Abstracts

Malaysian Journal of Medical Sciences
Vol. 14, No. 1, January 2007

Abstracts of Theses Approved for the M.Sc., M.Med. and Phd. Degrees at the School of Medical Sciences, University Sains Malaysia, Health Campus, Kubang Kerian, Kelantan, Malaysia.

A COMPARISON OF PLAIN ROPIVACAINE 0.5% WITH PLAIN BUPIVACAINE 0.5% IN SPINAL ANAESTHESIA FOR ORTHOPAEDIC SURGERY

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Introduction : Bupivacaine is a popular local anaesthetic drug used for spinal anesthesia, it is relatively cardiotoxic and has a longer duration of motor blockade leading to longer discharge time, research for newer local anaesthetic with less cardiotoxicity and minimal motor blockade is aimed. Ropivacaine is a relatively new long-acting local anesthetic used in spinal anaesthesia, which is structurally and pharmacologically closely related to bupivacaine. However, unlike bupivacaine, which is synthesized as a racemic mixture, ropivacaine is synthesized as a pure S (-) enantiomer. This characteristic feature of the drug may contribute to its faster return of motor function than bupivacaine, and with lower risk of cardiotoxicity.

Methodology : A double blind randomized clinical trial on 72 ASA grade I- II patients who were scheduled to undergo orthopedic surgery of the lower limb with duration of operation less than 3 hours were included in the study. These patients received an intrathecal injection of either: 15 mg of 0.5% plain ropivacaine (3 ml), or 15 mg of 0.5% plain bupivacaine (3 ml) for the above procedure.

Results : The mean onset of sensory block at T12 dermatome was 4 minutes (SD ±3.4) in bupivacaine group and in ropivacaine group it was 5.1 minutes (SD ±3.3) (P<O.207). Where as to reach T10 in bupivacaine group was 6.4 minutes (SD ±3.3) and in ropivacaine group reached in 9.3 minutes (SD ±5.2) (P<0.015). Regarding sensory block at T4, 20 patients (55.5%) in bupivacaine group reached this level with mean onset of sensory block in 6.9 minutes (SD ±3.7). Where as only 4 patients (11%) in ropivacaine group were able to reach the level of T4 in 15 minutes (SD ±4.08) (P<0.001). The duration of sensory block was assessed by the patient's first request for analgesia. In bupivacaine group the mean duration of time of sensory block was 5.4 hours (SD ±1.2) and in ropivacaine group it was 6.5 hours (SD ±2.44) (P<0.02). The mean onset of motor block to reach Modified Bromage Score (MBS1) in bupivacaine group was 1.4 minutes (SD ±0.8) and in ropivacaine group it was 2.1 minutes (SD ±1.5) (P<0.01). And to reach MBS2, in bupivacaine group and in ropivacaine group was 1.6 minutes (SD ±0.9) and 3.0 minutes (SD ±2.0) respectively (P<0.001). While to reach MBS3 bupivacaine group was 2.1 minutes (SD ±1.1) and in ropivacaine group it was 3.6 minutes (SD ±1.8) (P<0.001). In the bupivacaine group the mean duration of motor block was 4.7 hours (SD ±1.1) and in ropivacaine group was 3.5 hours (SD ±1.4) (P<0.001).

Conclusions : Ropivacaine in a dose of 15 mg as 0.5% solution can be used with an acceptable onset of sensory and motor blockade with a longer duration of analgesia and early mobilization for lower limb orthopedic surgery of duration less than three hours and a level of lower than T 12 dermatome.

Ghandev Phutane : Supervisor
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ANAESTHETIC COMPLICATIONS OF LIMB SALVAGE SURGERIES

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Objectives : Our purpose was to study the incidence of perioperative anaesthetic complications and morbidity following limb salvage surgeries as well as to determine the extent of contribution of preoperative status and duration of surgery towards incidences of these perioperative 'complications. Apart from that we aimed to study the extent and quality of postoperative care in limb salvage surgeries

Methodology : The medical records of 120 patients who underwent limb salvage surgery were traced and studied for incidences of perioperative anaesthetic complications in 4 categories hematological, temperature, cardiovascular and pulmonary. Necessary information were tabulated into individual data collection sheets (Appendix A).

Results : There were no significant findings in the demographic data. Intraoperative hypothermia appeared to be the only significant perioperative anaesthetic complication. We were able to demonstrate a significant relationship between the duration of surgery I anaesthesia and the development of intraoperative hypothermia. Almost half the patients were ventilated postoperatively whereby majority of care was instituted in the intensive care unit.

Conclusions : Intraoperative hypothermia is an proven perioperative anaesthetic complication of limb salvage surgery. Incidences of hypothermia in limb salvage surgery are directly proportional to the duration of surgery and anaesthesia. Ventilation in the intensive care unit appears to be the most common postoperative care.

Assoc. Prof. Dr. Nik Abdullah Nik Mohamad : Supervisor
Dr. Vishwanathan Thirumayan : Co-Supervisor

THE EFFECT PF PHENYLEPHRINE AND EPHEDRINE IN FETAL OUTCOME IN THE TREATMENT OF HYPOTENSION DURING SPINAL ANAESTHESIA FOR CAESAREAN DELIVERY

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Introduction : Sympathetic blockade manifested by hypotension is

one of the most common complications of the regional anaesthesia in obstetric patients. Its prophylaxis and treatment are primarily directed towards the concern that hypotension may result in decreased uteroplacental perfusion, thus compromised fetus and maternal. Various drugs and methods have been used in attempts to attenuate this response but all have limitations. Many studies using phenylephrine or ephedrine as a prophylaxis drug to suppress these reflexes had shown promising results and reduce the occurrence of fetal acidosis. As both phenylephrine and ephedrine had rapid onset and short duration of action, we formulated a comparative study to evaluate the capability of this drug to reduce the fetal acidosis in the treatment of hypotensive response to spinal anaesthesia.

