SSIM-Kongress Lissabon 2.- 5. September 2008
Berichterstattung von Frau Dr. Reinhild Link (Chair EMDG)

Vom 2. bis zum 5. September fand in Lissabon das jährliche Symposium der Society for the Study of Inborn Errors of Metabolism (SSIEM) statt. Für alle im Stoffwechselbereich aktiven oder interessierten Diätassistenten und Ökotrophologen bot sich ein vielseitiges Programm aus Vorträgen und Postern, sowie einem „Nutrition and Dietary Treatment Workshop“ und einem „Dietitians Workshop“ an zwei aufeinander folgenden Tagen.

Auch in diesem Jahr war es wieder aufgrund der Einladung durch Firmen einigen interessierten deutsch-sprachigen Kolleginnen, die im Stoffwechsel tätig sind, möglich an dem Symposium teilzunehmen – vielen Dank für die Übernahme der Kongressgebühren für diese KollegInnen für die beiden diätetisch ausgerichteten Tage! Für die Teilnahme der nicht englisch-sprechenden DiätassistentInnen und ÖkotrophologInnen wurde die Simultan-Übersetzung der englisch-sprachigen Vorträge angeboten. Es bestand in diesem Jahr nicht die Möglichkeit, deutschsprachige Beiträge einzureichen, weshalb es keine deutschen Beiträge gegeben hat.

An dem Workshop nahmen ca. 200 Diätassistentinnen aus unterschiedlichen Ländern teil.

Vor Beginn des Dietitians Workshop trafen sich die Mitglieder der **European Metabolic Dietetic Group (EMDG)**, die sich in London im März 2008 gegründet hatte und zu deren ersten Vorsitzenden Dr. Reinhild Link benannt wurde. Es waren 18 Kolleginnen und Kollegen aus 10 europäischen Ländern (Deutschland, Österreich, Schweiz, Schweden, Dänemark, Norwegen, England, Belgien, Portugal, Türkei) erschienen. Die Gründungspräsidentin der Internationalen Metabolic Group (**GMDI=Genetic Metabolic Dietitians International**), Frau Prof. Rani Singh aus Atlanta, USA, war eingeladen für einen Gedankenaustausch mit dem Titel: **„EMDG meets GMDI“,** um gegenseitige Erfahrungen bei der Gründung der Internationalen Gruppe und der europäischen Gruppe auszutauschen und vielfältige Unterstützung von Frau Singh zu erhalten.

Der nächste Dietitians Workshop wird 2010 in Istanbul stattfinden und von unserer Kollegin Hulya Gokmen Ozel aus Ankara organisiert.

Beim Dietitians Workshop in Lissabon war das Hauptthema:**„Fettsäureoxidationsstörungen: Gibt es einen Konsens bei der diätetischen Behandlung“.**

Dazu wurden Frau Dr. Rani Singh aus Georgia, USA, die die amerikanische Perspektive und Frau Prof. Ute Spiekerkötter aus Düsseldorf, die die deutsche Perspektive darstellte, eingeladen, sowie Frau Elles van der Louw aus Rotterdam, die die praktischen Aspekte vortrug. Die beiden ersten Beiträge können in beiliegender Publikation nachgelesen werden.

Für die Session **„Freie Vorträge“** am Nachmittag wurden aus den eingereichten Abstracts folgende Beiträge aus den unterschiedlichsten Stoffwechselbereichen ausgewählt, die in den folgenden Abstracts nachzulesen sind.

The Ketogenic Diet; more than just fat?!

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The Ketogenic Diet (KD) is a normocaloric, high-fat, low carbohydrate diet stimulating the generation of ketonbodies which are used as alternative fuel for the brain.
The KD has been used for decades to treat children with drug-resistant epilepsy. Now KD is also an accepted treatment of diseases of brain energy metabolism: GLUT1 deficiency syndrome (GLUT-1) and Pyruvate Dehydrogenase Deficiency (PDHC). Children with mitochondrial disease (Complex 1 deficiency) can also benefit from KD. The principles and use of KD doesn't really differ depending on the indication of use.
In the Netherlands, every year, 45-50 patients with intractable epilepsy and/or metabolic disease start with KD and are monitored by a team of caregivers.
In cooperation with the Dutch Multidisciplinary Ketogenic Diet Group, the evidence-based dietary guideline Ketogenic Diet was published in 2007. The Guideline contains theoretical and practical information for caregivers about both the classical- and MCT-version of KD.
The amount of prospective scientific studies of KD and epilepsy is international growing but the experience and research of its use in metabolic disease is still scarce.
In 2005 the Dutch national database KD was realized and data of 90 patients are registered and currently analyzed. Thus, all conditions are met for future scientific research.
The authors want to share experiences with colleagues about the pitfalls during the process of writing, implementation and use of the guideline, the creation and use of the nationwide database and discuss the experience of the treatment with KD in patients with metabolic diseases.

