

# ABSTRACTS

**UNIVERSITY SAINS MALAYSIA  
MEDICAL ALUMNI SOCIETY (PADU)  
NATIONAL SCIENTIFIC MEETING  
4<sup>TH</sup> OCTOBER 2003**

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**HOTEL RENAISSANCE  
KOTA BHARU, KELANTAN  
MALAYSIA**

**Scientific Committee**

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Prof. Rogayah Ja'afar  
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## **DO DIABETIC PATIENTS ON REGULAR HEMODIALYSIS REQUIRE HIGHER DIALYSIS PRESCRIPTION FOR BETTER QUALITY OF LIFE?**

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### **ABSTRACT**

#### **Background:**

Diabetic patients on regular hemodialysis generally have lower quality of life (QOL) compared to non-diabetic patients. This study was done to prove that the lower quality of life in diabetic patients on regular hemodialysis was due to inadequate dialysis therapy.

#### **Method:**

This was a cross sectional study done from January to June 2003 in all hemodialysis patients who fulfilled our selection criteria. They were interviewed using WHOQOL-BREF questionnaire (Malay version) to assess the four domains of QOL including physical health, psychological aspect, social relationships and environment. In addition, their dialysis treatment parameters were measured by using urea kinetic modeling (Kt/V).

#### **Results:**

The mean physical domain score in diabetic was significantly lower compared to non-diabetic patients ( $11.4 \pm 2.53$  Vs.  $13.2 \pm 2.39$ ) and similarly, the mean psychological score was also significantly lower in diabetic compared to non-diabetic patients ( $11.9 \pm 2.56$  Vs  $13.5 \pm 2.75$ ). However, the mean social and environmental score and dialysis prescription were not significantly different between these two groups.

#### **Conclusion:**

Despite similar dose of dialysis given, diabetic patients on regular hemodialysis therapy still have lower physical and psychological component of QOL. This may suggest that diabetic patients may require higher dialysis prescription for better QOL.

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## **DETECTION OF FUNGAL KERATITIS BY PCR**

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#### **Introduction:**

Microbial keratitis is a serious ocular infection. It is often difficult to establish microbial keratitis that is due to fungal infection. Inadequate therapy and delayed diagnosis of fungal keratitis leads to generally poor visual outcomes.

#### **Objective:**

The objective of this study is to determine sensitivity, specificity, positive predictive value and negative predictive value of PCR to detect fungal aetiology in microbial keratitis.

#### **Methodology:**

In this study, a PCR method was compared to the conventional method to detect fungal aetiology in microbial keratitis. Thirty cases of microbial keratitis were studied. The corneas were scraped and the

corneal scrapings were sent for Gram staining, culture and PCR analysis. The PCR was performed with primers pair F1,R2 and F3,R4 from two consecutive regions in the 18S rRNA gene. The presence or absence of this amplified target sequence was determined by agarose gel. Positive result for PCR was considered when there was presence of this amplified target sequence in both primer pairs F1,R2 and F3,R4.

**Results:**

The fungal pathogen was identified in 11 of 30 samples of microbial keratitis by conventional method (gram stain & culture). PCR detected 10 of 11 samples that were positive by conventional method. One of the 19 samples that were negative by conventional method, was positive by PCR. A statistical diagnostic test revealed that the PCR has a sensitivity of 90.0% and a specificity of 94.7% to detect fungal aetiology in microbial keratitis. The positive predictive value was 90.0% and a negative predictive value was 94.7%.

**Conclusion:**

PCR is a rapid, sensitive and a useful method to detect fungal aetiology in microbial keratitis.

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**IMMUNOHISTOCHEMICAL LOCALIZATION OF RET AND P53 MUTANT PROTEIN OF THYROID LESIONS AND ITS PROGNOSTIC IMPLICATIONS**

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**ABSTRACT**

**Introduction**

This study aims to investigate the expression of ret/PTC and p53 in the local normal, benign and malignant thyroid lesions in order to shed light on the pathogenesis of papillary carcinoma and explain the high prevalence of this condition among the nodular hyperplasia (multinodular goiter) cases in the local population.