Objectives : The objectives of this double-blinded, randomized study were to compare the fetal outcome after given phenylephrine or ephedrine as a treatment of hypotension in spinal anaesthesia during caesarean delivery.

Methodology : Fifty four patients, ASA physical status I or II, undergoing elective lower segment caesarean section surgery were assigned randomly in a double blind, to receive bolus dose of either ephedrine (6mg/ml) or phenylephrine (200mcg/ml), given intravenously as a treatment of hypotension post spinal anaesthesia. Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were recorded prior to spinal anaesthesia as baseline T and every minute after spinal anaesthesia until delivery of the fetus. At delivery, the umbilical artery blood was obtained and acid base analysis performed. Apgar scores at 1 and 5 mm after delivery was recorded. Patients were also monitored for complications such as nausea, vomiting and arrhythmia.

Results : Both ephedrine and phenylephrine groups showed the increase of SBP, DBP and MAP in the treatment of hypotension. Phenylephrine group showed mean umbilical artery pH 7.314 when compared to ephedrine (control) group 7.279. The entire increased in umbilical artery pH was significant statistically. Total overall complications were also significantly lower in phenylephrine group when compared to ephedrine (control) group.

Conclusion : Phenylephrine was able to increase the mean fetal umbilical artery pH in the treatment of hypotension in post spinal anaesthesia patients when compared to ephedrine (control) group. The total complications also were lower in patients treated with phenylephrine.

Assoc. Prof. Dr. Nik Adullah Nik Mohamad : Supervisor
Dr. Hendra Hardy bin Mohd Zaini : Co-Supervisor

A STUDY OF ADVERSE EVENTS OF INTRA-IIOSPITAL TRANSPORTATION OF CRITICALLY ILL PATIENTS FROM THE EMERGENCY DEPARTMENT, HOSPITAL UN! VERSITI SAINS MALAYSIA

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Introduction : The transports of critically ill patients always involve some degree of risks to the patient and sometimes to the accompanying personnel. It has been stated that when a patient is transported from an ICU to a diagnostic area such as a radiology suite, they are not in a hospital, but only close to one. Intrahospital transport refers to transportation of patients within the hospital for a purpose of undergoing diagnostic or therapeutic procedures, or transfer to a specialised unit. The basic reason for moving a critically ill patient is the need for additional care, either technology and/or specialists not available at the patient's current location.

Objectives : The objectives of this study are to determine the prevalence of adverse events during transfer of critically ill patients from emergency department to other specialised unit in HUSM, to determine the prevalence for the requirement of therapeutic interventions during transport as well as, to determine the factors predicting the occurrences of adverse events and the requirement for major therapeutic intervention during the intrahospital transport.

Results : A total of 257 transportations involving 247 critically-ill patients fulfilling the inclusion and exclusion criteria arrived to emergency department were included in this study over the period of twelve months. From this study, it was found out that there were no adverse events in 157 transports (61.5% ± 0.48). There was a significant in at least one variable in 100 transports (3 8.9% ± 0.48%). Of these 100 transports, 68 (26.5%) had derangement in only the physiologic variables, 15 (5.8%) had both a physiologic derangement and an equipment-related event, and 15 (5.9%) required at least one major intervention. At least one equipment-related adverse event occurred in 18 transports (7.0%). At least one major therapeutic intervention was performed in 15 transports (5.9%). Death during transport. The requirement for a major procedure was 9.3% in mechanically ventilated patients versus 3.4% in non-ventilated patients. Only pretransport Therapeutic Intervention Scoring System was significantly associated with the development of physiologic deterioration and the requirement for major intervention. The age and sex of the patient, and the number of escort personnel accompanying the transport did not affect the frequency of adverse event.

Conclusions : This study revealed that majority of the critically ill patients transported from the Emergency Department developed serious physiologic adverse events during intrahospital transport. Some of the clinical predictors such as blood pressure, heart rate, respiratory rate and oxygen saturation by pulse oxymeter were shown to be a significant indicator in the development of adverse events during transport of critically ill patients. Severity of illness as shown by Therapeutic Intervention Scoring System (TISS) is significantly associated with the physiological occurrence of adverse event and major interventions. The team composition and equipment required on transport must be commensurate with the pretransport severity of illness.

Dr. Rashidi bin Ahmad : Supervisor
Dr. Idzwan bin Zakaria : Co-Supervisor

RANDOMIZED, DOUBLE BLIND, CROSS OVER, PLACEBO CONTROLLED STUDY ON THE EFFECT OF REDVINE HERBAL BEVERAGE ON HEALTHY VOLUNTEER

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Introduction : Redvine herbal beverage has an antioxidant effect due to the presence of phenolic compounds, anthocyanidins and resveratrol. The anti-oxidant effect protects LDL from oxidation. Resveratrol has been shown to inhibit the COX pathway and influence platelet aggregation.

Objectives : The aim of this study is to assess any significant effect of Redvine herbal beverage on inhibition of platelet aggregation, reduction of LDL-cholesterol, reduction in leg volume test, increase in total antioxidant status and increase in arterial compliance.

