Materials and Methods

and intervention in Romania. A disciplinary clinical research protocol, which allows early diagnostic implementation of molecular genetic/epigenetic tests and to develop interdisciplinary cooperation for the treatment of childhood feeding, obesity, cognitive deficiencies. Our aims are to emphasize the importance of early diagnostic. Interdisciplinary clinical criteria, karyotype, FISH and methylation analysis (MS-PCR, MS-MLPA) are the main steps for a successful diagnostic protocol. Genetic tests results show a particular molecular profile in Romania with only 47% positive methylation results unlike literature (99%).

Background and Aims

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Abstract

Turner syndrome (TS) is defined by total or partial sex of the X chromosomes. Features vary widely including short stature and ovarian failure inconstant associated with characteristic face, skeletal malformations, renal and cardiac anomalies and endocrine disorders.

We analyzed the clinical and cytogenetic profiles of 37 TS children diagnosed with TS from January 2007 to December 2011 in the aim to establish genotype-phenotype correlations.

Growth delay and hypothyroidism were noted respectively in 89.2% and 19.4% of patients. Diabetes and celiac disease was observed in 5.6% of cases. 55% of our cohort had a 45, X karyotype, 81% had 45, X/47, XXX mosaicism and 5.4% have 45, X/46, XY mosaicism. Interestingly, FISH revealed the presence of SRY gene. The remainders had structural abnormalities: 55.1% had iso-chromosome Xq which was homogenous in roughly half of cases. 10.8% were diagnosed with a terminal deletion Xp and 5.4% with a ring of chromosome X.

There was no correlation between genotypes and clinical features. The short stature in girls with TS is thought to be related to the haploinsufficiency of the SHOX gene on Xp22.3. As a result, treatment with GH is now routinely adopted even if the GH hormone is normally secreted. The higher risk of autoimmune diseases in women with TS could result from haploinsufficiency of the FOXP3 gene on Xp11.23.

Otherwise, we highlight the importance of detection of 45, X/46, XY mosaicism which may be cryp to requiring SRY probe FISH screening a condition that exposes to gonadoblastoma and special chirurgical preventive treatment.

Materials and Methods

This study is part of a multicenter research project (CNMIP/Partnerships, 2008–2011), on 19 Romanian PWS patients, 12 females, 7 males, between 6 months and 29 years. For diagnostic, were used major and minor criteria (Gunay-Aygun) as clinical methods and 5 genetic tests.

Results

All patients have a clinical diagnostic score above 5, 63% of them having a maximal major criteria number with 100% neonatal hypotonia, 95% feeding difficulties at infants and hyperphagia after and a BMI till 18.2kg/m². 15% of patients have all minor criteria positive, with lethargy at infants, viscous saliva and small extremities predominance. 5% of patients have a positive 15q11–q13 micro-deletion, 79% a FISH positive and for 47% patients MS-PCR is positive. Techniques like MS-MLPA were late introduced in Romania, 20% of our patients having them.

Conclusions

The study indicates a relative correlation between clinical score and cytogenetic/molecular PWS confirmation and

emphasizes the importance of early diagnostic. Interdisciplinary clinical criteria, karyotype, FISH and methylation analysis (MS-PCR, MS-MLPA) are the main steps for a successful diagnostic protocol. Genetic tests results show a particular molecular profile in Romania with only 47% positive methylation results unlike literature (99%).

Abstract

Many of these transcripts are involved in synaptic transmission and metabolism. Interestingly, we also found changes in several histone clusters and histone deacetylases.

Conclusions

This is the first study to investigate whole genome expression in a preconditioning and asphyxia model that includes the fetal-to-neonatal transition and therefore truly resembles perinatal asphyxia. Our results warrant further research into epigenetic mechanisms of neuroprotection.

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Background and Aims

PWS-a rare genetic disease with a 1/12000–1/15000 newborn frequency, caused by deletion of some genes on paternal origin or maternal disomy of 15th chromosome.

Main clinical manifestations are: neonatal hypotonia, excessive feeding, obesity, and metabolism. Interestingly, we also found changes in several histone clusters and histone deacetylases.