**Materials and methods**

Archival blocks from 50 follicular adenomas, 66 nodular hyperplasia and 53 papillary carcinoma cases were retrieved from HUSM pathology department files. They were studied by immunohistochemistry for the presence of ret/PTC and p53 mutant protein. Normal tissues from 74 cases served as controls.

**Results**

5.4% normal thyroid tissue, 18% follicular adenomas, 22.7% nodular hyperplasia cases and 71.7% papillary carcinomas expressed ret/PTC mutation. Ret/PTC expression in papillary carcinoma was not associated with coexistence of nodular hyperplasia lesion. P53 is expressed by 17% of papillary carcinoma. No association was found between p53 expression of nodular hyperplasia with or without coexisting papillary carcinoma. p53, not ret/PTC was an excellent predictor of tumour lymph node metastasis and capsular invasion. It is also a significant prognosticator of survival outcome.

**Conclusion**

Ret/PTC mutation is highly prevalent in local papillary carcinoma, indicating a significant role in the pathogenesis of this tumour; with no apparent role in tumour behaviour and survival outcome. P53 on the other hand appear to be a significant factor in the latter events. The two genes appear to act in two different pathways; the former being the initiator, and the later perpetuator of papillary carcinoma.

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## **CLINICAL RELEVANCE OF CYP2D6 GENETIC POLYMORPHISM ON THE PHARMACOKINETICS OF TRAMADOL.**

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### **Introduction:**

Tramadol hydrochloride is metabolised by CYP2D6; a highly polymorphic enzyme. Because tramadol has an active metabolite, the extensive metabolisers (EMs) suffer more from its side-effects while the poor metabolisers (PMs) may suffer from breakthrough pain. The problem is compounded with the existence of wide interethnic variabilities in the capability to metabolise this drug. Furthermore, drug dosages of tramadol are commonly based on Caucasian data. This study was therefore developed to elucidate the correlation between pharmacogenetics and pharmacokinetics among Malaysian subjects.

### **Methods:**

The study was approved by the local Ethics Committee. A new HPLC method to analyse serum tramadol and O-desmethyltramadol (M1) levels was first developed and validated. PCR methods were then optimised to detect mutations common among Asians: *CYP2D6*\*1, \*3, \*4, \*5, \*9, \*10, \*17 and the *duplication* gene. Patients (n=138) received a 100 mg intravenous (IV) dose of tramadol, infused over 2-3 min. Blood was sampled at 0 min and subsequently at 15 min, 30 min, 1 h, 2 h, 4 h, 8 h, 16 h, 20 h and 24 h for serum tramadol HPLC analysis. NPEM2 was then used to determine population pharmacokinetic parameter values of tramadol.

### **Results:**

The developed HPLC method was selective and linear for concentrations ranging from 50 to 3500 ng/ml (tramadol) and 50 to 500 ng/ml (M1) with mean recoveries of 94.36±12.53% and 93.52±7.88% respectively. Limit of quantitation (LOQ) was 50 ng/ml. For tramadol, the intraday accuracy ranged from 95.48 to 114.64% and the interday accuracy, 97.21 to 103.24%. Good precision (0.51 and 18.32% for intra and inter-day respectively) was obtained at LOQ. About half of the subjects possess the wild-type allele with the "Asian" *CYP2D6*\*10 coming a close second at 40.22%. Of the three null alleles determined (*CYP2D6*\*3, \*4 and \*5), only the latter two were detected among the subjects, occurring at an overall frequency of 3.99% and 2.17% respectively. The most common genotype was *CYP2D6*\*1/\*10 (36.23%) followed by \*1/\*1 (30.43%) and \*10/\*10 (14.49%). None of the genotypes predicted poor metabolism. 26.81% of the subjects had genotypes that predicted intermediate metabolism (IMs) while 2.90% were ultra-rapid (URs) metabolisers with the rests making up the extensive metabolisers (EMs). There was a significant difference in the side effect profiles of the various genotype groups with the slower metabolisers (IMs) suffering more dizziness, headache, nausea, sweating and dry mouth compared with the EMs and UMs. The slower metabolisers also had higher serum tramadol levels compared to the EMs and UMs at 8, 16 and 24 h. There was a correlation between total clearance values (CLT) and the genotype groups ( $r = 0.5579$ ,  $p < 0.05$ ).