Methodology : The study was a randomized, double blind, cross over, placebo controlled study on the effect of Redvine herbal beverage on 50 healthy volunteers. The duration of the study was 16 weeks. Before entering treatment phase, washout period was done for 2 weeks. The volunteers were divided into 2 groups, namely group A and group B. During the first phase of the treatment, group A and B were given

placebo and Redvine herbal beverages (verum) in 80m1 bottle respectively daily dose for 6 weeks. Rest time was given for a week before entering second phase of treatment that began at week 7 and medications were crossed over for another 6 weeks. All the volunteers were then rested for a week and no medication were given during this week. At the end of 14 weeks final examination on the volunteers were done. Measurements were taken once except for leg volume test for each visit. Leg volume test was taken for three times and took an average reading. Other parameters were platelet count, platelet aggregation test, total cholesterol, triglyceride, high density lipoprotein, low density lipoprotein, very low density lipoprotein, total cholesterol/high density lipoprotein, leg volume test, plasma total antioxidant status and augmentation index.

Results : There was no significant effect in all the parameters namely platelet count, platelet aggregation test, total cholesterol, triglyceride, high density lipoprotein, low density lipoprotein, very low density lipoprotein, total cholesterol/HDL ratio, leg volume test, total antioxidant test and augmentation index .There was no adverse effect reported among the volunteers during study period.

Conclusion : All parameters namely platelet count, platelet aggregation test, total cholesterol, triglyceride, high density lipoprotein, low density lipoprotein, very low density lipoprotein, total cholesterol-HDL ratio, leg volume test, plasma total antioxidant status and augmentation index showed no significant effects and there was no adverse effect reported about Redvine herbal beverage.

Dr. Shaiful Bahari Ismail : Supervisor
Assoc. Prof. Dr. Syed Hatim Noor : Co Supervisor

A STUDY ON ACCURACY OF PREDEFINED SCREENING CRITERIA FOR SELECTIVE ORDERING OF CHEST X-RAY IN ROUTINE MEDICAL EXAMINATION AMONG STUDENTS ENROLLING INTO HIGHER LEARNING INSTITUTION ATTENDING HOSPITAL UNIVERSITI SAINS MALAYISA

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Introduction : The practice of doing chest x-ray in routine medical examination (RME) is still prevalent in Malaysia although many studies argue the benefit of routine chest x-ray in asymptomatic individuals. There is no standardized RME form used by various institutions in Malaysia. There are also no clear guidelines on who should have a chest x-ray and who should not. Therefore, there is a need to develop a set of screening criteria for selective ordering of chest x-ray in RME to reduce health care cost and to avoid unnecessary radiation risk.

Objectives : The objectives of the study were to develop an accurate set of screening criteria from literature review, to determine the sensitivity, specificity, positive predictive value and negative predictive value of the predefined screening criteria. The set of screening criteria is intended to be used as a screening tool for selective ordering of chest x-ray in RME, to determine the prevalence of abnormal chest x-ray in routine medical examination and to determine the sensitivity, specificity, positive predictive value and negative predictive value of chest x-ray interpretation made by medical officers. The agreement between medical officers and radiologist is also determined.

Methodology : A total of 408 students who came to Hospital Universiti Sains Malaysia between 1st June 2004 and 31 December 2004 participated in the study. They were screened by the predefined screening criteria developed by the researcher. The decision on chest X-ray requirement was determined based on the screening criteria. All the chest x-rays were reported both by medical officers and an appointed radiologist.

Results : The results from this study showed that the predefined screening criteria developed by the researcher has a sensitivity, specificity, positive predictive value and negative predictive value of 26.1%, 66.8%, 4.5% and 93.8% respectively. The prevalence of abnormal chest x-ray is 5.64% (95% C.I: 0.03-0.08). The sensitivity, specificity, positive predictive value and negative predictive value of chest x-ray interpretation by medical officers are 17.4%, 98.2%, 36.4% and 95.2% respectively The agreement on chest x-ray interpretation between medical officer and radiologist was poor (kappa=0.206).

Conclusions : From this study, it can be concluded that the prevalence of abnormal chest x-ray in RME is low. The set of screening criteria developed by the researcher is not accurate to be used as a screening tool for detecting abnormal chest x-ray in RME. However, the high negative predictive value means that the probability if a student is not indicated for chest x-ray to have a normal result is high. There is considerable discrepancy between medical officers' chest x-ray interpretation and that of trained radiologist. Chest x ray findings did not influence the decision of fitness for enrolment. Further research needs to be done to improve the accuracy of the screening criteria.

Dr. Harmy Mohd Yusoff : Supervisor
Dr. Ezane Abdul Aziz : Co-Supervisor

A STUDY ON THE EFFECT OF ORAL HYPOGLYCEMIC AGENTS ON ARTERIAL STIFFNESS AMONG MALAY PATIENTS WITH TYPE DIABETES MELLITUS

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Objective : The purpose of this study is to see whether there was any significant difference in arterial stiffness (as measured by augmentation index) between diabetic and non diabetic subjects and to see whether there was any significant difference between two different oral hypoglycaemic agents(OHA) regimens, (sulphonylurea monotherapy and metformin in combination with sulphonylurea therapy) on arterial stiffness.

Methodology : This was a case control study conducted in the Klinik rawatan keluarga(KRK) and Diabetic clinic, HUSM from May 2004 till May 2005. Hundred and two diabetic subjects and hundred and two age- and sex-matched non-diabetic control subjects were recruited after obtaining verbal consent following explanation of study protocol. Augmentation index (AI) was measured using the Sphygmocor apparatus and all measurements were performed by the researcher after an earlier validation study. These mean augmentation index measurements were then analyzed.

