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Biomarkers of hypHypoxic-ischemic encephalopathy in umbilical cord blood: a systematic review

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ADMINISTRATIVE INFORMATION

Support - ALF.

Review Stage at time of this submission - Risk of bias assessment.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 28 October 2024 and was last updated on 28 October 2024.

INTRODUCTION

Review question / Objective Could elevated biomarkers in umbilical cord blood correlate to the degree of hypoxic ischemic encephalopathy?

Rationale Hypoxic ischemic encephalopathy (HIE) is one of the most common causes of morbidity and mortality. Biomarkers detectable in umbilical cord blood, to guide diagnoses and prediction, would be a valuable support to clinical decision-making in the crucial timeframe for starting therapeutic hypothermia. The aim of this systematic review is to do a summary of the research done of biomarkers in umbilical cord blood and HIE over the last decades.

Condition being studied Hypoxic ischemic encephalopathy.

METHODS

Search strategy An article search was conducted in four different databases on 10 May 2021: PubMed, Embase, Cochrane Library and Cinahl. Updated searches were done on 17 April 2023 and 1 March 2024.
MeSH terms: Brain injury, Hypothermia, Hypoxic ischemic encelphalopathy, Newborn hypoxia, Brain hypoxia, Asphyxia, Brain damage, Biological markers, Interleukins, Neonatal, Newborn, Perinatal, Umbilical cord, Umbilical cord blood, Cord blood, Umbilical blood, Inflammation mediators and Infant.

Participant or population The population was term newborns, ≥35 weeks, with intrapartum asphyxia.

Intervention The intervention was measured levels of biochemical asphyxia markers in umbilical blood.

Comparator Healthy term newborns without HIE, neonatal encephalopathy (NE) or PA.

Study designs to be included Cohort studies and case-control studies.
Eligibility criteria Exclusion criteria: Reports with a population that was preterm and/or low gestational weight were excluded.
So were studies analyzing blood that was not from the umbilical cord, urin or cerebrospinal fluid (CSF). Studies that had other outcome than HIE were also excluded.

Information sources Electronic databases.

Main outcome(s) Hypoxic ischemic encephalopathy.

Additional outcome(s) Hypothermia, neonatal seizures, death of the baby (intrapartal, neonatal or perinatal), Cerebral pares, serious perinatal morbidity or death (composite outcome as reported in studies), hypothermia treatment, NICU or Apgar < 4 at 5 minutes.

Data management We conducted a systematic review following the PRISMA guidelines.
Records identified from: PubMed (n = 162); Embase (n = 171); Cochrane Library (n = 25); Cinahl (n = 59).
Records removed before screening: Duplicate records (n = 145).
Records screened (n = 272).
Records excluded (n = 198)
Reports sought for retrieval (n = 74).

Quality assessment / Risk of bias analysis Quadas 2.

Strategy of data synthesis Information about location, type of study, biomarker, the technique used to analyze the biomarker, diagnostic criteria, the assessment of the grade of HIE, inclusion criteria, exclusion criteria, sample size, if it was arterial, venous or mixed cord blood that was analyzed, p-value, AUC, and if bed-side test is available will be extracted.

Subgroup analysis Long term follow up outcome.

Sensitivity analysis Area under the receiver operating characteristic curve.

Language restriction Our search was limited to reports published in English.

Country(ies) involved Sweden.

Keywords Perinatal Asphyxia, Umbilical cord blood, Biomarkers, Hypoxic ischemic encephalopathy.

Contributions of each author
Author 1 - Hanna Toorell - The search strategy and study eligibility were performed by HT and YC. Disagreements were resolved by consensus of HT, YC and HH. Quality assessment were performed by HT, YC and HH. The evaluation was performed independently by HT, YC and HH.
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Author 2 - Ylva Carlsson - The search strategy and study eligibility were performed by HT and YC. Disagreements were resolved by consensus of HT, YC and HH. Quality assessment were performed by HT, YC and HH. The evaluation was performed independently by HT, YC and HH.
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Author 3 - Henrik Hagberg - The search strategy and study eligibility were performed by HT and YC. Disagreements were resolved by consensus of HT, YC and HH. Quality assessment was performed by HT, YC and HH. The evaluation was performed independently by HT, YC and HH.
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