Forty patients with persistent, non-focal congenital hyperinsulinism: Urgent need for new treatment modalities

UNIVERSITY OF SOUTHERN DENMARK

Amalie Greve Rasmussen[1,2], Maria Melikian[3], Evgenia Globa[4], Sönke Detlefsen[5,6], Lars Rasmussen[5,7], Henrik Petersen8, Klaus Brusgaard9, Annett Helleskov Rasmussen1, Henrik Thybo Christesen1,2,5, *

[1] Hans Christian Andersen Children's Hospital, Odense University Hospital, Odense, Denmark [2] Department of Clinical Research, University of Southern Denmark, Denmark [3] Endrocrine Research Centre, Moscow, Russia, Department of Pediatric Endocrinology [4] Ukrainian Research Center of Endocrine Surgery, Pediatric Endocrinology Department, Kyiv, Ukraine [5] OPAC, Odense Pancreatic Centre, Odense University Hospital, Odense, Denmark [6] Department of Pathology, Odense University Hospital, Odense, Denmark [7] Department of Surgery, Odense University Hospital, Odense, Denmark [8]Department of Nuclear Medicine, Odense University Hospital, Odense, Denmark [9]Department of Clinical Genetics, Odense University Hospital, Odense, Denmark

* Presenting author

CONCLUSION

Persistent, non-focal CHI remains difficult to manage. Neurological impairment in 30% suggests a frequent failure of prompt and adequate treatment. A high rate of problematic treatment status at follow-up demonstrates an urgent need for new medical treatment modalities.

BACKGROUND

Congenital hyperinsulinism (CHI) may be divided in focal, diffuse and atypical CHI. While focal CHI is cured surgically, non-focal CHI is a much greater challenge to manage.

We aimed to review the medical and surgical treatment of non-focal CHI in a consecutive cohort of patients at one international CHI center, to evaluate the need for improved treatment options.

SUBJECTS AND METHODS

Retrospective evaluation of the treatment and outcome of a cohort of 40 patients with non-focal, persistent CHI admitted to the International Hyperinsulinism Center, Denmark from January 2000 to May 2017. The patients were referred from Denmark, Norway, Sweden, Latvia, Russia, Ukraine, Kazakhstan, Belarus and Greenland. In case of no surgery, diffuse CHI was defined by genetics and/or 18F-DOPA PET/CT. Problematic treatment status at last follow-up was defined as lack of hypoglycemia control, severe medical side effects, tube feeding, or diabetes.

RESULTS

- Baseline

  Mutations found: 52.5% (n = 21), TABLE 1

  55% could not be managed with medical monotherapy (diazoxide or octreotide).

  Severe potential side effects to medication: 15%

- Surgery

  Surgically treated: 43% (n = 17). Extend of pancreatic resection median 90%, range 66%-98%

  Early post-surgical complications: 5.9% (n = 1)

  Surgically treated patients had more frequently K_{ATP}-channel mutations (p = 0.013), highly severe disease (p = 0.025) and clinical onset <30 days of age (p = 0.004).

- Follow-up

  Follow-up median (range) age: 5.3 (0.3-31.3) years

  Patients receiving treatment at last-follow up: 80% (n = 32), including 12/17 (71%) with surgery.

  Diabetes post-surgically: n = 1 (98% pancreatic resection).

  Problematic treatment status: 17.5% (n = 7). FIGURE 1

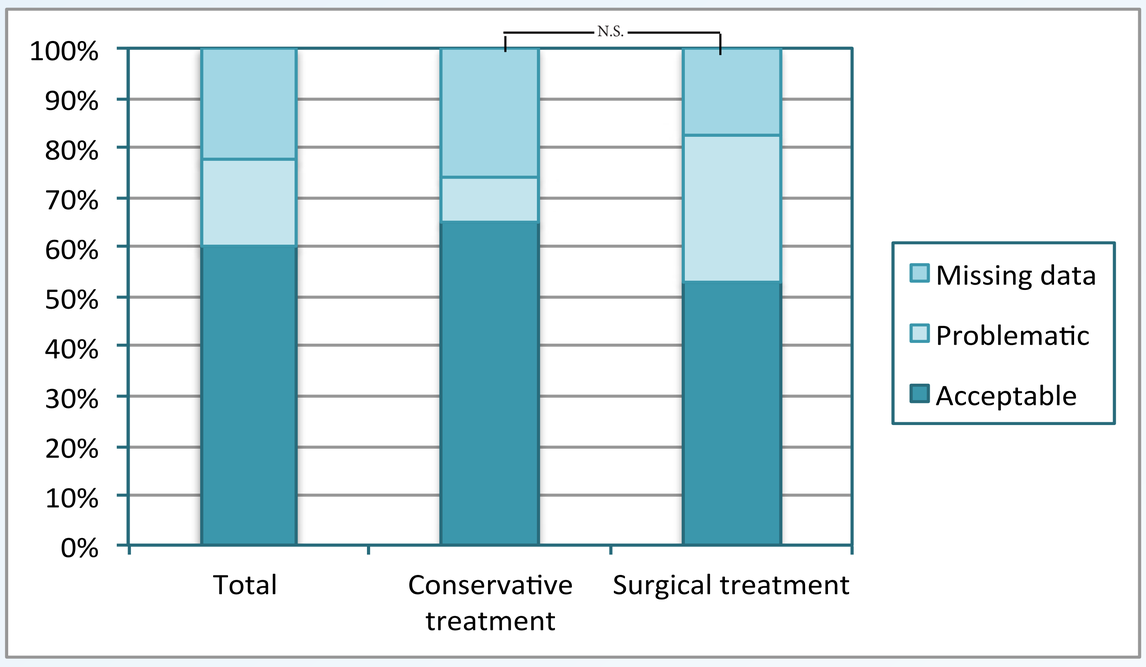
  Clinical remission: 20% (n = 8) (conservative, n=3, surgical, n=5)