PKU management across Europe

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Background: Since the start of the European Society of PKU (ESPKU) 1987, parental organizations of 27 member countries joined in order to share knowledge. There are huge differences in treatment within Europe. A survey among professionals was done to determine goals and practice. However, not all countries were really active at ESPKU level.
Method: A questionnaire was sent out to professionals of all member countries, addressing the following issues: diagnostic and treatment procedures, numbers necessary for a PKU centre, guidelines followed, numbers of patients treated and professionals involved in care, target phenylalanine concentrations, availability of products, amount of protein prescribed, frequency of monitoring and clinical visits, need for follow up of various clinical/biochemical data, the importance of various abnormalities and definition of poor compliance.
Results: At that time 11 countries (14 centers) answered, and 14 countries could not be reached or did not respond. Differences in care do not only apply to the target phenylalanine concentration. Only at few points there is general consensus.
Conclusion: PKU treatment varies a lot between the European countries. Knowing these differences and the lack of clearness about goals (apart from phenylalanine concentrations), the ESPKU started to organize meetings for professionals besides the already existing program for parents/patients. Discussion with all kind of professionals taking care of PKU patients may lead to an European guideline, which definitely needs to address more than target plasma phenylalanine concentrations.

THREE OR FOUR PROTEIN SUBSTITUTES PER DAY IN PRE-CONCEPTION AND MATERNAL PHENYLKETONURIA (PKU)?

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Background:
It has been well documented that recommended phenylalanine (phe) control during pregnancies of PKU women can prevent fetal abnormalities including congenital heart disease, mental retardation, microcephaly and low birth weight. We recently demonstrated fluctuations of phe, even within target ranges, has a negative impact on offspring outcome (Maillot et al 2008). A study in children (MacDonald et al 2006) has suggested even distribution of protein substitute throughout 24 hours may produce more stable phe control and contribute to minimising phe fluctuations. No published adult study has assessed this.

Methods:
We assessed whether frequency of protein substitute influenced phe fluctuation over a 24hr period in adult pre-conception or pregnant patients. By retrospective analysis 20 patients (aged 20-41 years) were classified according to 3 (n=14) or 4 protein substitutes/day (n=6). Patients collected five finger-prick blood spots over a 24 hour period, taken before meals and at bedtime.

Results:
All patients were on diet with phe < 500µmol/l. Four protein substitutes/day resulted in a consistently higher, although not statistically significant, mean compared to 3/day (245.47 and 187.05 respectively). A smaller fluctuation was observed in those that took 4 substitutes per day compared to 3 per day (48 and 55.9 respectively).

Conclusion:
This small study has not shown any differences in stability of phe when taking 3 or 4 protein substitutes/day, contrary to the one previous report. Indeed taking protein substitute more frequently was associated with higher average phe concentrations. A larger, more controlled study would be useful to examine these issues further.

ASSESSMENT OF BODY COMPOSITION OF GSD TYPE I PATIENTS

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Background: Glycogen Storage Disease type I (GSD I) is an inherited metabolic disorder, caused by a defect in glucose-6-phosphatase, leading to short fast hypoglycaemia. Due to particular food patterns and associated morbidity of GSD I, these patients are more susceptible to malnutrition status.

The aim of this study was to assess body composition (total body water, fat and free fat body mass), basal metabolism and body mass index (BMI) in GSD I children followed as outpatients.

Methods: Five patients (one female), aged 2 to 14 years (median 10y) with GSD Ia (n=3) and GSD Ib (n=2) were studied. Control group included 13 healthy subjects, matched for age. Body composition was assessed using a tetrapolar bioelectrical impedance analyser Akern.. Mann-Whitney test was used for statistical analysis.

