas exchange, which is linked to asphyxia. Asphyxia is listed as one of the main risk factors for IVH in a children delivered before week 37 of gestation and infants weighing less than 1500 g. severe hypoxia, which is defined as an Apgar score of ≤3 at 1 and 5 minutes [17]. Neonatal brain injury including IVH, is closely linked to infections and inflammatory responses. The chance of periventricular\intraventricular hemorrhage in premature infant worsening was more than three times higher in mothers with fewer genital tract infections. Sepsis, funisitis, and chorioamnionitis can raise a preterm infant's risk of developing PV-IVH. One of the key ways that intrauterine infections spread is through maternal lower reproductive tract infections. Newborns with PV-IVH worsening had higher ratios of elevated white blood cell (WBC) count and C-reactive protein (CRP) level in addition to the ratio of mother lower reproductive tract infection. The idea that cytokines generated during prenatal infection are a direct cause of harm to the developing brain is supported by recent clinical and experimental data. PV-IVH risk was found to be higher in preterm newborns with elevated cytokine levels [18].

Preterm birth risk factors are often associated with an increased incidence of IVH. One well-researched risk factor for preterm birth is multiple births. If multiple births and IVH are causally related, then there should be a substantial risk of IVH even when gestational age is taken into account. However, after gestational age was taken into account, having multiple births was not shown to be a risk factor for IVH [19].

Conclusion:

Intraventricular hemorrhage in the preterm infant is critical issue that have high prevalence overall the world in preterm infant; there is no proven cure for IVH, and the intrusive procedures carry a significant risk of infection. Furthermore, little information exists about how invasive and non-invasive techniques affect the long-term results of neurodevelopment. Numerous neonatal intensive care unit have recently implemented a number of strategies, including caesarean delivery, delayed cord clamping, minimal handling of infants, avoiding head down position, head positioning in the midline for 72 hours, maintaining the head of the bed raised at 15 to 20 degrees, slow fluid infusion, and prenatal corticosteroid administration for the prevention of IVH, provide highly qualified incubator in hospitals for preterm infant. It will be particularly beneficial in managing IVH and its related mortality as well as long term neurodevelopment results once the standard treatment is established.

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