### **Discussions:**

Generally, the mean total clearance predicted from NPEM2 was lower (19.66 L/h) and the half-life longer (5.99 h) compared to the general values of 28 L/h and 5.2 h respectively reported among the Western populations. This might be due to the differences in the *CYP2D6* genotype with higher frequency of the *CYP2D6*\*10 allele among our Asian subjects which contributes to the IM phenotype. In general, the UMs and EMs had 2.65 and 1.30 times faster total clearances compared to the IMs respectively. Mean total clearance values were 15.89, 18.23, 23.24 and 42.15 L/h while mean half-lives were 7.10, 6.78, 5.56 and 3.78 h among the IMs, EM1, EM2 and UMs respectively.

### **Conclusion:**

Tramadol's pharmacokinetics is influenced by *CYP2D6* polymorphism. Patients that have genotypes predicting lower enzyme activity had slower clearance rates and longer half-lives and suffered from more side-effects. Drug dosages among our Asian subjects should therefore be adjusted accordingly.

**Keywords:** *Tramadol, CYP2D6, genotype, population pharmacokinetic, NPEM.*

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### **VALIDATING THE FDMKAP QUESTIONNAIRES FOR TYPE 2 DIABETIC PATIENTS AND RAMADAN FASTING**

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The FDMKAP questionnaire was developed to assess the level of knowledge, the direction of attitude and the practice of type 2 diabetic patients with regards to Ramadan fasting. Pretest was done to test the validity and reliability of this questionnaire. 33 type 2 diabetic patients on oral medication were given a self-administered questionnaire. A health educator and two diabetologists reviewed face and content validity. Good construct validity was demonstrated by high factor loading of each sub domain ranges from 0.53 to 0.95 with Eigen value of more than one. The total variance explained by the common factors was more than 40%. Acceptable reliability was demonstrated by the internal consistency coefficient ranges from 0.54 to 0.75. This study indicates that the FDMKAP questionnaire offers a valid and reliable assessment of the knowledge, attitude and practice of type 2 diabetic patients with regards to Ramadan fasting.

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### **A STUDY OF PREMARITAL SEXUAL ACTIVITY AMONG SECONDARY SCHOOL STUDENTS IN KOTA BHARU, KELANTAN.**

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#### **Objective**

To evaluate the knowledge, attitude and practice regarding premarital sexual activity and its prevalence among secondary school students in Kota Bharu, Kelantan.

#### **Methodology**

A cross sectional study was carried out among all Form 4 to Upper 6 students in two secondary schools in Kota Bharu, Kelantan in September 2001. Self administered questionnaires (Bahasa Malaysia) based on the modified and validated Sex Knowledge and Attitude Test – Form II (SKAT-II) were distributed in the two secondary schools and completed in one hour. The data was analysed on various domains using the SPSS version 9.0 for Windows.

#### **Results**

Among the 1408 students in the study, there were 812 (57.7%) female and 596 (42.3%) male students. There were 1357 (98.5%) Malay, while Chinese were 8 (0.6%), Indian were 10 (0.7%) and others were 3 (0.2%). Statistical analysis showed sexuality knowledge score was significantly associated with sex and age, but not associated with race of the students. Female and older students were more conservative in heterosexual relations attitude. The overall attitude score was relatively high rejection of sexual myths. Female students have liberal view of abortion as an acceptable method of birth control. Male students were more experienced than females on sexual practice. The prevalence of premarital sexual activity among the secondary school students was 7.3% (103), male 14.1% (84) and female 2.3% (19). Among the student who were sexually active about 55 (41%) did not use any protection, 55 (41%) used condom,

while 11 (8.2%) used oral contraceptive pill or traditional method. Majority of the students 58.1% (818) had never discussed about sexual matters with their parents.

### **Conclusion**

The prevalence of sexual activity among secondary school student age between 16 to 19 years was lower compared with previous studies among adolescents in this country. The students have relatively high sexuality knowledge but conservative in their sexual attitude.

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## **CHARACTERISTICS OF PATIENTS WITH REPEATED ADMISSION FOR ASTHMA**

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### **Introduction:**

Asthma is responsible for much morbidity and mortality with an increasing trend in many countries in the recent decade. This report describes the characteristics of patients with repeated admissions for asthma compared with asthmatic patients who had no repeated admissions over a same period of one-year duration.