TABLE 1: Mutations and histology in non-focal CHI

Mutations	All	Surgery		No surgery	
		Diffuse	Atypical	Predicted diffuse *	Unknown
K_{ATP}Channel (*ABCC8/KCJN11*)	18	12		6	
Homozygous	1	1			
Compound heterozygous	9	8		1	
Heterozygous	8	3		5	
Paternal	4	2		2	
Maternal	1			1	
De novo	3	1		2	
GLUD1	1			1	
HNF-Alfa	1			1	
11p15UPD	1		1		
Unknown	19	1	3		15
Total	40	13	4	8	15

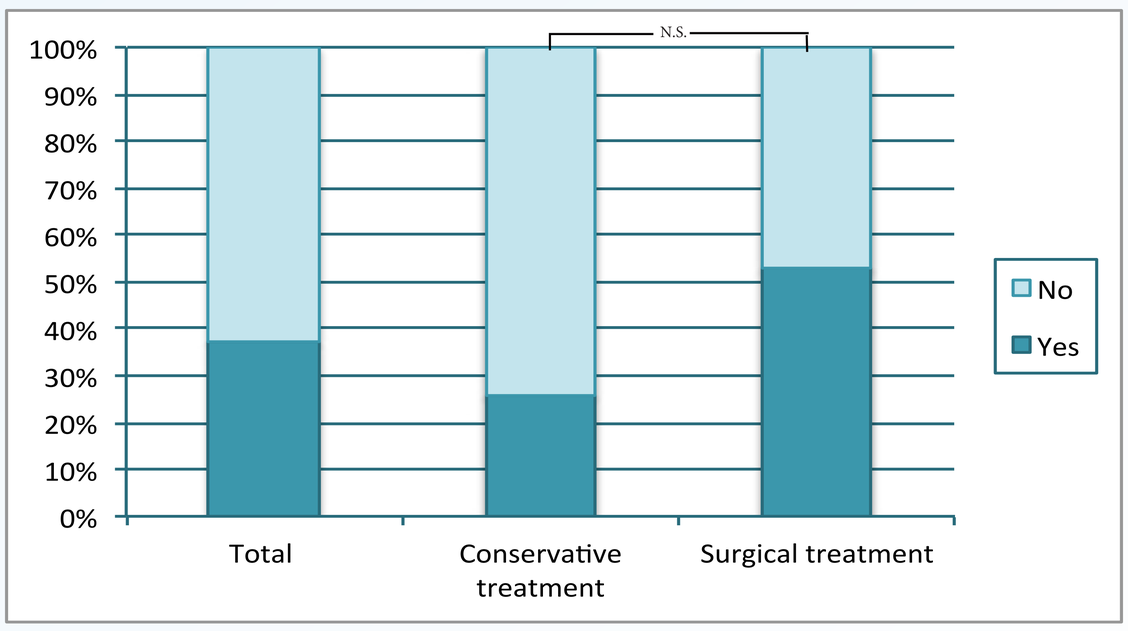
*) by genetics and/or 18-DOPA

FIGURE 1:Treatment status at last follow-up



Problematic: lack of hypoglycemia control, severe medical side effects, tube feeding, or diabetes.

FIGURE 2: Patients with neurological impairment at last follow-up



Neurological impairment: presence of psychomotor retardation, epilepsy, cerebral palsy or blindness.

This study was funded by: novo nordisk fonde