

**5th Congenital Hyperinsulinism
International Family Conference
Milan, September 17 - 18**

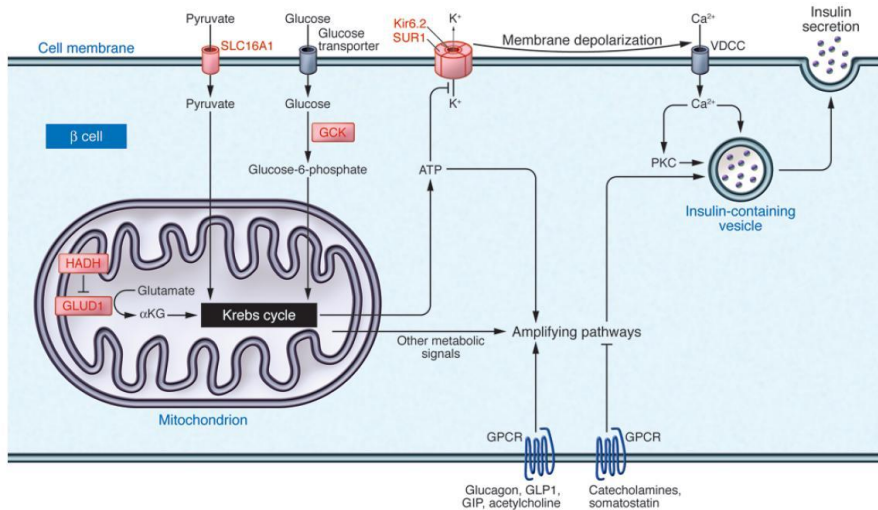


Remission in Non-Operated Patients with Diffuse Disease and Long-Term Conservative Treatment.

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University Children's Hospital Düsseldorf



Unterschiedliche genetische Defekte

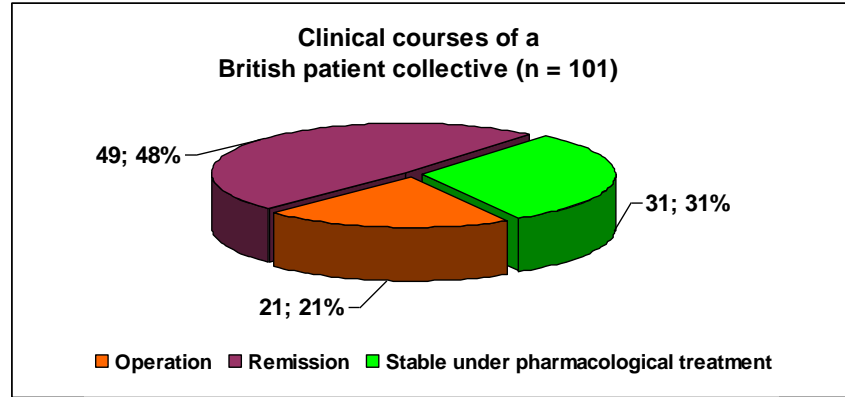
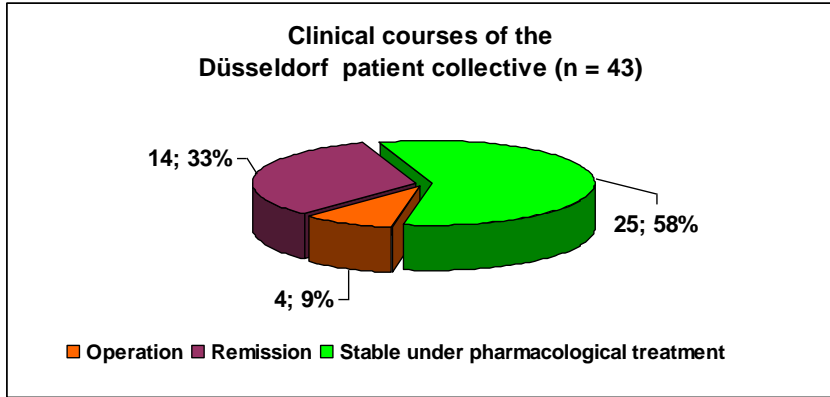