### **Methodology:**

This was a cross-sectional comparative study which involved 30 asthmatic patients with repeated admission for asthma compared with another 30 asthmatic patients who had no repeated admission over a same period of one-year duration. The sociodemographic, clinical characteristics and evaluation data were collected. An evaluation included measurement of expiratory peak flow meter (PEFR), inhaler technique skill and questionnaires on knowledge of asthma.

### **Results**

There was no difference in sociodemographic characteristics, PEFR and inhaler technique skill in between both groups. In clinical characteristics, there was difference in history of allergy, absenteeism, asthma symptoms and use of medications. In asthma knowledge scores, the repeated admissions group scored 49.7% vs. 59.19% in the group with no repeated admissions.

### **Conclusion:**

Asthmatic patients with repeated admissions trend to had past history of allergy, more absenteeism, more frequent asthma and more use of inhaler steroids. They also had poor inhaler technique and lesser asthma knowledge about asthma management and skills compare to those who without repeated admissions.

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## **A STUDY ON COMMON SEXUALLY TRANSMITTED DISEASE (STD) INFECTION IN INTERTILE FEMALE IN HOSPITAL UNIVERSITI SAINS MALAYSIA, KUBANG KERIAN KELANTAN.**

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### **Objectives:**

1. To determine local prevalence of common organism in STD infection (Chlamydia, Gonorrhoeae and Syphilis) in infertile females in HUSM
2. To determine the clearance rate of Chlamydial and Gonorrhoea infection after a course of Azithromycin 1 gram

### **Study Method:**

A prospective study involving 150 infertile females under follow up at infertility clinic HUSM between 1<sup>st</sup> of

March 2002 till 28<sup>th</sup> of February 2003. Endocervical samples were obtained to detect Chlamydia trachomatis by direct immunofluorescence, Neisseria gonorrhoea by Gram smear and culture & sensitivity. Blood samples were also obtained for VDRL testing and for 1g M antibody toward Chlamydia. For VDRL testing positive patient another blood sample for Treponema pallidum haemagglutination assay (TPHA) will be taken. In a patient with a positive Chlamydial or Gonorrhoea or both infections, she and her partner will be treated with a single dose of Azithromycin 1 gram orally. After 2 weeks of Azithromycin, the respective investigation(s) will be repeated to determine the clearance of such infection(s).

**Results:**

Chlamydia infection was present in 6 (4.0%) patients. There was no incidence of gonorrhoea or syphilis infection in the studied population. All repeated investigations after Azithromycin for Chlamydial infection showed a negative testing. The clearance rate of Gonorrhoea or Syphilis is unable to determine as there is no incidence of the infection in the studied group.

**Conclusion:**

The prevalence of Sexually Transmitted Disease (Chlamydia, Gonorrhoea and Syphilis) infection in infertile female is low in our studied group. The clearance rate of Chlamydia infection by Azithromycin is good. This is not a true representation of Malaysian populations as it is a hospital-based study. A larger scale study involving a few centers is needed in order to obtain a better representation of Malaysian populations.

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**A COMPARATIVE STUDY ON THE SEVERITY OF DRY EYES BETWEEN MENOPAUSAL WOMEN NOT ON HORMONE REPLACEMENT THERAPY (HRT) AND THOSE ON HRT IN HUSM**

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**Introduction:**

It is a known fact that Dry Eyes Syndrome (DES) occurs more commonly in females of older age group compared to men. Menopausal women have lack of hormones that may contribute to dry eye. Hormone replacement therapy, therefore, is expected to prevent the occurrence of dry eye. However, this has never been scientifically proven.

**Objective:**

To investigate the occurrence and severity of Dry Eye in menopausal women in HUSM and to compare the results between women taking hormone replacement therapy and those not taking any hormone replacement therapy.

**Methodology:**

Menopausal women in HUSM underwent eye examination consisting of the Schirmer's test, the tear film breakup time and the rose bengal staining. At least 2 of the tests need to be abnormal to diagnose dry eye. After the ocular examination, blood was taken from every patient for estradiol, progesterone and dehydroepiandrosterone sulfate levels.