Result : The mean of AI of diabetic subjects was significantly higher than non diabetic subjects (140.32 ± 12.0% Vs 128.77 ± 10.69%, P <0.0001). However, there was no significant difference in mean AI between two different OHA regimen groups in diabetic subjects (140.51 ± 11.42 Vs 140.14 ± 12.86, 95% C -4.40, 5.15, p = 0.877).

Conclusion : Diabetic patients have increased arterial stiffness compared with age- and sex-matched non diabetic subjects, which may partly explain why diabetes mellitus are associated with increased cardiovascular risk. This study also showed that two different groups of oral hypoglycaemic agents have no effect in relation to arterial stiffness.

Dr. Juwita Shaaban : Supervisor
Prof. Dr. Abdul Rashid Abdul Rahman : Co-Supervisor

A COMPARISON OF SUTURING TECHNIQUE FOR REPAIR OF EPISIOTOMY

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Objectives : To determine the outcome of episiotomy repair between 2 suturing techniques- continuous subcuticular technique and transcütaneus interrupted technique among Malay primigravida.

Methodology : A 6 months prospective randomized study over a total of 200 Malay primigravida in Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan, who had spontaneous vaginal delivery (SVD) from August 2005 till January 2006. This study was conducted to compare the outcome of two suturing techniques—continuous subcuticular technique and transcutaneous interrupted technique. The outcome measured were perineal pain at 24 hours, 10 days and 3 months and also dyspareunia after 3 months post-delivery.

Results : A total of 200 patients (100%) were able to be reviewed at 24 hours, 148 patients (74%) at day 10 and 131 patients (65.5%) were reviewed at 3 months post- delivery. There was significantly less time taken to repair episiotomy in subcuticular continuous technique compared with transcutaneous interrupted technique (17.2 mm vs 24.8 mm, p<O.O5). However, there was no significant difference in perineal pain score at 24 hours (2.4 vs 2.3, p=O. 10 days (2.3 vs 2.6, p=O.36l) and 3 months (1.3 vs 1.3, p post-delivery. There was no difference in dyspareunia at 3 months post-delivery review in both groups (p=O.33l). The perineal pain at 24 hours was significantly correlated with episiotomy length after repaired (r: -0.185, ,=o.oo9). However, there was no significant difference in pain on ambulation at 24 hours (p and 10 days (p=O. use of analgesia at 24 hours (p 0.841), 10 days (p= 0.909) and 3 months (p= 0.3 34) post-delivery. There was no difference in urinary or bowel problems for both groups at 24 hours and 10 days (p > 0.05). There was no statistically significant difference in wound morbidity of both group studied at 24 hours and 10 days post- delivery (p> 0.05)

Conclusions : Subcuticular continuous technique should be given as an option when repairing an episiotomy. Even though there was no reduction in the symptoms of perineal pain and dyspareunia, this method significantly required less repairing time.

Prof. Madya Dr. Nik Mohd. Zaki : Supervisor

THE INFLUENCE OF BETA2-ADRENORECEPTOR POLYMORPHISMS ON SPIROMETRIC CHANGES IN GLAUCOMA PATIENTS RECEIVING TOPICAL TIMOLOL-XE

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Introduction : Timolol is a non selective beta adrenoreceptor antagonist without intrinsic symphatomimetic activity. It is one of the preferred monotherapy drug of choice in the treatment of primary open angle glaucoma in Malaysia. Unfortunately, a certain amount of these eye drops is absorbed through the nasopharyngeal mucosa and into the systemic circulation and by blocking the beta-adrenoreceptors in the heart and lungs, they can cause bradycardia and respiratory impairment.

Objectives : To evaluate the extent of impairment of respiratory function in newly diagnosed glaucoma patients on topical timolol-XE therapy and to study the influence of beta2- adrenoreceptor gene polymorphisms in altering the respiratory function among glaucoma patients receiving topical timolol-XE 0.5%.

Methodology : Sixty-three consecutive newly diagnosed primary open angle glaucoma and normotensive glaucoma patients without any history of obstructive airway disease were recruited. Spirometry, pulse, blood pressure were recorded before starting topical therapy with timolol-XE 0.5% and repeated again at 1 month, 3 months and 6 months follow up. Five ml of blood was taken from each patient for DNA extraction and multiplex PCR to determine the beta2-adrenoreceptor (b2AR) (genotyping (polymorphism) for allele 16, - 47, 27,-20, and 164. Patients demonstrating a greater than 15% reduction in FEy were deemed to have reversible airways obstruction.

Results : Six patients developed respiratory outflow obstruction. The allele frequencies in the group who developed respiratory outflow obstruction versus no respiratory impairment were Argl6 (50% vs 75%), G1y16 (50% vs 25%), G1n27 (83% vs 88%), G1u27 (17% vs 12%), Thr164 (100% vs 100%),-20C (58% vs 21%), -20T (42% vs 79%), Argl9 (17% vs 9%), Cysl9 (83% vs 91%).

Conclusions : Genetic variation in the beta2-adrenoreceptor and its associated proteins is common. The presence of single nucleotide polymorphism in the beta2-adrenoreceptor gene is probably disease-modifying and can contribute to the development of respiratory outflow disease. The SNP G1y16 could predispose patients on topical timolol-XE to the development of outflow impairment. Conversely, the SNP T-20 may afford a protective effect against outflow disease.

Dr. Liza Sharmini Mohd. Tajudin : Supervisor
Dr. Zilfalil bin Alwi : Co-Supervisor

VISION SCREENING AMONG PRESCHOOL CHILDREN AGED 4 TO 6 YEARS IN KOTA BHARU, KELANTAN

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Objective : Vision screening was performed in Kota Bharu District, to determine the prevalence of visual impairment, refractive error, strabismus and amblyopia among preschool children between 4-6 years of age.