Beta-Zelle Pankreas*

- irreguläre Insulinsekretion
- unklar, wann Unterzuckerungen Hypoglykämien machen

* Figure from Glaser, Benjamin (2011): Lessons in human biology from a monogenic pancreatic β cell disease. In: *J. Clin. Invest.* 121 (10), S. 3821–3825

Comparison of therapeutic approaches in clinical practice



Pharmakotherapie: Diazoxide, wenn effektiv, sonst Octreotid oder Octreotidanaloga

Definition der Remission: keine Hypoglykämien, normale Ernährung, keine Medikamente

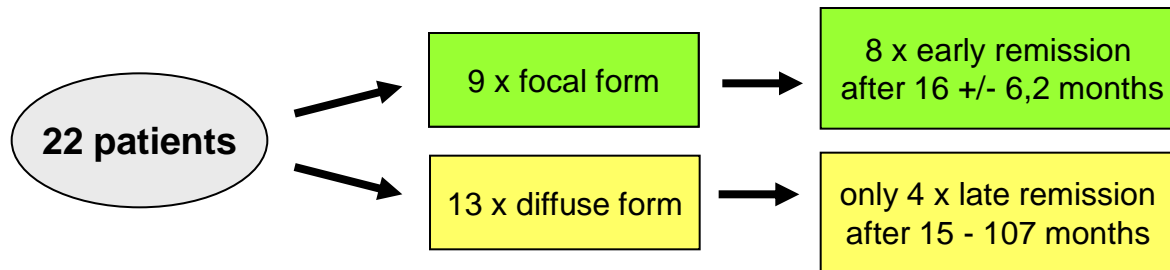
Surgical intervention, especially a near-total pancreatectomy in case of a diffuse form, must be well considered with regards to long-term effects.

It may be a helpful device if a focal form is confirmed by a PET-Scan of the pancreas.

* Data from: Banerjee, I.; Skae, M.; Flanagan, S. E.; Rigby, L.; Patel, L.; Didi, M. et al. (2011): The contribution of rapid KATP channel gene mutation analysis to the clinical management of children with congenital hyperinsulinism. In: *Eur. J. Endocrinol.* 164 (5), S. 733–740

Publizierte Daten: Wahrscheinlichkeit der Remission

Israelisches Team waren die Pioniere (90er Jahre)



Wahrscheinlich Fokale Region: Programmierter Zelltod erhöht, frühe Remission

In 2011, Banerjee und Kollegen (Manchester) suchten prognostische Faktoren:

Positive Korrelation:

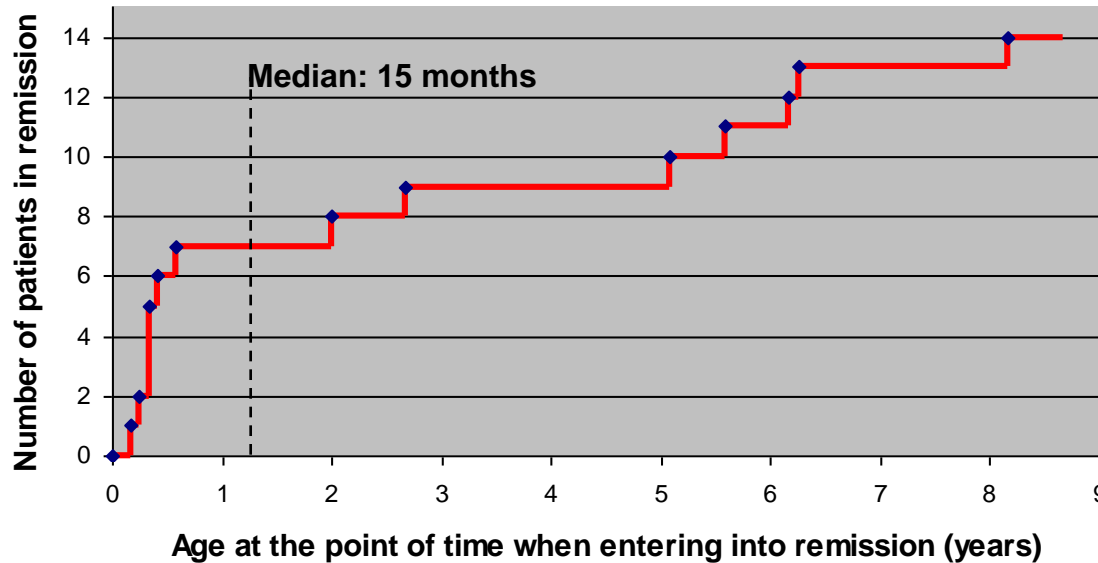
- Ansprechen auf Diazoxid
- Keine Mutation nachweisbar