**Results:**

Fifty-four women were examined, 30 (55.6%) of which were on hormone replacement therapy (HRT group), while 24 (44.4%) women were not on any hormone replacement therapy (control group). In the HRT group, 11 patients were on estrogen (Estrogen group) and 19 patients were on combined estrogen and progesterone (Combined group). Dry eye was found in 29.2% of patients in the control group and in 70.0% of patients in the HRT group [ $p < 0.05$ ]. Comparing the patients in the HRT group, dry eye occurred more frequently in the combined estrogen and progesterone group (84.2%) as compared to the estrogen only group (45.5%) [ $p < 0.05$ ]. When analysed separately, the only dry eye test found to be statistically significant was a positive BUT test between the Combined group (94.7%) and the Estrogen group (45.5%) [ $p < 0.05$ ]. The severity of dry eye was not statistically significant between groups.

**Conclusion:**

Dry eye was found more commonly in menopausal women who took hormone replacement therapy in Hospital Universiti Sains Malaysia. Combined estrogen and progesterone therapy was associated with a higher occurrence of dry eye compared to estrogen only therapy. These results, therefore, are in contrast to the previous assumption that HRT would prevent dry eye.

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**A STUDY ON RISK FACTORS OF REPEATED ADMISSION AMONG SCHIZOPHRENIC PATIENTS IN HOSPITAL KOTA BHARU**

<sup>1</sup>*SB Draman*, <sup>1</sup>*MR Merchant*, <sup>1</sup>*M Harny* <sup>2</sup>*Tg Arif*, <sup>1</sup>*SB Ismail*, <sup>3</sup>*SS Jasmit Singh*.

<sup>1</sup>*Department of Family Medicine*, <sup>2</sup>*Dept. of Community Medicine, School of Medical Science, Universiti Sains Malaysia, Health Campus*, <sup>3</sup>*Department of Psychiatric Hospital Kota Bharu*.

**Introduction:**

The number of people with psychological problems in the world has reached 1.5 billion in 1996, but only one percent of them have received treatment. (10<sup>th</sup> International Psychopathology Conference). Schizophrenia is a difficult disease that many choose to conceal. Relapse and frequent readmissions among schizophrenic patients are common and various risk factors have been associated with them. These further enhance the existing societal stigma which causes pain to the patients, their family and friends.

**Objective:**

To identify the risk factors of readmission less than 6 months from the previous admission among schizophrenic patients in Hospital Kota Bharu.

**Methodology:**

A total of 120 outpatients and 120 inpatients who fulfilled DSM IV criteria for schizophrenia from Hospital Kota Bharu between January 2002 until June 2002 were interviewed using a validated questionnaire. The questionnaire includes questions on patients' sociodemographic data, compliance, insight, family support and life events.

**Results:**

Using multiple logistic regression analysis, it was shown that young age, poor compliance, poor insight and poor family support are significant risk factors of repeated admissions. Other variables such as marital status, income, education, distance and life events showed no significant associations.

**Conclusion.**

Age, number of previous hospitalization, poor compliance, poor insight and poor family support are important.

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**THE EFFECTS OF TOPICAL ANTIGLAUCOMA DRUGS ON CONJUNCTIVAL CELL PROFILE**

<sup>1</sup>*Liza Sharmini AT*, <sup>1</sup>*Tan SH*, <sup>1</sup>*Abdul Mutalib O*, <sup>2</sup>*M. Madhavan*, <sup>1</sup>*Elias H*

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**Introduction**

Subclinical inflammation of the conjunctiva induced by topical antiglaucoma drugs were implicated to cause excessive scarring of filtering bleb, which is usually associated with trabeculectomy failure.



### **Objective**

Our aim is to investigate the effects of topical antiglaucoma drugs on conjunctival cell profile when compared to conjunctiva not exposed to the drugs. The effects of duration of treatment and number of drugs on conjunctiva cell profile were also evaluated.

### **Methodology**

Quantitative histological analysis was done on twenty-two (22) superior bulbar conjunctival biopsies using light microscope. Four (4) biopsies were obtained from glaucomatous eyes exposed to single topical treatment undergoing primary trabeculectomy surgery. Seven (7) biopsies from glaucomatous eyes exposed to multiple topical treatment. Eleven (11) age-matched biopsies were obtained from non-glaucomatous eye undergoing cataract surgery and free from any topical drugs.

