Risk factors for brain injury after transient or persistent hyperinsulinemic hypoglycemia in neonates

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Background

Congenital Hyperinsulinism (CHI) is a rare condition and the most common cause of persistent hypoglycemia in infants and children. Despite improved treatment options, up to 50 % of children with CHI still suffer from long-term neurodevelopmental impairment.

Aim of this study:
To identify possible explanations why brain damage still occurs in neonates with transient or persistent hyperinsulinism.

Material and Methods:
Retrospective medical chart review was conducted at the University Children's Hospital Düsseldorf, Germany. The study was approved by the ethics committee of the Medical Faculty at the University of Düsseldorf. Data was analyzed descriptively using SPSS®. Figure 1 shows the cohort definition in our analysis.

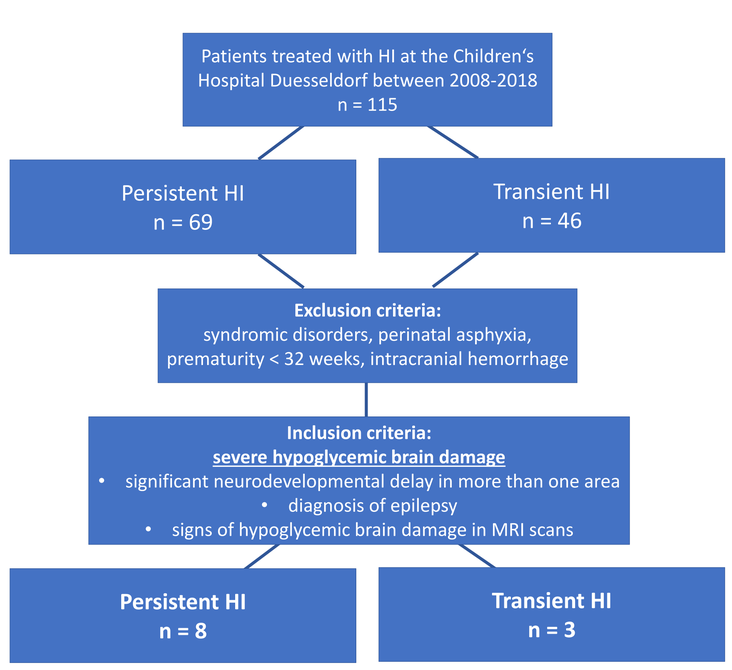

Fig. 1: cohort definition

Results

Table 1: Characteristics and Outcome of 11 children with hyperinsulinism

	Form of CHI	Place of birth	Risk factor for neonatal hypoglycemia	Lowest plasma glucose	Signs of brain injury in MRI scans	Epilepsy	Neurodevelopmental delay	Impaired vision	Other neurological deficit	Hypoglycemic seizures
Patient 1	transient	Germany	no	0.1	yes	unknown	unknown	unknown	unknown	yes
Patient 2	transient	Germany	no	0.7	yes	yes	yes	yes	no	yes
Patient 3	transient	Germany	no	0.7	yes	yes	yes	no	no	yes
Patient 4	persistent	Germany	no	0.8	yes	yes	yes	no	microcephaly	yes
Patient 5	persistent	Turkey	no	0.8	yes	yes	yes	no	microcephaly, cerebral palsy	yes
Patient 6	persistent	Syria	yes	0.4	no	no	yes	no	no	yes
Patient 7	persistent	Syria	no	1.2	yes	yes	yes	no	no	yes
Patient 8	persistent	India	yes	0.1	no	yes	unknown	no	unknown	yes
Patient 9	persistent	Iraq	no	1.1	unknown	yes	yes	yes	microcephaly, cerebral palsy	unknown
Patient 10	persistent	Germany	yes	0.2	yes	yes	yes	yes	no	yes
Patient 11	persistent	Germany	no	1.0	no	no	yes	no	no	yes

Mean of lowest blood glucose levels was 0.7 mmol/l (range 0.1 – 1.2 mmol/l). In 8 patients, the lowest known blood glucose concentration was recorded in the initial glucose measurement. Only two neonates had a blood glucose checked within the first 48 hours of life and they both had risk factors for hypoglycemia. All patients had symptomatic hypoglycemia. 9 children initially presented with unspecific symptoms and 2 with seizures. 10 patients had at least one episode of hypoglycemic seizures during the course of their disease. The prevalence of severe hypoglycemic brain injury was not significantly different in children with transient and persistent hyperinsulinism (3/46 (7 %) vs. 8/69 (12 %); p = 0.52).