Results: Comparing with controls, our patients had statistically significant higher percentage of body fat and BMI. Patients less than 10 years-old showed lower total body water ($p<0,05$). There was no significant difference between GSD Ia and GSD Ib patients in all parameters. All patients presented low total body water and a medium basal metabolism of 36,6 kcal/kg.

Conclusions: GSD I patients are submitted to frequent meals with high carbohydrate content, leading to fat accumulation and higher BMI values than healthy individuals. When managing GSD I, attention should be paid not only to glucose requirements but also to nutritional status. Bioimpedance is a useful, non invasive method for assessing body composition of GSD I patients in outpatient clinics.

DIETARY THERAPY IN ISOVALERIC ACIDAEMIA

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Introduction

Long-term treatment of Isovaleric Aciduria (IVA) follows the principles of other organic acidurias: carnitine supplementation and protein or leu- restricted diet. Glycine is also used. IVA appears less severe than PA or MMA and there is little evidence that diet confers any extra benefit over medication alone. Many extended newborn screening programmes include IVA making it important to understand the necessity of diet in this condition.

This study in an unscreened population details the neurological outcome in IVA children correlating outcome with diet restriction.

Methods & **Results**

Seven patients (2 male), age range 4m – 15y were reviewed. Six presented neonatally and one aged 5y with psychomotor retardation. Acute management was cessation of protein and IV carnitine. Five had oral glycine.

Low protein diet (minimal requirements) was commenced in 5 of 6 neonatal cases. One breast-fed infant was weaned onto low protein foods. Diet was relaxed in 3 of 6 cases at 2 = – 8y. Only 1 of 7 cases had a further decompensation at age 1y; she was diet treated.

Neurodevelopment is normal in 3 of 7 cases. Two have moderate psychomotor retardation. Two siblings have severe retardation with autism. The neurological outcome was unrelated to the degree and compliance with protein restriction.

Conclusions

The degree of protein restriction does not correlate with neurological outcome or number of decompensations in IVA. Medication alone may be sufficient to manage this group once stabilised; further studies including those from screened populations would help address this issue.

NUTRITIONAL MANAGEMENT OF PKU IN SAUDI ARABIA

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Background: Inborn errors of metabolism are common in Saudi Arabia (incidence estimated at 5 times that in the US). Adherence to a special diet is essential to prevent developmental disability in phenylketonuria (PKU). Our aim is to identify risk factors for poor outcome in PKU patients at King Faisal Specialist Hospital & Research Center in Saudi Arabia and to improve nutritional management.

Methods: Qualitative study: Assessed nutritional knowledge, attitudes and practices through interviews (n=5) and focus groups (2) with health care providers; interviews with patients (6); and families (17).
Quantitative study: Took anthropometric measurements, dietary intake, phenylalanine blood

levels, developmental assessments, and questionnaires with 40 PKU patients and their families.

Results: Major qualitative themes: Lack of sufficient services; inadequate dietary knowledge; limited resources; social and emotional attitudes towards diet and compliance.
Quantitative initial results: Factors contributing to poor outcome (IQ <80) include: 1.Delayed diagnoses. Mean IQ's (±1SD) according to age at diagnosis were: diagnosed <1month: IQ 90 (±12.3)*; diagnosed 1month - 1year: IQ 74 (±21.8); diagnosed >1year: IQ 55 (±28.5)*. *Significantly different ($p<0.005$). 2.Inadequate dietary phenylalanine control. Patients with mean phenylalanine above 480µmol/L were 3.8 times more likely to have developmental disability.

Conclusion: In Saudi Arabia targeted nutrition management programs need to be developed to capitalize on the expanding neonatal screening program. Education and metabolic care services need major improvements to be able to deliver optimal care for patients and their families.