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dissimilarity index which indicate the percentage of the peak area of the fragment (operational taxonomic unit: OTU) was used.

**Results** Two fecal samples of 1 CC infant and 14 fecal samples of 7 BA infants were obtained. Nine predominant OTUs were detected with Bsl I digestion. The microbiota consisted of microbial communities of Bifidobacterium, Lactobacillales, Bacteroides, Prevotella, Clostridium clusters IV, XI, and XVIII, and Clostridium subcluster XIVa. The Bifidobacterium, Bacteroides, and Clostridium clusters were detected predominantly in CC than BA group. Lactobacillales was most predominat group in BA feces.

**Conclusions** Bacterial DNA showed marked differences in the composition of fecal microbiota in CC and BA infants. Molecular analysis of colonic microbiota using 16s rRNA gene libraries and T-RFLP might be useful to differentiate CC from BA.

**734** **ASSESSMENT OF DNA DAMAGE USING COMET ASSAY AND DETECTION OF OXIDATIVE STRESS PARAMETERS IN DOWN SYNDROME**

**Background** Down syndrome is one of the commonest numerical chromosomal aberrations. Recent studies showed that oxidative stress is an important pathological factor in Down syndrome.

**Objective** To estimate the level of oxidative stress and DNA damage in Down syndrome patients.

**Patients** and methods: Fifteen Egyptian patients clinically diagnosed and cytogenetically proven to have Down syndrome. Fifteen Egyptian healthy controls were recruited from the outpatient clinic of Clinical Genetics Department, National Research Centre. Oxidative stress parameters including total antioxidant capacity (TAC), Superoxide dismutase (SOD) enzyme activity and Malondialdehyde (MDA) biomarkers were estimated. DNA damage was determined using the alkaline comet assay.

**Results** The MDA and SOD levels in Down syndrome patients were significantly higher than control group (p=0.000 & 0.01, respectively). Total antioxidants levels were non-significantly higher than control group (p=0.54). Statistical analysis of DNA damage levels in DS patients compared to controls showed significant increased levels (p=0.000). There was a positive correlation of DNA damage levels with age in DS patients but not reaching a significant value (p=0.536). A non-significant positive correlation was detected between DNA damage levels and both MDA and TAC levels (p=0.8 & 0.37, respectively). Also a non-significant negative correlation of DNA damage levels with SOD levels was noticed (p=0.14).

**Conclusion** Oxidative stress plays a major role in DS pathogenesis.

**735** **CONTRIBUTION OF ALKYLATING AGENTS IN THE CYTOTOGENETIC DIAGNOSIS OF FANCONI ANEMIA**

**Background and Aims** Fanconi Anemia (FA) is an autosomal recessive disease characterized by heterogenous phenotype which includes a bone marrow failure, diverse abnormalities and increased predisposition to develop leukemia. The cytogenetic diagnosis of FA cells to bifunctional alkylating agents, resulting in greatly increased chromosomal breakage and radial stuctures induced by cross-linking agents. To estimate the sensitivity and the specificity of the Mutomycin C (MMC) and the Diepoxybutan (DEB), two alkylating agents used in the diagnosis of the FA, we studied the chromosomal instability on 22 patients using type and concentrations of these alkylating (25 and 40 ng/ml of MMC, 0.1 μg/ml of DEB).

**Methods** Heparanized venous blood samples were collected and were processed for the cytogenetic methodology in this study. After culture, 100 of metaphases were analysed to evaluate the frequency of chromosomal aberrations.

**Results** The MMC test at 25ng/ml was High sensitive for FA. The DEB test showed a better specificity. The study of the mitotic segregation of sexual chromosomes by FISH took away any abnormality of the segregation to cells FA.

**Conclusions** A molecular study of the sensitivity and the specificity of the alkylating agents used according to the group of complementation will come refine the diagnosis of FA by establishing a gold standard.
Cyst from Biliary Atresia

Fecal Samples to Differentiate Choledochal Cyst from Biliary Atresia

T Okada, S Honda, H Miyagi and A Taketomi

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