Analysis of intracranial hemorrhage grade in preterm singleton pregnancies delivered vaginally or by cesarean section

Analiza stepena intrakranijalnih hemoragija kod preterminskih monofetalnih trudnoća završenih vaginalnim putem ili carskim rezom

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Abstract

Background/Aim. Preterm birth is the leading cause of neonatal mortality. Periventricular hemorrhage–intraventricular hemorrhage (PVH–IVH) remains a significant cause of both morbidity and mortality in infants prematurely born. The aim of the study was to evaluate the perinatal outcome regarding IVH of premature babies according to the mode of delivery. Methods. A total of 126 women in preterm singleton pregnancies with vertex presentation and 126 neonates weighted from 750 g to 1,500 g at birth were enrolled. The outcomes of 64 neonates born vaginally were compared to 62 neonates born by cesarean section. Results. There was no significant difference in the incidence of IVH among both groups. Conclusion. Our data is consistent with the hypothesis that the mode of delivery does not influence IVH and consequently perinatal outcome in preterm neonates.

Key words: intracranial hemorrhages; infant, premature delivery, obstetric; cesarean section; mortality.

Introduction

Premature birth is one of the most delicate conditions in reproductive medicine. It is responsible for a large percentage of early neonatal death and early and/or late neonatal morbidity. Problems that may occur in premature born babies are related to organic immaturity and directly to gestational age. The most significant morbidity includes respiratory distress syndrome, persistent ductus arteriosus, bronchopulmonary dysplasia, necrotizing enterocolitis, intraventricular hemorrhage, retinopathy, hyperbilirubinemia and neonatal sepsis. In contrast to the period two decades ago, when the survival of these children was accompanied by a significant rate of disability (blindness, cerebral palsy or mental retardation), today the risk for disabilities exists in newborns weight below 1,500 g and lower gestational age.

Statistically, the percentage of premature births has not significantly decrease in recent decades, despite drug therapy, cerclage application or bed rest. Despite the known risk factors for preterm birth: socioeconomic status, preterm membrane rupture, infection, maternal medical or obstetric complications, a large percentage of women can be classified into a group of patients with so-called idiopathic preterm labor. The pathophysiology of preterm labor initiation is unknown, but there are three possible theories: progesterone theory, the theory considering oxytocin initiating factor and oxytocin...
the theory of organic communication, based on the fact that amniotic fluid contains many substances (prostaglandins, arachidonic acid, platelet activating factor and cytokines) whose activation initiates labor.\textsuperscript{5,6}

Different authors make different risk-scoring systems in order to identify the risks for preterm birth.\textsuperscript{7–9} Despite the applied criteria for the detection of preterm delivery, the diagnosis remains difficult. Cervical dilatation, as one of the important clinical signs, may not be accompanied by registered uterine activity and vice versa. More than 80% of women treated for premature delivery, gave birth at term, because uterine activity (Braxton-Hicks contractions) was not accompanied by cervical changes.\textsuperscript{10} The use of tocolytic therapy, which may be applied in 17–20 weeks of gestation in women at high risk for preterm delivery, is widespread in the last 3–4 decades. Different agents are used to inhibit preterm delivery: beta-agonists, prostaglandin inhibitors, nitric oxide donor drugs, etc. For many of these agents there are data on their benefits in terms of extending the duration of gestation, but the accuracy of such data is questionable because it is difficult to make the diagnosis of premature birth. There is also a lack of data on the possible impact of these agents to the rate of perinatal morbidity and mortality. Many reports talk about the metabolic complications of prematurity: maternal hypokalemia and hyperglycemia and neonatal hypoglycemia.\textsuperscript{11}

Prematurity is an important predisposing factor for the occurrence of cerebral damage in the neonatal period and neurological sequelae are three times more frequent than in term neonates. A damage is caused by anatomical and physiological events in the brain, depending on the degree of maturation. Brain state blood vessels, cerebral tissue specificity and cerebrovascular autoregulation are the basis for understanding hemorrhage and hypoxic-ischemic cerebral changes in neonates.

Subependimal germinative matrix, formed between 10 and 20 weeks of gestation, is located lateral to the chamber system, proliferates in fetus during pregnancy and is responsible for the maturation of fragile blood vessels.\textsuperscript{12} In early gestation the endothelium of blood vessels is thin, the vessels are prone to rupture. Over 80% of periventricular-intraventricular hemorrhage (PVH-IVH) can be explained by developments in the germinative matrix. The structure of arteries in the premature brain is responsible for hypoxic-ischemic changes. A relative resistance of the cerebral cortex to the development of hypoxic-ischemic stroke can be explained by rich anastomosis between meningeal arteries.