Methodology : Vision screening was conducted on 252 kindergarden children aged between 4-6 years The first step was to assess visual acuity in all children in the selected kindergardens using Snellen chart, Snellen letters, Tumbling E, Sheridan Gardiner, and Cardiff acuity cards in decreasing order of cognitive difficulty. They were also assessed for presence of any strabismus and/or amblyopia. Refraction was done using portable hand-held refractokeratometer . Those with vision equal or less than 6/12 were referred to a tertiary centre for complete ocular examination and refraction to determine the cause of poor vision.

Results : Of the 252 students screened, 50.8%(n=128) were males and the remaining females. Among them, 70.2% (n=177) were Malays, 29.8% non-Malays (Chinese 73, Indians 2). About 16.7% (n=42) students had uncorrected visual acuity equal or less than 6/12 in the better eye. This was further reduced to 1.6% after best corrected visual acuity. The prevalence of refractive error was 21%(n=53) of students with hyperopia (11.1%, n=28) more commoner than myopia (9.9%, n= 25) as the cause of visual impairment. Amblyopia was found in 2 % (n students, refractive error being the major cause. Strabismus was noted only in one student (0.4%). There was a trend towards myopia in the older age group compared to the younger age group. However, there was no significant relationship between the refractive error and

the gender of the students.

Conclusion : Visual impairment due to refractive error was found to be the main cause for poor vision which is comparable to other similar studies. Hyperopia is found to be more common than myopia but myopia was more prevalent among the older age groups compared to hyperopia. There was no significant relationship between the gender and refractive error. In view of above prevalence rate of refractive error and amblyopia, it can be concluded that there is a need for a vision-screening program among pre-school children so that vision disorders are detected early

Dr. Zunaina Embong : Supervisor
Dr. Wan Hazabbah Wan Hitam : Co-Supervisor

THE STUDY OF PREVALENCE OF REFRACTIVE ERROR AMONG MALAY PRIMARY SCHOOLCHILDREN IN KOTA BHARU, KLEANTAN

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Objective : To determine the prevalence of refractive error and visual impairment among primary school children of Malay ethnicity in Kota Bharu, Kelantan.The possible associated factors inducing refractive error will also be studied.

Methodology : A school-based cross sectional study carried out from January to July 2006. Random selection of primary school children was performed on standard 1 to standard 6 students of 10 primary schools in the Kota Bharu district. Information sheet, questionnaire and consent were given to parents before the examination day. Ophthalmic examination was carried out in all selected schools. Visual acuity assessment for presenting, uncorrected and best corrected acuity was measured by using logMAR ETDRS chart. Positive predictive value of uncorrected visual acuity equal or worse than 20/40, was used as a cut-off point for further evaluation of refractive error by automated refraction and retinoscopic refraction. Ocular motility, strabismus examination, anterior segment and non-dilated fundus examination were also performed.

Results : Of the total 840 enumerated students, 705 were examined. The main presenting visual acuity measured was 20/20. The prevalence of uncorrected visual impairment was seen in 54 (7.7 %) children. The main cause of the uncorrected visual impairment was refractive error, contributing 90.7% of the total, with 7.0% prevalence for the studied population. Other causes of visual impairment such as corneal or retinal problem and amblyopia were not common. Myopia was the commonest type of refractive error (5.4 %), followed by hyperopia (1.0 %) and astigmatism (0.6 %). Only 24 (48 %) of students with refractive error wear glasses on the examination day. A significant positive correlation, was noted between myopia development with increasing age ($p< 0.005$), more hours spent in reading books ($p< 0.005$) and background history of siblings with glasses ($p< 0.005$) and those parents with higher education ($p< 0.005$).

Conclusion : There was a relatively low prevalence of visual impairment and refractive error among primary school children observed in Kota Bharu. Uncorrected refractive error was the commonest cause of visual impairment. Significant number of children with refractive error was not on glasses.

Dr. Wan Hazabbah Wan Hitam : Supervisor
Dr. Mohtar Ibrahim : Co-Supervisor

A STUDY ON PREVALENCE OF HEARING IMPAIRMENT AND EAR DISEASE IN KELANTAN

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Objective : To determine the prevalence of hearing impairment and ear diseases in Kelantan.

Methodology : It was a prospective population based cross-sectional study. The study was conducted in the chosen subjects that based on two-stage stratified random sampling in nine districts in Kelantan. Enumeration blocks (EB) were selected from each district. Eight living quarters were selected from each EB. All households who live in the living quarters and consented to get involved in the study were screened for hearing impairment and ear diseases by using questionnaire, ear examination and audiological test at their house. Each participant was subjected to otoacoustic emission test. Subjects were then underwent behavioral test according to their age. The behavioral tests include distraction test and pure tone audiometry (air conduction only).

Result : A total of 502 participants were screened. For the ear diseases, 500 were able to be examined and the prevalence was 11.8%. Impacted wax was the most common ear disease found followed by chronic suppurative otitis media. Whereas for the hearing impairment, the prevalence based on OAE was 30.2% and this figure was reduced to 16.8% when the participants were screened with behavioral tests. Presbyacusis was most common finding of the cause of hearing impairment followed by noise induced hearing loss.

Conclusion : Result from the study has shown that significant prevalence of ear diseases and hearing impairment among population of Kelantan and effort should continue even harder to tackle the problems. Providing education toward good ear care and screening program to detect hearing impairment as early as possible and thus early rehabilitation should be carried out.