Keine Korrelation:

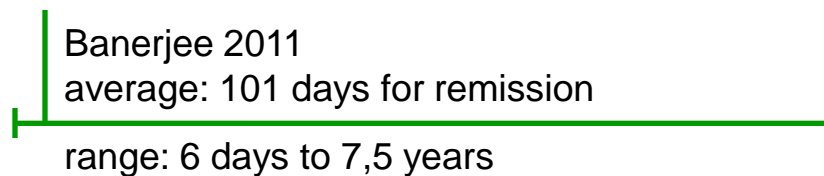
- Glukosebedarf
- Geburtsgewicht

* Data from Glaser, B.; Ryan, F.; Donath, M.; Landau, H.; Stanley, C. A.; Baker, L. et al. (1999): Hyperinsulinism caused by paternal-specific inheritance of a recessive mutation in the sulfonyleurea-receptor gene. In: *Diabetes* 48 (8), S. 1652–1657

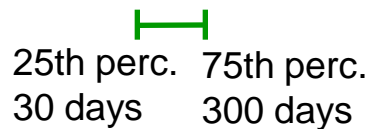
Düsseldorf Erfahrungen mit Remission



Jeder blaue Punkt ist ein Patient in Remission und es ist das Alter dazu gezeigt.



Wahrscheinlichkeit der Remission deutlich höher bei Patienten mit Octreotidtherapie (Odds-Ratio $\approx 3,519$)



* Data were analysed by means of IBM® SPSS® Statistics for Windows, Version 20.0 (IBM Corporation, Armonk, New York). The p-value of the Odds-Ratio was determined using the Mantel–Haenszel test.

Case report of a non-operated patient with diffuse disease and long-term pharmacological treatment

Fallbericht

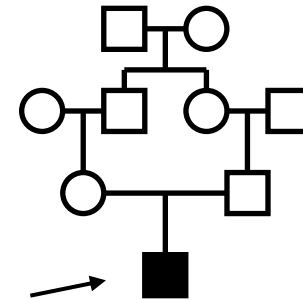
- 5.320 g Geburtsgewicht; 54 cm Geburtslänge → macrosomic
- schwerer Hyperinsulinismus

Genetische Analyse: homozygote KCNJ11 Mutation

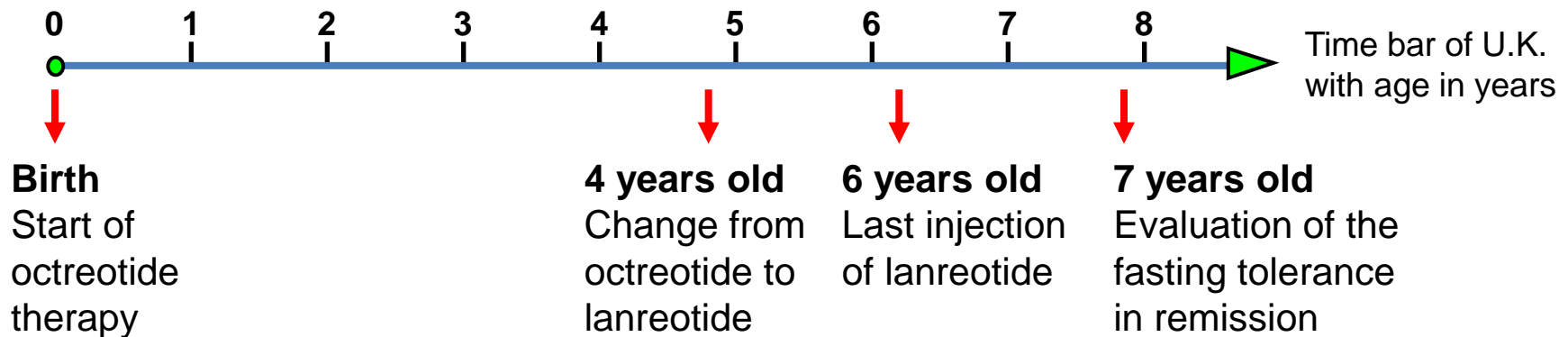
→ K_{ATP} -Kanalerkrankung

→ Diffuse Form

Patient U.K.



