

Plasmapheresis Combined with Leukocytapheresis for Patients with Immunoglobulin-Refractory Kawasaki Disease

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BACKGROUND: Early treatment with intravenous immunoglobulin (IVIG) reduces the risk for coronary artery lesions of Kawasaki disease (KD). (CAL). However, a study found that 15.8% of KD patients were IVIG-refractory and of them 38.5% developed CAL (2). We previously reported the efficacy of plasmapheresis (PE) to prevent CALs in IVIG-refractory KD (E J Pediatr 163:263-4,2004). By now over 50 patients have been treated with PE in our institute. PE significantly reduced the incidence of CALs about 15% of them. Autoimmunity is related to the pathogenesis of KD. Especially, activated neutrophils migrate, attach to the vascular wall and infiltrate it. Leukocytapheresis (LCAP) may prove effective in KD, but there has been no report up to now.

OBJECTIVE: To investigate the efficacy of PE/LCAP combination therapy for IVIG-refractory KD, and compare it with PE therapy alone.

DESIGN/METHODS: After obtaining the parents' informed consent and the approval from the ethical committee of our hospital, PE/LCAP was performed in 11 children (6 males, 5 females, 10 months old ~ 5 years 8 months old) with IVIG-refractory KD. For PE, 1~1.5 plasma volume was replaced with 5% albumin per day; for LCAP, leukocytes were removed from 1~1.5 blood volume per day. PE/LCAP was continued until the resolution of fever.

RESULTS: Nine patients successfully recovered without CAL. One patient showed transient mild dilatation. One patient had moderate dilatation and needed warfarin therapy, but this patient had already presented moderate dilatation at the time of the initiation of PE/LCAP. The average duration of the therapy was 2.7 ± 1.1 days, which was about one day shorter than PE therapy alone (3.6 ± 1.1 days). There was no severe adverse events.

CONCLUSIONS: LCAP/PE therapy prevented the development of CAL in these patients. Although the number of patients was small, PE/LCAP was as effective as PE, and shortened the duration of blood purification therapy. At the same time, we established the method for LCAP using the leukocyte removal filter for blood transfusion even in small infants (lowest weight was 7 kg). Further studies involving a larger number of cases will be needed to elucidate the mechanism for the efficacy of LCAP in KD patients.

Genetics / Inborn Errors of Metabolism

3:00 pm-6:30 pm

P_Sat_021_3747.12 Poster Board 65**Studies on Mutations in ATP7A Gene in Male Patients and a Female Patient with Menkes Disease**

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BACKGROUND: Menkes disease is an X-linked recessive disorder of copper metabolism characterized by progressive neurological degeneration and connective tissue abnormalities. The disease is caused by mutations in the ATP7A gene, which encodes a copper-transporting P-type ATPase. ATP7A gene consists of 23 exons spanning a genomic region of about 150 kbp. Mutations in the ATP7A gene have been reported to show variety in patients with Menkes disease. Only few female patients with Menkes disease and chromosomal abnormalities have been reported.

OBJECTIVE: We examined the mutations in the ATP7A gene in 43 unrelated male patients and a female patient. The female patient had a normal chromosome karyotype of 46 XX.

DESIGN/METHODS: Genomic DNA was prepared from peripheral blood lymphocytes, cultured fibroblasts or amniocytes, and amplified by PCR. The direct sequencing of exons was performed with a DNA analyzer. RT-PCR was also examined from the samples

RESULTS: Forty different mutations were identified in the 43 male patients; 10 nonsense mutations, 6 missense mutation, 10 splice-site mutations, and 14 insertion/deletion mutations. No mutation was found in the female patient. Mutation was not found in the genes of HAH1, a chaperon protein of copper, and CTR1, a transporter of copper on the plasma membrane, in the female patient. RT-PCR of ATP7A cDNA revealed that ATP7A of the female patients is normal.

CONCLUSIONS: These results indicate that mutations vary from a patient to a patient with Menkes disease. These results suggest that there is an unknown regulation mechanism of copper which is disturbed in the female patient.

Differences in the Plasma Proteome of Patients with Kawasaki Disease

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BACKGROUND: Kawasaki disease (KD) is an acute multi-systemic vasculitis syndrome of unknown etiology occurring mostly in children <5 yr of age. It is also the leading cause of acquired heart disease during childhood in the developing countries.

OBJECTIVE: In this study, our goal was to elucidate potential differences in plasma between KD and control groups.

DESIGN/METHODS: Plasma samples of 10 KD and 10 fever control groups were enrolled in this study and compared with proteomics technology. Using proteome analysis, two-dimensional gel electrophoresis detected more than 200 spots per gel.

RESULTS: A differential protein expression was discovered between KD and fever control groups. Fibrinogen beta and gamma chains, alpha-1-antitrypsin were increased in KD plasma, whereas CD5 antigen-like precursor (CD5L), immunoglobulin lambda chain, clusterin were decreased.

CONCLUSIONS: Our results show that proteomic profiling is a useful approach for detecting protein expression in Kawasaki disease. Further studies are needed to explore the roles of these candidate proteins.

P_Sat_022_3747.16 Poster Board 69**Descriptive Epidemiology of Birth Defects in Malaysian Births: A Population-Based Study**

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BACKGROUND: Data on birth defects from population-based studies originating from developing countries such as Malaysia are lacking.

OBJECTIVE: The objectives of this study are to determine the epidemiology of birth defects and to identify risk factors for major birth defects in Malaysian births.

DESIGN/METHODS: This is a descriptive study of all Malaysian births with major birth defects identified over a 14-month period using a case-controlled population-based birth defect register. All major birth defects in infants 500 g (or more or 22 weeks) till one week of life, in Kinta district, state of Perak, Malaysia are enrolled. Ethical approval and parental consents were obtained. The mothers of the cases were interviewed. All the affected babies were examined by attending doctors and clinical photographs were taken, after informed consent was obtained. Blood samples were sent for chromosomal studies. The abnormalities were classified by an organ system classification according to ICD10. Two normal controls for each case from same institution of birth, matched for sex and ethnic group were chosen.

RESULTS: There were 253 babies with major birth defects in 17720 births, giving birth prevalence of 1 in 70 (1.43%) (95% CI: 0.87-1.99). The exact syndromic diagnosis of the babies with multiple birth defects could be identified in 62/82 (77.5%) babies. Isolated major birth defects were cardiovascular (13.8%), cleft lip and palate (11.9%), clubfoot (9.1%) and central nervous system abnormalities (7.9%). The babies with major birth defects were lighter, more premature, had higher Caesarean section rates, required prolonged hospitalization and more specialist care and had a perinatal mortality rate of 25.2%. Mothers with affected babies were older, had birth defects themselves or in their relatives, had a consanguinity rate of 2.4%, and had higher rates of previous abortions. Risk factors identified for birth defects using multivariate logistic regression were maternal insulin-dependent diabetes, previous abortions, maternal recall of exposure to teratogens during pregnancy but not lack of periconceptional folate supplementation.

CONCLUSIONS: Pre-natal screening for insulin dependent diabetes, counselling and investigating causes for previous abortions and public education on avoidance of teratogens may reduce birth defects in this population. A Birth Defect Register must be set up to monitor these developments in Malaysia.