Assoc. Prof. Dr Dinsuhaimi Sidek : Supervisor
Dr. Mohd. Khairi Mohd. Daud : Co-Supervisor
Dr. Baharuddin Abdullah : Co-Supervisor

A HEALTH RELATED QUALITY OF LINE ASSESSMENT TREATED HEAD AND NECK CANCER PATIENTS IN EAST COAST OF MALAYSIA

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Introduction : Length of survival and tumour recurrence has long been used as the assessment of treatment outcome in Head and Neck cancer patients. However for the past 20 years with reduction in tumour recurrence and increasing survival rates, quality of life (QOL) of the survivors has becoming the measure of treatment outcome. Recent data from United State indicated that the number of patients with Head and Neck cancer is increasing over the years and the trend is probably similar in Malaysia. QOL is a broad concept which covers four essential components which are physical function, psychological state, social interaction and somatic sensation. There are many validated instruments available worldwide and the University of Washington quality of life (UWQOL) questionnaire is the most commonly used in United Kingdom as well as United States. As in other parts of the world, there has been an increasing demand for Malaysian researchers nowadays to assess the QOL in their Head and Neck cancer patients.

Objectives : The main objective in this study is to evaluate quality of life in the treated Head and Neck cancer patients.

Methodology : This is a cross-sectional study in a treated Head and Neck cancer patients conducted in Ear, Nose and Throat clinic (ENT) of Hospital Tengku Ampuan Afzan (HTAA) Kuantan in the state of Pahang and ENT clinic of Hospital Universiti Sains Malaysia (HUSM) Kubang Kerian in the state of Kelantan. Those Malay patients who fuilfihled the inclusion and exclusion criteria were recruited into this study. Standard validation process were followed which include forward and backward translation of the originial version UWQOL. Patients were asked to answer the Malay version UWQOL. Data were analysed using statistical software SPSS version 12.0 for Windows.

Results : Reliability was tested by inter-item correlation coefficient with Cronbach' s alpha value of 0.80. Test-retest reliability as reflected by intraclass correlation coefficient was 0.85. Patients with early stage tumour (stage I and II) tend to score higher than advance stage tumour (III and IV). Site of tumour and mode of treatment does not significantly affect the patients QOL.

Conclusions : This data suggest that Malay version of UWQOL is reliable and valid questionnaire when applied to a sample of Head and Neck cancer patients in Malaysia. Tumour stage was the strongest determinant of quality of life in Head and Neck cancer patients.

Dr. Suzina Sheikh Ab Hamid : Supervisor
Prof. Dr. Abd. Rani Samsudin : Co-Supervisor

A SERIAL EVALUATION OF THE EFFECTS OF SEA CUCUMBER EXTRACT ON THE HEALING PROCESS OF TRAUMATIC TYMPANIC MEMBRANE PERFORATIONS IN GUINEA PIGS

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Introduction : Gamat, a local name for sea cucumber extract (SCE) has a strong role in the practice of traditional and complementary medicine in health care in Malaysia. Its effectiveness is species specific and dose dependant. Tympanic membrane (TM) perforations are common Otorhinolaryngology problems. Alternatives to surgical treatment of tympanic membrane perforation have been evaluated. In the future, it is hoped that SCE will proved beneficial in the healing process of tympanic membrane perforations. The traumatic TM perforation in guinea pigs is a proven model of TM healing.

Objective : The objective of this study was to serially evaluate the effects of 5mg/mi concentration of Gamat on the healing process of traumatic tympanic membrane perforations in guinea pigs, both in the rate of healing process and the quality of resultant neomembranes.

Study Design : This was a prospective, and blinded animal study.

Methodology : A total of 40 Guinea pigs were selected and subjected to anterior quadrantic excision of the tympanic membranes under anaesthesia. The test and control substances were placed at the perforation. In any animal one ear acts as control to the other ear. Results were obtained following euthanasia at day three, five, nine and fourteen post perforation. Each group consisted of 10 guinea pigs. The results were assessed using an operating microscope. The tympanic membrane were dissected out and subjected to macroscopic and histopathology examinations.

Result : The results showed that gamat at 5mg/mi promote the quality and quantity of wound healing in traumatic tympanic membrane perforations of guinea pigs particularly during first 9 days following injury. Histologically there were increased production of epithelium at early phase of wound healing in the SCE group. However, there were no significant difference in the formation of granulation tissue layers between the two groups.

Assoc. Prof. Dr. Dinsuhaimi Sidek : Supervisor
Prof. Syed Mohsin Syed Jamalulail : Co-Supervisor
Assoc. Prof. Dr. M. Madhavan : Co-Supervisor

THE EFFECT OF MILD HEARING LOSS ON ACADEMIC PERFORMANCE OF PRIMARY SCHOOL CHILDREN IN KUALA TERENGGANU

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Objectives : The objective of this study was to report on the prevalence of mild hearing toss and the association between academic school performance and mild hearing toss among standard 5 primary schoolchddren in the district of Kuala Terengganu.

Methodology : This was a comparative cross sectional study done between August to October 2004. A total of 257 standard 5 students from 5 randomly selected national schools in Kuala Terengganu were screened. Students in Class A were considered to have good academic performance where as students in Class C as poor academic performance. Student selection into these classes was based on their final term examination Cumulative Grade Point Average (CGPA) in standard 4. The students were screened for hearing impairment using otoscopy, tuning fork tests (Rinne's and Weber's) and TEOAE. Those who failed hearing screening were further evaluated using pure tone audiometry for hearing threshold in a sound treated room at ORL specialist clinic Hospital Kuata Terengganu.