Therapy: Octreotid und häufige Mahlzeiten



BMI \approx 23,4 ($>$ 3 SD)

→ Insulinresistenz ?

Strukturierte Literaturrecherche

- Schlagwortsuche in den Datenbanken Medline (ab 1947) und Embase (ab 1988)
- 1261 Patienten mit kongenitalem Hyperinsulinismus
- Auswertung des Therapieregimes für 619 langfristig medikamentös behandelte Patienten
- Nebenwirkungsprofil für 1039 “medikamentöse Anwendungen”

Ziel

- Informationen bezüglich Dosierung, Therapiedauer und Nebenwirkungen
- Bessere Beratung der Eltern der Patienten
- Therapieempfehlungen

The screenshot displays the JADMET software interface, which is used for managing bibliographic data. The main window shows a table of entries with columns for 'Entrytype', 'Author', 'Title', 'Year', and 'Journal'. The entries are sorted by author, with 'Other' entries listed first, followed by 'Z'raggen et al.', 'Zaffanello et al.', 'Zammarchi et al.', 'Zani et al.', 'Zhang et al.', 'Zhou et al.', 'Zuniga et al.', 'Zunkler', and 'Zuppinger'. The 'Other (Yap2004)' entry is highlighted, and its full citation is shown in a pop-up window at the bottom: 'Yap, F., Hogler, W., Vora, A., Halliday, R. & Ambler, G. Severe transient hyperinsulinaemic hypoglycaemia: Two neonates without predisposing factors and a review of the literature 2004, -'. The interface also includes a sidebar with 'Groups' and 'Settings' options, and a top menu with 'File', 'Edit', 'View', 'BibTeX', 'Tools', 'Web search', 'Plugins', 'Options', and 'Help'.

Entrytype	Author	Title	Year	Journal
Other	Z'raggen et al.	Severe recurrent hypoglycemia ...	2008	Obesi...
Other	Zaffanello et al.	Neonatal hyperinsulinemic hyp...	2002	Miner...
Other	Zammarchi et al.	Different neurologic outcomes i...	1996	Child'...
Other	Zammarchi et al.	Different neurologic outcomes i...	1996	Child'...
Other	Zani et al.	The predictive value of preoper...	2011	Journ...
Other	Zhang et al.	Conformational transition pathw...	2006	Proce...
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Other	Zhang et al.	Lys169 of human glucokinase i...	2009	PLoS ...
Other	Zhang et al.	Lys169 of human glucokinase i...	2009	PloS ...
Other	Zhou et al.	Persistent leucine sensitivity foll...	2009	Diabe...
Other	Zuniga et al.	Persistent leucine sensitivity foll...	1983	Ameri...
Other	Zunkler	Human ether-a-go-go-related (...	2006	Phar...
Other	Zuppinger	Disorders of the endocrine pan...	1983	Progr...
Other	Zuppinger	Disorders of the endocrine pan...	1983	Progr...
Other	Zuppinger	Conservative management of c...	2008	Natur...

- Remission immer bei Ashkenazi Jews in Isreal
- Vergleich Manchester zu Düsseldorf: Unsere Patient kommen später in Remission. Mehr transiente CHI-Fälle in der Manchestergruppe?
- Ermutigende Daten für eine medikamentöse Dauertherapie
- Bei den Düsseldorfer Patienten Remission häufiger unter Octreotid (oder Analoga)
- Wahrscheinlichkeit der Remission noch schwer vorherzusagen (Wann, mit welcher Chance?). Dies sollte Ziel weiterer Studien sein.

Danke!

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