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Exploring the Correlation Between MAGIC Values in Lesion Areas and Serum Bilirubin in Neonates with Hyperbilirubinemia Using Magnetic Resonance MAGIC Imaging Technology

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Abstract: ***Objective:*** *To investigate the application value of magnetic resonance MAGIC (Multi-Acquisition Gradient Echo Imaging with Contrast) imaging in neonatal hyperbilirubinemia, analyze the correlation between MAGIC values in cerebral regions of interest (ROI) and total serum bilirubin (TSB) levels, and evaluate the potential of MAGIC imaging for early identification of bilirubin-induced brain injury.* ***Methods:*** *A retrospective collection of 62 full-term neonates with hyperbilirubinemia admitted to our hospital's neonatal department from January 2022 to June 2024 was conducted. Patients were categorized into mild (TSB <257 μmol/L), moderate (257 μmol/L ≤ TSB <342 μmol/L), and severe (TSB ≥342 μmol/L) groups based on TSB levels. Additionally, 20 healthy full-term neonates without jaundice or neurological abnormalities were selected as controls. All subjects underwent cranial MAGIC sequence scans within 72 hours to 14 days after birth. ROIs were manually delineated in the bilateral globus pallidus, putamen, and thalamus to measure MAGIC values. Peak TSB levels were recorded for each group. One-way ANOVA was used to compare MAGIC value differences across groups, and Pearson correlation analysis was performed to assess the relationship between globus pallidus MAGIC values and peak TSB levels.* ***Results:*** *The MAGIC values of the bilateral globus pallidus in the severe hyperbilirubinemia group were significantly higher than those in the control group, mild group, and moderate group, with statistically significant differences (P < 0.05). No statistically significant differences in MAGIC values were observed among groups in the putamen and thalamus (P > 0.05). The MAGIC values of the globus pallidus showed a significant positive correlation with peak serum TSB levels (r = 0.726, P < 0.001).* ***Conclusion:*** *MAGIC magnetic resonance imaging can quantitatively detect signal changes in the globus pallidus. The MAGIC values of the globus pallidus exhibit a clear correlation with serum total bilirubin levels, making them a non-invasive imaging indicator for early screening and assessment of neonatal bilirubin-induced brain injury.*

Keywords: Newborn, Hyperbilirubinemia, Bilirubin Encephalopathy, Magnetic resonance imaging, MAGIC, Globus pallidus.

1. Introduction

Neonatal hyperbilirubinemia is one of the most common conditions during the neonatal period. A large amount of unconjugated bilirubin can cross the blood-brain barrier and deposit in the basal ganglia region, particularly the globus pallidus, causing neuronal damage. In severe cases, it progresses to bilirubin encephalopathy, resulting in permanent neurological sequelae such as hearing impairment, cerebral palsy, and intellectual disability. Conventional MRI routine sequences have limited sensitivity for early bilirubin-induced brain injury. Signal abnormalities are often detected only after significant neurological symptoms appear, making early warning challenging.

MAGIC imaging is a multi-echo gradient echo quantitative magnetic resonance technique that enables quantitative measurement of tissue susceptibility-related signals. It is sensitive to trace substance deposition and microscopic susceptibility changes in brain tissue, allowing detection of microscopic brain alterations even when conventional MRI reveals no significant morphological abnormalities. Current research on MAGIC in neonatal bilirubin-induced brain injury remains limited. This study employs MAGIC imaging to quantitatively measure MAGIC values in the basal ganglia region, analyzing their correlation with serum total bilirubin levels, with the aim of exploring the clinical application value of MAGIC imaging in the early diagnosis of neonatal bilirubin-induced brain injury.

2. Materials and Methods

2.1 Research Subject

A total of 62 term neonates with hyperbilirubinemia admitted to the Department of Neonatology at our hospital from January 2022 to June 2024 were retrospectively enrolled.

Inclusion criteria: 1) Gestational age 37-42 weeks (term neonates); 2) Birth weight 2500-4000g; 3) Clinically confirmed neonatal hyperbilirubinemia; 4) Completed cranial MAGIC MRI scan with qualified image quality; 5) Complete dynamic monitoring data of serum total bilirubin, recording peak TSB levels.

Exclusion criteria: 1) Premature birth or low birth weight; 2) Complicated by intracranial hemorrhage, hypoxic-ischemic encephalopathy, or congenital brain malformations; 3) Infectious meningitis or inherited metabolic disorders; 4) Motion artifacts in images preventing ROI measurement; 5) Incomplete clinical data.

Control group: 20 healthy term neonates without jaundice during the same period, showing normal neurological examinations, no history of perinatal asphyxia, and no abnormalities on cranial MRI.

Grouping: Mild group with 22 cases, moderate group with 21 cases, severe group with 19 cases, and control group with 20 cases. This study was approved by the hospital ethics committee (Ethical Approval Number: 2022-LL-036), and informed consent forms were signed by the guardians of all pediatric patients.

2.2 Inspection Method

Using a 3.0T superconducting MRI scanner, neonates were orally sedated with 10% chloral hydrate before examination, with earplugs for hearing protection. The scanning sequences included conventional T1WI, T2WI, T2-FLAIR, and MAGIC sequences. The MAGIC sequence employed a multi-echo gradient echo sequence to acquire multi-echo images, with post-processing reconstruction generating MAGIC quantitative maps.