The pathogenesis of PVH-IVH is multifactorial and refers to intravascular, vascular and extravascular factors: cerebral blood flow disorder, increased cerebral venous pressure, coagulation disorder, fragile germinative vascular matrix, increased fibrinolytic activity and possible reduction of extravascular tissue pressure. Intrapartal asphyxia is relatively common and follows a high rate of incidence of neonatal cardiorespiratory problems.

Unconjugated hyperbilirubinemia of newborns with a deposit of bilirubin in the basal ganglia (kernicterus) can lead to microscopic neuronal destruction in the brain. Although not proven that previously determined risk factors: sepsis, asphyxia, acidosis, hypoglycemia and hypothyroidism, may be the cause of kernicterus, it cannot be prevented and in premature infants it presents risk for cerebral damage.

Prevention of neonatal cerebral hemorrhage can be divided into: antepartal (prevention of prematurity, intrauterine transport and pharmacological therapy – phenobarbital and vitamin K), intrapartal and postpartal.

According to the literature, the mode of delivery does not affect the development of neurological sequelae in neonates below the weight of 1250 g.\textsuperscript{4} Another study, for the same weight, indicates that the mode of delivery has no effect on neonatal mortality in vertex presentation, but also indicates that neonatal mortality is significantly lower after cesarean section in malpresentations.\textsuperscript{1} The same study, for the neonatal weight of 1,250 g to 1,500 g indicates a higher neonatal mortality, but not significantly after cesarean section. Another study suggests that the method of delivery did not affect the incidence of IVH in the neonates under 2,500 g.\textsuperscript{13} Other authors conclude that the duration of active phase of labor carries greater risk of PVH-IVH than the method of labor.\textsuperscript{14} A long-term uterine activity is a mechanical force that can lead to cerebral venous pressure elevation. Also, uterine contractions lead to an increase in fetal blood pressure resulting in the simultaneous increase in cerebral flow of preterm fetus who has immature cerebral autoregulation.

A relation between the occurrence of neonatal intraventricular hemorrhage and the mode of delivery is controversial, according to numerous studies. According to some studies, the risk of PVH-IVH is significantly reduced in neonates born by cesarean section, while other authors believe that cesarean section should be done only in extreme prematurity (28 weeks or less). Considering specific factors in the etiopathogenesis of PVH-IVH, the mode of delivery is determined by individual and optimal procedure.

The aim of this study was to evaluate the perinatal outcome of preterm newborns, in terms of the occurrence of IVH, compared to the mode of delivery. The study excluded malpresentations, as well as women with fetal intrauterine growth retardation.

**Methods**

A total of 126 women in preterm singleton pregnancies with vertex presentation and 126 neonates weighted from 750 g to 1,500 g at birth were enrolled. The outcomes of 64 neonates born vaginally were compared to 62 neonates born by cesarean section. We analyzed the rate of neonatal IVH compared to the mode of delivery, women’s age, gestational age, use of tocolytic therapy and dexamethasone use. Neonatal outcomes were monitored by the appearance of IVH.

The data from this study were statistically analyzed and presented as figures and tables.

**Results**

We analyzed the occurrence of neonatal IVH in relation to the mode of delivery and the results were presented in Table 1.

Occurrence of the intraventricular hemorrhage (IVH) in relation to the mode of delivery

<table>
<thead>
<tr>
<th>Type of delivery</th>
<th>IVH [n (%)]</th>
<th>Total number of newborns (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginal</td>
<td>No 20 (31.3)</td>
<td>Yes 44 (68.8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>64 (100.0)</td>
</tr>
<tr>
<td>Cesarean section</td>
<td>No 27 (43.5)</td>
<td>Yes 35 (56.5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>62 (100.0)</td>
</tr>
<tr>
<td>Total</td>
<td>47 (37.3)</td>
<td>79 (62.7)</td>
</tr>
</tbody>
</table>

There was no statistically significant difference in the incidence of IVH in newborns compared to the mode of delivery, but a slightly higher percentage of IVH in vaginally born neonates was found.

Figure 1 shows the incidence of IVH in newborns as compared to the age of mothers.

Mother’s age not affect the incidence of IVH in neonates, regardless the mode of delivery.

The effect of the applied tocolytic therapy on the incidence of IVH is presented in Table 2.