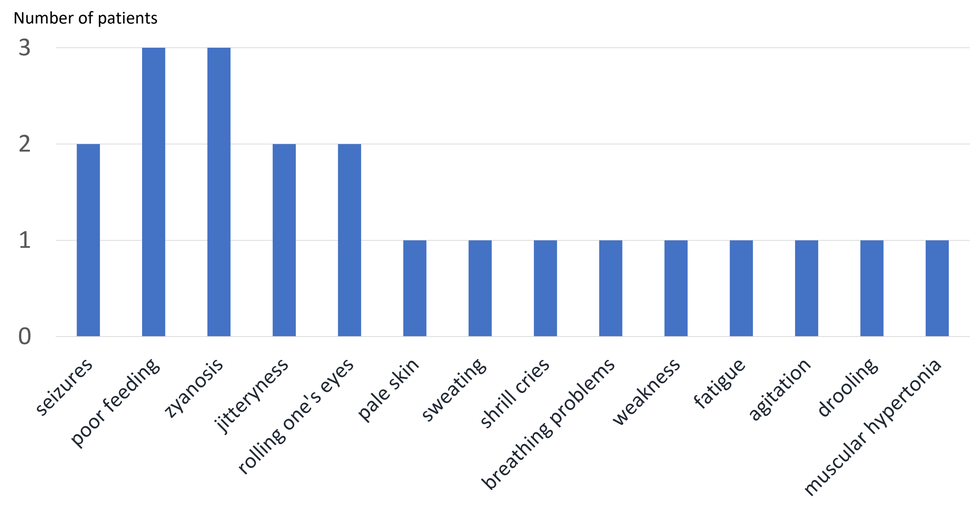

Fig. 2: First noted symptoms of hypoglycemia

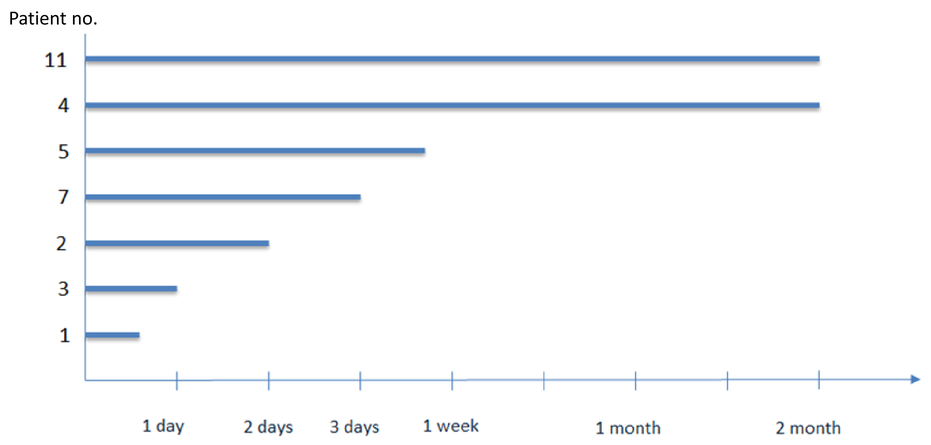

Fig. 3: Delays between first symptoms and first blood glucose measurement

Conclusions

Brain damage particularly occurred in newborns without risk factors for postnatal hypoglycemia as for these newborns blood glucose screenings are not standard procedure. Brain damage in transient hyperinsulinemic hypoglycemia was a relatively frequent finding in our cohort, even though it is regarded as a mild hyperinsulinemic condition. Inferior neurological outcome was notably associated with a delay between first clinical symptoms, diagnosis and initiation of adequate treatment. Additionally, hypoglycemic seizures and associated very low blood glucose levels (mean 0.7 mmol/l) were prevalent in those with brain damage. Therefore research and education of midwifes, nurses and neonatologists is needed to improve early identification of patients with high risk for brain damage within the large group of neonates with physiological postnatal hypoglycemia.

References

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Fetal, neonatal endocrinology and metabolism (to include hypoglycaemia)

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