### **Results**

There were statistically significant increased in lymphocytes and plasma cells count in conjunctiva exposed to topical antiglaucoma drugs compared to control. Mean duration of treatment was  $22.82 \pm 16.12$  months (1.9 years). Number of topical antiglaucoma drugs and duration of treatment showed no statistically significant changes on conjunctival cell profile.

### **Conclusion**

Although hampered by small sample size, there was early evidence of conjunctival cell profile changes in eye exposed to topical antiglaucoma drugs, which may be responsible to excessive scarring of the bleb.

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## **A STUDY ON RISK FACTORS OF REPEATED ADMISSION AMONG SCHIZOPHRENIC PATIENTS IN HOSPITAL KOTA BHARU**

<sup>1</sup>SB Draman, <sup>1</sup>MR Merchant, <sup>1</sup>M Harmy, <sup>2</sup>Tg Arif, <sup>1</sup>SB Ismail, <sup>3</sup>SS Jasmit Singh.

<sup>1</sup>Department of Family Medicine, <sup>2</sup>Dept. of Community Medicine, Universiti Sains Malaysia, Health Campus, <sup>3</sup>Department of Psychiatric Hospital Kota Bharu.

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### **Results:**

Using multiple logistic regression analysis, it was shown that young age, poor compliance, poor insight and poor family support are significant risk factors of repeated admissions. Other variables such as marital status, income, education, distance and life events showed no significant associations.

**Conclusion:**

Age, number of previous hospitalization, poor compliance, poor insight and poor family support are important factors in determining repeated admissions among schizophrenic patients. In the management of these patients, good family support need to be emphasized as it plays a significant role.

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**THE EFFECTS OF TOPICAL ANTIGLAUCOMA DRUGS ON CONJUNCTIVAL CELL PROFILE**

**<sup>1</sup>Liza Sharmini AT, <sup>1</sup>Tan SH, <sup>1</sup>Abdul Mutalib O, <sup>2</sup>M. Madhavan, <sup>1</sup>Elias H**

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**Conclusion**

Although hampered by small sample size, there was early evidence of conjunctival cell profile changes in eye exposed to topical antiglaucoma drugs, which may be responsible to excessive scarring of the bleb.

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**THE SMN GENES ANALYSES OF MALAY PATIENTS WITH SPINAL MUSCULAR ATROPHY**

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**Introduction**

Most spinal muscular atrophy (SMA) patients show homozygous deletion of the SMN1 gene. Some patients also show homozygous deletion of the NAIP gene. In Malaysia, SMA is diagnosed based on the clinical observation with or without muscle biopsy, but molecular analyses of the SMA-related genes

have not been available so far. In this preliminary study, we searched for homozygous deletion of SMN1 exons 7 and 8 in Malay patients with SMA.

**Objective**

To identify the homozygous deletion of SMN1 exons 7 and 8 in Malay patients with SMA.

**Materials and methods**

Three Malay patients who fulfilled the diagnostic criteria for SMA as defined by the International SMA Consortium were enrolled into the study. Genomic DNA was extracted from 3 ml of whole blood from the patients after obtaining their informed consent. The analysis was performed according to the method of van der Steege et al. PCR was done to amplify the gene using primer sets for SMN exon 7 and another primer set for exon 8. To discriminate between the SMN1 and SMN2 gene products, the PCR product was then subjected to Dra I and Dde 1 restriction enzyme treatment. Dra I restriction enzyme digests only the exon 7 of SMN2 gene products, and not the SMN1 gene products, while Dde1 restriction enzyme digests only the exon 8 of SMN 2 and not the SMN 1 gene products. The final products were electrophoresed in 3% agarose gel and visualized by ethidium bromide staining.

**Results**

In control samples, non-digested and digested products of exons 7 and 8 were seen on the gel. However, in these three patients, non-digested products of exons 7 and 8 were not seen, but only digested products of exons 7 and 8 were seen on the gel. According to the findings, SMN1 exons 7 and 8 were completely absent, but SMN2 exons 7 and 8 were retained in these patients.

**Conclusion**

We identified homozygous deletion of SMN1 exon 7 and 8 in Malay patients with SMA. To the best of our knowledge, these are the first SMA cases diagnosed at the molecular level in Malaysia. The analyses of NAIP exon 5 are now under way.

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