Tocolytic use and the incidence of the intraventricular hemorrhage (IVH)

<table>
<thead>
<tr>
<th>Tocolytics use</th>
<th>IVH [n (%)]</th>
<th>Total number of newborns (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>No 21 (30.9%)</td>
<td>Yes 47 (69.1%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>68 (100)</td>
</tr>
<tr>
<td>Yes</td>
<td>No 26 (44.8%)</td>
<td>Yes 32 (55.2%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>58 (100)</td>
</tr>
<tr>
<td>Total</td>
<td>47 (37.3%)</td>
<td>79 (62.7%)</td>
</tr>
</tbody>
</table>

In the monitored groups, there was no statistically significant difference regarding the use of tocolytic therapy and the incidence of IVH, regardless the mode of delivery.

Analysis of the dexamethasone use in relation to the incidence of neonatal IVH is presented in Table 3.

The use of dexamethasone in relation to intraventricular hemorrhage (IVH)

<table>
<thead>
<tr>
<th>Dexamethasone use</th>
<th>IVH [n (%)]</th>
<th>Total number of newborns (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>No 38 (37.3%)</td>
<td>Yes 64 (62.7%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>102 (100)</td>
</tr>
<tr>
<td>Yes</td>
<td>No 9 (37.5%)</td>
<td>Yes 15 (62.5%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>24 (100)</td>
</tr>
<tr>
<td>Total</td>
<td>47 (37.3%)</td>
<td>79 (62.7%)</td>
</tr>
</tbody>
</table>

There was no statistically significant difference in the incidence of IVH in relation to the use of dexamethasone.

Analysis of the incidence of IVH in preterm newborns from vaginal deliveries and cesarean section in relation to the gestational age is presented in Table 4.

Gestational age and the incidence of IVH

There was no statistically significant difference in the incidence of IVH in the preterm newborns from vaginal deliveries and cesarean section in relation to the gestational age, but there was a higher incidence of IVH in vaginal delivery of lower gestations.

In relation to the newborns body weight the incidence of IVH was monitored according to the mode of delivery and the results were presented in Figure 2.

There was statistically significant difference in the incidence of IVH regarding the body weight of newborns.

Discussion

Prematurity is an important predisposing factor for the occurrence of cerebral damage in the neonatal period and
neurological sequelae are three times more frequent than in term neonates. A damage is caused by anatomical and physiological events in the brain, depending on the degree of maturation. Blood vessels state of the brain, cerebral tissue specificity and cerebrovascular autoregulation are the basis for understanding hemorrhage and hypoxic-ischemic cerebral changes in neonates.

The mode of delivery is one of major concerns in preterm birth modern obstetrics. It depends on obstetric indications, severity of maternal diseases and facility of hospital. Recommendations of mode of delivery in preterm birth still remain controversial and not yet clearly established. Some studies show a significant beneficial effect of cesarean delivery on neonatal mortality. Other studies report that mode of delivery affected very little adverse neonatal outcomes, either mortality or psychomotoric outcomes. There are limited studies evaluating the association between mode of delivery and neonatal outcomes in preterm birth.

The purpose of this study was to compare neonatal outcomes between modes of delivery in preterm births.

The main finding in this study is that the mode of delivery had no influence on the incidence of IVH in preterm neonates with vertex presentation. However, we registered a higher percentage of IVH at vaginal delivery compared to cesarean section at lower gestational age (from 29 to 31 weeks) and in relation to lower body weight of newborns that is consistent with the literature data.

Mother’s age does not affect the incidence of neonatal IVH, regardless the mode of delivery.

Meta-analysis from Haas et al. stated that administration of β-mimetics may facilitate a 48 h delay in delivery in comparison with no treatment/placebo, but do so at the cost of placing both the mother and fetus/neonate at greater risk of unwanted side effects than other types of tocolytics. It is also stated that the use of β-mimetic agents has been associated with an increased risk of many neonatal side effects including neonatal intraventricular hemorrhage. However, our study failed to confirm these data, since the results indicate that the tocolytic use (beta agonists) did not affect the incidence of IVH.

Our study indicates that the use of corticosteroid therapy has no effect on reducing the occurrence of IVH, despite some studies showing that corticosteroids reduce the incidence of IVH.

Although the majority of premature children had a low degree of IVH (I and II level), long-term prognosis is unpredictable.

We think that the mode of delivery in preterm birth should be determined by individual and optimal procedure.

Conclusion

Our data is consistent with the hypothesis that mode of delivery does not influence IVH and consequently perinatal outcome in preterm neonates.

REFERENCES


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