Two radiologists independently delineated regions of interest on MAGIC pseudo-color maps: bilateral globus pallidus, putamen, and thalamus, avoiding blood vessels, cerebrospinal fluid, and artifact areas. Each ROI was measured three times, with the average value recorded as the MAGIC value.

2.3 Clinical Data Collection

Collect the gestational age, birth weight, and postnatal age at scan of newborns, and record the peak total serum bilirubin (TSB). Bilirubin levels were measured using an automated biochemical analyzer with venous blood samples.

2.4 Statistical Methods

Statistical analysis was performed using SPSS 26.0 software. Measurement data were expressed as mean ± standard deviation (\(\bar{x} ± s\)). Multiple group comparisons were conducted using one-way ANOVA, while pairwise comparisons between groups were performed using the LSD test. Correlations were analyzed using Pearson correlation analysis. A (P < 0.05\) was considered statistically significant.

3. Result

3.1 General Data Comparison

The comparison of gestational age, birth weight, and age at scanning among the four groups of newborns showed no statistically significant differences (P > 0.05), indicating comparable baseline data. The severe group had a significantly higher peak TSB level than the other three groups (P < 0.05). See Table 1.

Table 1: Comparison of general clinical data among four groups of newborns ($\bar{x} \pm s$)

Group	Number of cases	Gestational age (weeks)	weight (g)	Scanning age (days)	TSB Peak (μmol/L)
Control group	20	39.2±1.1	3326±245	6.1±1.8	112.3±21.5
Mild group	22	38.9±1.2	3289±261	6.4±2.0	234.6±18.7
Moderate group	21	39.1±1.0	3315±238	6.2±1.9	296.4±22.3
Severe group	19	38.8±1.3	3274±252	6.5±2.1	387.2±31.6
F	-	0.412	0.275	0.336	326.741
P	-	0.745	0.844	0.799	<0.001

Note: TSB: Total serum bilirubin.

3.2 Intergroup Comparison of MAGIC Values in Different Brain Regions

Globus pallidus MAGIC values: Control group < Mild jaundice group < Moderate jaundice group < Severe jaundice group. The severe group showed significantly increased globus pallidus MAGIC values with statistically significant intergroup differences (P < 0.05). No statistically significant differences were observed in MAGIC values of the putamen and thalamus across groups (P > 0.05). See Table 2.

Table 2: Comparison of MAGIC Values in Different Brain Regions Among Four Groups of Newborns (mean ± standard deviation)

CC	Number of cases	Globus pallidus	Putamen	Thalamus
Control group	20	102.4±11.3	110.6±12.5	107.3±10.8
Mild group	22	114.7±13.2	113.2±11.9	109.1±11.4
Moderate group	21	128.5±14.6	115.8±13.1	111.5±12.0
Severe group	19	156.2±17.4*#△	118.4±14.2	114.2±13.1
F	-	42.137	1.526	1.374
P	-	<0.001	0.213	0.253

Note: Compared with the control group, *P<0.05; compared with the mild group, #P<0.05; compared with the moderate group, △P<0.05.

3.3 Correlation Analysis

In all neonates with jaundice, the MAGIC values of the globus pallidus showed a positive correlation with peak serum TSB levels, r=0.726, P<0.001; the MAGIC values of the putamen and thalamus showed no significant correlation with TSB (P>0.05).

4. Discussion

The primary target area of brain injury caused by neonatal hyperbilirubinemia is the globus pallidus, where bilirubin deposition alters the magnetic susceptibility characteristics of brain tissue. Conventional MRI sequences often only reveal T1 hyperintensity in the globus pallidus during the late stages of bilirubin encephalopathy, lacking quantitative indicators and making it difficult to assess early microscopic damage. MAGIC, as a multi-echo gradient echo quantitative technique, can quantitatively reflect changes in brain tissue magnetic susceptibility, capturing subtle tissue signal changes caused by bilirubin deposition before macroscopic morphological alterations occur.

The findings of this study demonstrate that only the MAGIC value of the globus pallidus increased with rising bilirubin levels, while no significant changes were observed in the putamen or thalamus, consistent with the pathological mechanism of bilirubin preferentially depositing in the globus pallidus. The MAGIC value of the globus pallidus showed a significant positive correlation with peak TSB, indicating that higher bilirubin load leads to more pronounced magnetic susceptibility changes in the globus pallidus. MAGIC quantitative values can serve as an objective imaging biomarker to compensate for the limitations of conventional

MRI qualitative diagnosis, aiding in the early identification of bilirubin-related cerebral alterations and providing imaging evidence for clinical intervention.

This study has limitations: it is a single-center retrospective study with a limited sample size; long-term follow-up of neurodevelopmental outcomes was not conducted, and the association between MAGIC values and long-term neurological prognosis could not be confirmed. Future studies should expand the sample size, conduct prospective follow-up, and further validate the predictive value of MAGIC imaging for the prognosis of bilirubin encephalopathy.

5. Conclusion

MAGIC magnetic resonance imaging can quantitatively assess the susceptibility changes in the globus pallidus, with a significant positive correlation between the MAGIC value of the globus pallidus and the peak serum total bilirubin level. MAGIC imaging enables non-invasive and early detection of microscopic changes in the globus pallidus of neonates with hyperbilirubinemia, and has the potential to serve as an imaging tool for the early assessment of bilirubin-induced brain injury in newborns.

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