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Future perspectives on neonatal brain injury

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Abstract

Neonatal brain injury (NBI) is a complex and challenging area of research and critical care. Advances in understanding and treating NBI are crucial for improving the long-term adverse neurological outcomes of the affected neonates. Future perspectives in NBI are focused on systematic antenatal education, personalized medicine and profiling, stem cell and neuroprotective therapies, biomarkers in biological fluids with an emphasis on multimodal biomarker panels, collaborative research projects and considerations regarding ethical issues. Although substantial efforts have been made recently to restrain NBI, its incidence is still high on a global scale. Therefore, future management of NBI will involve a multidisciplinary approach that integrates genetics, individualized therapy, and medical advancements, with particular attention to early detection and intervention. The ultimate goal is to reduce the prevalence of NBI and improve the affected neonates' long-term prognosis. It is critical to remember that this field of study is still being investigated, and it could be years before many of these advancements are widely applied in standard clinical practice.

Keywords: Future perspectives; Neonatal; Brain; Injury; Advancements

1. Introduction

Neonatal brain injury (NBI) refers to damage or abnormalities in the brain of a neonate, typically occurring within the first few days or weeks of life. In neonates, NBI is a leading cause of mortality and morbidity and is strongly associated with significant impacts on the child's development and long-term adverse neurological outcomes [1, 2]. There are several potential causes of NBI but it is usually a complex and multifactorial clinical situation.

More specifically, hypoxia-ischemia is one of the most common causes of NBI, occurring when there is a lack of oxygen (hypoxia) and blood flow (ischemia) to the neonate's brain. This may result from perinatal complications such as prolonged labor [3].

Maternal infections or infections acquired by the neonate after birth can lead to brain injury mainly through inflammation [4]. Furthermore, prematurity, metabolic and certain genetic disorders can make a neonate more susceptible to brain injury or increase the risk of developmental issues [5]. Brain damage can also occur in neonates following trauma, such as head injuries resulting from accidents [6].

Exposure to toxins or drugs during pregnancy or after birth can harm the developing brain as well [7]. The consequences of NBI can vary widely, depending on the type, severity, and location of the injury. Common outcomes include

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developmental delays, intellectual disabilities, cerebral palsy, seizures, and other neurological problems [8, 9]. Early diagnosis and intervention are crucial for managing and mitigating the effects of NBI. Treatment may include medications, therapy (physical, occupational, and speech therapy), and supportive care to address the specific needs of the child. It is understandable that importance should be attached to the reduction of NBI's incidence and this may be achieved by preventive measures, such as systematic prenatal care to reduce the risk of premature birth [10] and ensuring a safe birthing environment. Healthcare professionals should closely monitor high-risk pregnancies and neonates to detect and address any potential issues promptly.

The field of NBI research continues to evolve and thus we aim to demonstrate several promising future perspectives and trends that may shape our deeper understanding of NBI. It is essential to consider advances in prevention, diagnosis, treatment and long-term management.

2. Antenatal education

Antenatal education plays a crucial role in preventing NBI by equipping expectant parents with the knowledge and skills necessary to promote a healthy pregnancy, labor, and delivery. Looking into the future, several key perspectives and trends in antenatal education to prevent NBI can be identified.

Personalized education, for instance, can become more prevalent. This can involve assessing risk factors and genetic predispositions to identify potential issues early and provide targeted information and support to parents. Tailoring antenatal classes to individual needs may also give emphasis on perinatal mental health. Addressing maternal mental health during pregnancy is critical as stress and depression have been significantly correlated with neonatal health [11, 12]. Such classes may likely include modules on stress reduction, emotional well-being, and coping strategies. Antenatal education may also incorporate sessions regarding potentially dangerous environmental factors that can impact on neonatal health, like exposure to toxins and microorganisms. Moreover, a focus on maternal nutritional education is undoubtedly vital as emphasizing the importance of a balanced diet, appropriate weight gain, and the avoidance of harmful substances, such as alcohol and tobacco, may contribute to the reduction of neonatal morbidity [13, 14]. The integration of advanced technology (e.g. virtual reality, telemedicine) can enhance antenatal education. These tools can provide realistic simulations of labor and delivery, helping parents understand potential complications and the importance of medical interventions, midwifery care and interdisciplinary approach. Technology can additionally support remote learning via online antenatal education programs, whose demand is constantly increasing as they provide accessible and convenient options for parents who may have limited access to in-person classes due to geographical or other constraints [15-17]. Ensuring that antenatal education is accessible to all parents, considering also cultural factors and population diversities, must be a future priority. Efforts to reduce disparities in access to education and healthcare resources will play a crucial role in preventing NBI. Lastly, antenatal education will increasingly emphasize the importance of building a support network for expectant parents. Connecting with other parents and support groups can provide emotional support and valuable insights [18].