Results : 159 (61.9%) students have passed hearing screening for both ears. 91 (35.4%) students failed hearing screening and were referred for PTA whereas 7 (2.7%) students were referred for treatment and PTA. 36 out of 68 students who had come for PTA were found to have mild hearing toss making a prevalence of 14%. Conductive hearing toss was the most common finding in 32 (88.9%) students and sensorineural hearing loss was found in four (11.1%) students. Chi-square test showed there was a significant association between mild hearing toss and academic performance.

Conclusion : The prevalence of mild hearing loss among standard 5 school children in Kuala Terengganu was 14%. School children with even mild hearing loss have poorer academic performance as compared to other students with normal hearing (p value <0.01). Hearing screening programmed among primary schoolchildren is necessary and beneficial and therefore is recommended.

Dr. Mohd Khairy Md Saud : Supervisor
Assoc. Prof. Dr. Dinsuhaimi Sidek : Co-Supervisor

DEPRESSION AND COPING STRATEGIES AMONG SEXUALLY ABUSE CHILDREN: A PRELIMINARY STUDY

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Introduction : Child sexual abuse is a complex life experience and it is associated with depression. Sexually abused children cope with the experiences differently. Depression is a major mental health concern

worldwide. There is no previous local study on screening for depression and coping strategies used in child sexual abuse in Malaysia.

Objectives : This study aimed to describe the psychosocial factors and coping strategies used and its association with depression in sexually abused children.

Methodology : The study consisted of 2 stages. First, the validation of the Malay version of CDI and followed by a cross sectional study of depression and coping strategies used, participated by 65 sexually abused children and adolescents attending HUSM. The following measures were used: general questionnaire, semi-structured questionnaire of coping strategies and the validated Malay version-CDl. Depression was defined as score above the optimum cut-off point on Malay version-CDl determined at the validation study.

Results : The validation study showed that at the cut-off score of 18, the CDI had 90% sensitivity and 98% specificity in detecting depression.

In the study sample, 16 (24.6%) participants had been depressed and 49 (75.4%) participants had not been depressed. In coping strategies, 57 (87.7%) used emotion-focused coping strategies, 6 (9.2%) used problem or task-focused coping strategies and 2 (3.1%) used both emotion and problem-focused. Among emotion-focused coping strategies, participants used (i) deciding than nothing can be done to change things, (ii) denial and (iii) suppression.

Conclusion : The screening of depression in the vulnerable group such as child sexual abuse was important, as for early detection and treatment. By recognizing the coping strategies used in sexually abused children, it can be helpful for clinician and counselor in their counseling session.

Key word: Child sexual abuse, Children Depression Inventory, depression, coping strategies.

Dr. Rohayah Husain : Supervisor
Assoc. Prof. Dr. Hasanah Che Ismail : Co-Supervisor

PRELIMINARY STUDY OF CT PERFUSION OF PENUMBRA IN PATIENT WITH HYPERTENSIVE INTRACRANIAL HAEMORRHAGE

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IIntroduction : Hypertension is a major illness in Malaysia with a prevalence of 24% (Zaher et al., 1998) and haemorrhagic stroke is its complications which much more likely to result in death or major disability than cerebral infarction(Broderick et al., 1993). Nonenhanced Computed Tomography (NECT) scan is the most common imaging modality used to diagnose intracranial haemorrhage (ICH). There were controversial issues whether medical or surgical treatment benefits these patients. CT perfusion (CTP) allowed the study of cerebral perfusion. Theoretically it is useful in selecting for treatment option. Modified Barthel index (MBI) was a reliable disability scale (Sulter et al., 1999) and used as outcome assessment.

Objectives : This preliminary study was aimed to determine perfusion characteristics of perihaematoma region and correlation with clinical outcome. These will be used as predictor of the outcome whether medical or surgical treatment benefits the patients. This study also aimed to find contributing factors of abnormal perfusion in perihaematoma of hypertensive ICH and factors affecting its clinical outcome.

Materials & Methodology : From July 2004 till November 2005, 10 patients were enrolled as they fulfilled the inclusion criteria and written informed consent obtained. NECT scan was done to confirm ICH then CTP was performed. The data were analyzed at the CT workstation. Haematoma volume and distance from skull were measured in NECT scan. Perihaematoma regions were divided into four sections in relation to distance from the skull. The regions of interest were drawn based on CTP colour mapping. Each parameters of perfusion were produced by the perfusion software and were analyzed whether selected region were normal, penumbra or umbra perfusion status. MBI was scored at presentation and 4 weeks.

Results : Significant statistical Spearman correlation at the 0.05 level (2-tailed) noted between ages and initial MB!, and haematoma volumes with haematoma distances to skull. Significant Pearson correlation of haematoma volume and ischaemic injury sizes at the 0.01 level (2-tailed) noted. Perfusion ischaemic injury were found in perihaematoma region however no statistical correlation of the perihaematoma area with clinical outcome.

Conclusions : CTP is a useful, easy and practical method in assessing intracranial perihaematoma perfusion however no correlation with clinical outcome. A bigger sample size may reverse these findings.

Dr. Salmah @ Win Mar : Supervisor
Assoc. Prof. Dr. John Tharakan : Co-Supervisor

A PRELIMINARY STUDY OF THE ULTRASONOGRAPHIC APPEARANCES OF GALL BLADDER AND BILIARY TRACT IN CLINICALLY SUSPECTED BILIARY ATRESIA

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Introduction : Biliary atresia is one of the congenital anomalies that has high mortality rate which is characterized by a fibrosclerosing obliteration of the extrahepatic duct that uniquely presents in the first months of life, It is also the most frequent cause of chronic end-stage liver disease in children and accounting for 40 to 50 % of all pediatric liver transplants. Ultrasonography has been one of the diagnostic workouts, where early and specific diagnostic tools are important in achieving the correct diagnosis for better prognosis of patients.

