B1

A Local Retrospective Review of Relapsed Acute Lymphoblastic Leukaemia

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Aim: Despite modern therapy, 1 in 5 children with acute lymphoblastic leukaemia (ALL) suffer from relapse of disease. Management and counselling of these patients are difficult as local data on relapsed ALL is lacking. Our aim is to provide more epidemiological data to facilitate better care.

Methods: We performed a retrospective review of 41 out of 46 (89%) children with relapsed ALL and data available at the National University Hospital between 1987 and 2005. Their demographics, laboratory investigations, relapse characteristics and treatment compliance were analysed.

Results: Thirty patients had initial diagnosis and management in NUH while 11 were referred. Most relapses were isolated (59%) or combined (24%) bone marrow relapses. A significant proportion (44%) suffered very early relapse (occurring <18 months from diagnosis). This was more common in patients defined as high risk at initial diagnosis using the NCI criteria, possessing unfavourable cytogenetics as well as being poorly compliant to treatment. Eight patients (27%) had poor treatment compliance, with a shorter time to relapse (1.03 years) compared to compliant patients (2.33 years). Reasons cited were preference for alternative medications (38%), cost (38%) and fear of chemotherapy (25%). Very early relapse was associated with a shorter survival time from relapse. In this group, those who received bone marrow transplant did not show a significant improvement in survival time.

Conclusion: A unique aspect of poor compliance locally is usage of alternative therapy, which is associated with a poorer outcome compared to patients compliant with established therapy. This information will facilitate counselling on compliance.

B2

Ethnic Differences in the N-3 and N-6 Fatty Acid Composition of Breast Milk in Singapore Women

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Aim: It remains controversial whether breastfeeding protects against allergy. Diets with lower ratios of n-6/n-3 fatty acids seem to be protective in animal studies. We postulate that variations in breast milk composition may affect the development of immune tolerance in early childhood. We investigated the n-6 and n-3 fatty acid composition of breast milk in Chinese, Malay, and Indian mothers in Singapore.

Methods: Breast milk samples were collected postnatally and mixed with ethanol and sulfuric acid (0.5M). The samples were extracted with a mixture of ether/heptane followed by aminopropyl column purification. n-6 (arachidonic acid, eicosatrienoic acid, eicosadienoic acid) and n-3 [docosahexaenoic acid, alpha-linolenic acid (LNA), eicosapentanoeic acid, docosapentaenoic acid (DPA)] fatty acid levels were determined by liquid chromatography tandem mass spectrometry. Differences in fatty acid levels among ethnic groups and multiple pairwise comparisons between ethnic groups were performed using non-parametric methods.

Results: Breast milk samples were obtained from 53 lactating women: 31 Chinese, 15 Indian and 7 Malay. Significant differences among the ethnic groups were found in %LNA (P = 0.002) and %DPA (P = 0.032). For %LNA, Chinese (14.3 ± 19.9) women had significantly lower levels compared to Indians (35.8 ± 29.0, P = 0.002) and Malays (40.7 ± 36.3, P = 0.010). Chinese (0.50 ± 0.93) women had higher n-6/n-3 fatty acid ratios than Indians (0.33 ± 0.42) and Malays (0.15 ± 0.30) but the difference was not statistically significant.

Conclusion: Like allergy prevalences, the long-chain polyunsaturated fatty acid composition of breast milk is different among Chinese, Indians, and Malays in Singapore. Whether these breast milk differences affect development of allergy requires further study.

B3

The Reactions of Polyaniline with NADH and NADPH

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Aim: The 2000 Nobel Prize in Chemistry was awarded for the study of certain electroactive polymers, e.g. polyaniline. Boasting unique electronic, chemical and physical properties, they show great potential as materials for biosensors and artificial membranes. However, no study has yet been done on the interactions of biological molecules with such polymers. Hence, we chose to investigate the reaction between NADH and polyaniline doped with different acids (PANi), as well as between PANi and NADPH. We then compared these to the reactions between PANi and inorganic redox agents.

Methods: PANi films were synthesised and doped with different acids. Redox potentiometry and UV-Vis spectrometry were used to follow the reaction of PANi with potassium ferricyanide, potassium ferrocyanide, NADH, and NADPH.

Results: PANi is able to reduce ferricyanide to ferrocyanide. It can also react in the opposite direction, producing ferricyanide from the reduced form. PANi film also reacted with NADH to produce NAD and with NADPH to produce NADP. The rate of reaction decreased in the sequence: PANi doped with camphor-sulphonic acid, doped with HCl and finally undoped. Reaction showed first-order kinetics with 2 phases.

Conclusion: The typical reaction rates per unit area of PANi are higher than that in liver. The reaction is not limited by the polymer surface; rather, the whole polymer volume participates in the process. PANi films can act both as oxidising or reducing agents and have potential to be used as artificial membranes for biological redox reactions. Further study should be carried out in this direction.

B4

Functional Polymorphisms of the Cytochrome P450 1A2 (CYP1A2) Gene and Prolonged QT Interval in Schizophrenia

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Aim: Prolonged QT-interval is a direct cause of torsades de pointes, a potentially fatal side effect associated with treatment with antipsychotics. A G>A polymorphism was identified in the 5'-flanking region of the CYP1A2 gene and was associated with a decrease in CYP1A2 activity. A C>A polymorphism on intron I was also associated with tardive dyskinesia in smokers. The aim of this study was to assess the clinical importance of the above polymorphisms in relation to risk for prolonged QT-interval.

Methods: Subjects were 69 patients with a DSM-IV diagnosis of schizophrenia, treated with known doses of antipsychotics. Venous blood samples were collected from consenting patients and QT-intervals measured on ECG and corrected for rate. DNA was extracted from whole blood (Qiagen) and analysed by PCR-RFLP.

Results: The average daily chlorpromazine-equivalent dose was 261 (+/-241) mg. Distribution of polymorphisms in the 5'-flanking region was 59.4% G/G, 33.3% G/A and 7.2% A/A, and that of intron I was 13.0% C/C, 39.1% C/A and 47.8% A/A. The G>A polymorphism was not associated with QT prolongation (QTc in ms G/G = 408, G/A = 409, A/A = 412, $P = 0.938$, ANOVA). However, a marginally significant result for the C>A polymorphism was noted at doses >340mg (C/C = 437, C/A = 416, A/A = 399, $P = 0.058$). Analysis of a subgroup of patients who smoked did not reveal any association in either polymorphism ($P = 0.430$, $P = 0.373$ respectively).

Conclusion: These data suggest that the C>A polymorphism may serve as a genetic risk factor for prolonged QT-interval in patients with schizophrenia. Further studies in independent samples are warranted to confirm these findings.