In summary, the future of antenatal education to prevent NBI will be marked by personalization, technological advancements, evidence-based practices, a holistic approach to maternal and neonatal health, and a commitment to addressing the diverse needs of expectant parents. By staying up-to-date and adapting to these trends, along with campaigns which raise awareness, healthcare providers and educators can play a significant role in reducing the incidence of NBI.

3. Personalized medicine and profiling

Personalized medicine and profiling in NBI represent promising areas of research and clinical development with significant potential to improve the diagnosis, treatment, and long-term outcomes of neonates at risk of or affected by brain injuries. Future perspectives in this field include genomics, pharmacogenomics, and biomarker profiling [19] in neonatal care. These will allow for the identification of genetic predispositions and specific biomarkers associated with NBI as well as the determination of the most effective and safe medications for treating brain injuries while minimizing potential side effects [20]. Understanding deeper the underlying causes and individual variations in NBI, targeted and precision therapies will become more common. This could include gene therapies, stem cell-based treatments, and neuroprotective interventions tailored to each neonate's needs. All these areas which aid in early diagnosis and personalized treatment strategies, will become increasingly important in future neonatal medicine. Artificial intelligence algorithms will play a pivotal role in analyzing numerous and complex data from various sources, including imaging, genetic, and clinical data. These algorithms can help identify patterns, predict outcomes, and optimize treatment plans tailored to each neonate [21].

Personalized medicine will extend beyond the acute phase of NBI. There will be a greater focus on long-term follow-up and rehabilitation programs designed to address the unique needs of each child based on their injury profile and developmental trajectory. Telemedicine and remote monitoring technologies will enable continuous tracking of neonates at risk for brain injuries, even after discharge from the hospital. This can help identify any signs of deterioration or the need for intervention in real-time [22]. Future comprehensive neonatal care will be in need of incorporating multidisciplinary collaboration, empowering families with information about personalized medicine options and involving them in decision-making processes and considering ethical and legal aspects, including consent for genetic testing, data privacy, and equitable access to cutting-edge treatments and diagnostics.

In conclusion, the future of personalized medicine and profiling in NBI holds immense promise for improving outcomes and reducing the long-term impact of brain injuries. Advances in technology, genomics, and data analysis, coupled with ethical considerations and a family-centered approach to neonatal care, will drive progress in this field.

4. Stem cell therapy

Stem cell therapy is a promising field of research for treating NBI as it offers a potential avenue for regenerating damaged brain tissue and improving outcomes. Mesenchymal stem cells can be derived from various sources, including umbilical cord blood, bone marrow, and placental tissue. They have been studied for their anti-inflammatory and neuroprotective properties which can help reduce further damage to the neonatal brain [23]. Neural stem cells have the potential to differentiate into various neural cell types and are being investigated for their ability to replace damaged neural tissue and promote recovery [24].

Preclinical studies in animal models have shown promising results, demonstrating the safety and efficacy of stem cell therapy in reducing brain injury and improving neurological function [25]. However, safety concerns, ethical and regulatory considerations surrounding the use of stem cells in neonates, must be addressed in human trials. Ongoing research aims to refine the protocols for stem cell therapy, optimize the choice of stem cell type, and establish the best routes of administration [26]. Combination therapies, including stem cells and other interventions, may hold promise for enhancing recovery.

While stem cell therapy for NBI is still in the experimental stage, it offers hope for improving outcomes in neonates being affected by such devastating conditions. Collaborative efforts between researchers, clinicians, and regulatory bodies are essential to further advance this field and ensure the safety and efficacy of these treatments. Neonates' families should consult with healthcare professionals and consider participating in clinical trials when appropriate to access the latest developments in stem cell therapy for NBI.

5. Neuroprotective Therapies

In the last few years, much more information on neuroprotective therapies has become available. This may include pharmacological agents, therapeutic hypothermia and other novel interventions designed to reduce inflammation, excitotoxicity and oxidative stress in the developing brain. Therapeutic hypothermia is currently one of the standard treatments for neonatal hypoxic-ischemic encephalopathy. Future developments may involve refining the timing, duration, and depth of cooling to optimize neuroprotection and minimize potential complications [27]. Moreover, modulating the inflammatory response in the neonatal brain is a critical focus. Immunomodulatory agents and anti-inflammatory strategies are being investigated to reduce the detrimental effects of neuroinflammation [28]. Growth factors and neurotrophic factors are being explored for their potential to promote neurogenesis and repair damaged neural tissue in experimental animal studies [29]. Nevertheless, in the future, a combination of pharmacological and non-pharmacological brain-focused clinical practices might be considered as the most promising protection and/or treatment provided in clinical practice to neonates at high risk of neuronal injury [30].