CESSATION OF PROTEIN SUBSTITUTE IN TYROSINAEMIA TYPE III

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There is no consensus about the long term benefit of a low tyrosine (tyr) diet in Tyrosinaemia III. In our centre, it is practice to start a low tyr diet if plasma tyr is ≥ 600 micromol/l.. Two Asian girls, one who demonstrated clinical improvement with diet, have required minimal dietary treatment (Subject 1: took protein substitute [PS] without tyr and phenylalanine (phen) only [1g/kg/day]; subject 2: required 1.5g/kg/day natural protein with 1g/kg/day PS) to achieve plasma tyr less than 200 micromol/l. In latter years, PS dose was not increased in either subject. Subject 2 relaxed natural protein intake without loss of tyr control. Dietary treatment was stopped in both girls.
Aim: To evaluate diet cessation in Tyrosinaemia III patients
Methods: Subject 1 diagnosed 16m (tyr 1820 μmol; phen 85 μmol) stopped PS at 13y. Subject 2 diagnosed 18m (tyr 1400 μmol and phen 100 μmol) stopped diet and PS at 13 y. Twice daily blood samples (fasting early a.m. and p.m.) were collected over 3 weeks and at monthly intervals post diet cessation.
Results: Plasma blood levels for tyr and phen remain well controlled off dietary treatment for 6 months in both subjects. Median fasting morning and evening tyr concentrations remained below 230 micromol/l (morning: subject 1: 180 [130-280]; subject 2: 120 [100-170]; evening; subject 1: 230 [150-320]; subject 2 160 [110-170]).
Conclusion: Dietary treatment for some patients with Tyrosinaemia III may only be required temporarily to achieve plasma tyr levels closer to normal reference levels.

IMPROVEMENT IN CARDIOMYOPATHY IN A CASE OF MALONYL-COA DECARBOXYLASE DEFICIENCY ON LCT-RESTRICTED/MCT SUPPLEMENTED DIET

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Introduction

Malonyl CoA decarboxylase (EC 4.1.1.9, MCD) deficiency is a rare inborn error of metabolism causing developmental delay, seizures, cardiomyopathy and acidosis. MCD is important in both lipid and carbohydrate function, although its precise role is unclear. Most children have been treated with a low fat/high carbohydrate diet but there is little evidence to support such a diet.

This case describes dietary intervention with a precise low fat/high carbohydrate diet with subsequent improvement in cardiac function.

Case Study

A term Pakistani infant was diagnosed with Malonic Aciduria following screening due to positive family history. At age 13 weeks echocardiography showed impaired LV function with ejection fraction of 18%. She was commenced on carnitine, an ACE inhibitor and a nutritionally complete infant formula, providing 1.5% energy from Long Chain Triglyceride (LCT), 20% Medium Chain Triglyceride (MCT) and 65% carbohydrate. Cardiac function was optimal at 23 months of age with a fractional shortening of 25% and good systolic function. Thereafter cardiac function deteriorated following a significant reduction in MCT intake. This reversed following improved intake of MCT.

Conclusions

Since the role of MCD is unclear it is difficult to know how best to influence disease progression. This case of Malonic aciduria with cardiomyopathy demonstrates improvement in cardiac function attributable to LCT restricted/MCT supplemented diet.

PRACTICALITIES OF EMERGENCY REGIMENS IN IMD

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Emergency feeds are used to prevent metabolic decompensation and encephalopathy during illness in many inherited metabolic disorders (IMD). They are commonly based on glucose polymer, although other high sugar drinks may be used. **Methods**: In order to ascertain patient/carer understanding and practical application of emergency feeds, 15 multiple choice questions were administered to 111 patients' carers with IMD requiring an emergency regimen. They had a median age of 5y (range 4 months to 28y). Forty five (41%) had fatty acid oxidation and 66 (59%) protein metabolism disorders. 21% (n=23) had non-English speaking mothers. **Results**: Almost all (87%; n=97) understood that emergency feeds were high sugar drinks, their function (87%; n=97) and when to use them. Most used (n=85; 77%) glucose polymer; the rest used commercial high sugar drinks. 12% (n=13) used emergency feeds at least monthly, and only 28% (n=31) used them less than annually. Although 62% (n=69) had their emergency feeds updated (carbohydrate and/or volume adjusted) in the last 2 years; 25% (n=28) of carers could not remember when they received an update or if they had ever had a written regimen. In 38% (n=42), preparing the emergency feeds was the specific responsibility of one parent only; 19% of carers kept no written emergency feed recipe; and 6% (n=7) used inappropriate drinks or measuring equipment. **Conclusions**: It is important health professionals check emergency feeds are updated annually, and verify carers understanding of their appropriate preparation and administration.