Emerging trends in neuroprotective therapies comprise also non-invasive brain stimulation. Techniques like transcranial magnetic stimulation and transcranial direct current stimulation are being investigated for their ability to enhance neuroplasticity and promote recovery in brain injury [31]. It is important to note that integrating novel neuroprotective therapies into clinical practice will require rigorous testing, regulatory approval, and consideration of ethical and safety concerns. Nonetheless, continuous research and innovations offer hope for improved outcomes and a better quality of life for neonates diagnosed with NBI.

6. Biomarkers

The field of biomarkers and NBI is constantly evolving and continuous advances are being made regarding biomarkers that predict the risk for NBI and enable rapid assessment in biological fluids. Early detection and diagnosis of NBI at its earliest stages, form primary goals for the early neonatal period as this would enable healthcare professionals to intervene promptly, potentially reducing the severity of the injury and improving long-term outcomes. Besides, individualized care and support planning may be provided. Furthermore, biomarkers may help guide potential treatment options, monitor progress and the effectiveness of therapeutic interventions [19, 32, 33]. Lastly, multimodal biomarker panels can provide a more comprehensive picture of NBI and thus, improve diagnostic accuracy and predictive power [2, 32, 34]. Nevertheless, the use of biomarkers in neonatal care should be standardized as they become more established. Guidelines and protocols should be developed and integrated into daily clinical practice.

7. Collaborative Research Efforts

Collaborative research efforts in NBI are essential for advancing our understanding of this complex and critical medical condition. Since NBI is a global issue, international collaborations are essential for understanding regional variations, sharing best practices, and addressing disparities in healthcare and research [35]. Collaborative research may also involve multiple institutions, researchers, healthcare professionals, and stakeholders working together to address various aspects of NBI. Multidisciplinary teams often involve experts from various disciplines, including neonatology, pediatrics, neurology, neurosurgery, radiology, nursing, midwifery and psychology [21, 30]. These teams can offer a comprehensive perspective on NBI. Besides, research consortia bring together researchers and institutions to work on NBI and facilitate as well, data sharing, access to patient populations, and the pooling of resources for large-scale studies. Establishing patient registries will help track neonates' outcomes, identify trends, and form future research directions [36].

Conducting multi-center clinical trials is essential to evaluate the effectiveness of potential interventions or treatments for NBI. Collaborative trials can enroll a larger and more diverse patient population, increasing the reliability of results [37]. Collaborations between basic science researchers and clinical researchers/providers should be encouraged as they may help bridge the gap between laboratory findings and clinical applications [38]. Understanding the cellular and molecular mechanisms underlying NBI is crucial for developing targeted treatments. Similarly, translation of research into practice has become a central issue in recent years. Disseminating research results, developing clinical guidelines, and training healthcare professionals in evidence-based practices utilizes research findings in clinical practice [39]. Finally, the input of families in the research process may help shape research priorities, improve study design, and ensure that research outcomes are patient-centered. Research collaborations undoubtedly help leverage the collective expertise and resources of multiple stakeholders, ultimately leading to better prevention, diagnosis, and treatment strategies for NBI.

8. Future ethical considerations

Neonatal brain injury raises a range of ethical considerations that are complex and sensitive. With the advancements of medical technologies and health sciences, ethical concerns regarding decision-making, consent, and the allocation of resources in neonatal critical care will continue to evolve [40].

Ensuring equitable access to treatments and respecting the autonomy of parents will be future challenges. It will remain ethically challenging to obtain informed consent for treatments, with parents and caregivers needing to be fully informed about their child's long-term consequences. Healthcare resources may continue to be limited, so ethical questions regarding how to allocate them fairly will remain relevant. Several ethical issues will arise regarding acceptable quality of life, who should make decisions about life-sustaining treatments, and when treatment should be withheld or withdrawn [40, 41]. There will be ethical considerations surrounding the appropriate use of genetic information, who should have access to it, and how to safeguard the privacy of the neonate and its family [42]. The best interests of the neonate shall be prioritized while respecting various cultural customs and traditions [43]. Last but not least, palliative and end-of-life care will continue to have a significant contribution to critical-ill neonates and their families. For the benefit of the neonate, decisions about when to switch from curative to palliative care must be made carefully [44].

9. Conclusion

Neonatal brain injury is a multifactorial and complicated situation. Although significant efforts have been made in recent years to restrain it, its prevalence remains globally high. In the future, NBI will be managed by a multidisciplinary strategy that combines genetics, customized treatment, and breakthroughs in medicine, with an emphasis on early detection and intervention. In the end, the objective is to lower the incidence of NBI and enhance the long-term optimal prognosis for affected neonates. It's crucial to keep in mind that research in this area is ongoing, and it might be years before many of these developments are widely used in routine clinical practice.

Compliance with ethical standards

Disclosure of conflict of interest

All authors declare that they have no conflicts of interest.

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