Methodology : and Materials : This is a retrospective cross sectional study, involving 32 clinically suspected biliary atresia infants with 32 normal infants as a control group. The aim of this study is to compare the gall bladder appearance and it measurements between disease and control group. Triangular cord was assessed in the porta hepatis from hepatobiliary ultrasonography done from January 2003 till December 2005 in HUSM between clinically suspected biliary atresia infants and normal control group.

Results : Most of the infants were term infants with normal birth weight. There was no significant difference noted between sex, race, gestational age and day of ultrasound performed between the clinically suspected biliary atresia and normal control subject. Significant difference was noted between the gall bladder wall thickness, length and width between the two group with p value of 0.009, 0.001 and 0.022 respectively.

Conclusion : There is a significant difference noted in the gall bladder length, width and wall thickness between the clinically suspected biliary atresia and normal control group. Gall bladder was present in 84.4 % of cases and triangular cord sign was present in 20.1 % in clinically suspected biliary atresia infants.

Assoc.Prof. Dr. Haji M. Abdul Kareem : Supervisor
Dr. Mohd. Ezane Aziz : Co-Supervisor

A PILOT STUDY OF POWER DOPPLER SONOGRAPHY USING TUMOUR VASCULARITY

PATTERN IN DIFFERENTIATING BENIGN FROM MALIGNANT BREAST LESIONS

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Objective : The objective were to determine the specificity and sensitivity the criterias of the tumour vascularity pattern using power Doppler sonography in differentiating benign and malignant breast lesion and to find any association between tumour vascularity pattern and size of benign and malignant breast lesion

Methodology and Materials : Ethics committee approval and informed consent were obtained. This study was carried out in Hospital USM, Kubang Kerian, Kelantan for 16 months from July 2004 until October 2005. Power Doppler sonography using 13.5MHz transducer was prospectively performed on a total of 40 patients with breast lesion. The tumour vascularity criterias assessed were the flow, distribution, vessel morphology and presence of penetrating artery. FNAC (Fine needle aspiration cytology) and/or HPE (Histopathological examination) were done for all cases. The power Doppler criterias and HPE were analysed using univariate analysis. The sensitivity, specificity, positive predictive value and negative predictive value calculated using diagnostic table.

Result : There was detectable blood flow in 13 infiltrating ductal CA and 16 benign lesions. The mean size of vascular lesion was 30.5mm with 1.8mm standard deviation. The size of the lesions may have played a part in the vascularity of the lesion with a p value of 0.005 for flow characteristics. In the vascular lesions, irregular vessel and presence of penetrating artery showed a significant p value of 0.004 and 0.011. There was no single vascularity pattern which was specific for benign and malignant breast lesion. The descriptors of vessel morphology, flow, distribution and penetrating artery were not found to be highly predictive of malignancy with positive predictive value of 50.0%, 54.5%, 5 6.0% and 63.1% respectively. High negative predictive values were interestingly noted in the following descriptors: peripheral distribution (100%), low flow (88.9%) and regular vessel (87.5%).

Conclusion : Power Doppler US provided only limited additional information in differentiating benign solid breast lesions from malignant lesions. Vascular assessment was helpful only when it supported a benign morphology.

Dr. Latifah Basheer : Supervisor
Dr. Salmah @Win Mar Jalaludin : Co-Supervisor
Dr. Effat Omar : Co-Supervisor
Dr. Zainal Mahamood : Co-Supervisor

A SONOGRAPHY MEASUREMENT OF KIDNEY DIMENSIONS IN A SAMPLE OF HEALTHY NEWBORNS

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Overview : Sonography is the best non-invasive imaging study to evaluate renal morphology in newborn. Because many renal disorders are associated with changes in the sizes of kidneys, normative standards for assessing kidney size have been developed. These standards rely upon comparison of the kidney dimensions with various somatic measurements, including weight, height, body surface area, and chronological age. These standards have been widely used as a standard reference. However, it is uncertain whether the population on which these standards are based comparable to our local patient population that differs in their genetic, ethnic, and socio-economic background.

Objectives : The main objective of this study was to determine the normal range of kidney dimension in Malaysian newborns and compare it with Western data. Other objective is to determine correlation between kidney dimension and somatic measurements of both the newborn and the mother.

Methodology : Two hundred and twenty healthy newborns delivered at the Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan from May 2005 until September 2005, were included in a cross-sectional, random, and prospective study. Sonographic examination was performed within first few days of life to determine various kidney dimensions, including length, anteroposterior diameter, width, volume and cortical thickness. Relationships of kidney dimensions with somatic variables of newborns and their mother were investigated.

Results : Five out of 220 newborns were excluded due to congenital anomalies, leaving 215 newborns for statistical analysis, consisted of 115 boys and 100 girls. Ninety-eight percent of the newborns were Malay. Their gestational age ranges from 35 to 41 weeks (mean 39 ± 1.4 weeks), and 180 were term newborns. In the term newborns, the mean kidney length was 4.04 ± 0.32 cm, mean kidney volume was 8.31 ± 1.53 cm and mean cortical thickness was 3.65 ± 0.49 mm. Significant linear relationship was found between both kidney length and kidney volume and gestational age, birth weight, height, and body surface area. The best correlation was observed with birth weight. Cortical thickness was correlated better with kidney length and width There was no significant relationship between newborn's kidney dimensions and maternal somatic measurements was observed. There was no significant difference was found between both sexes for kidney length and cortical thickness. Although both sexes differs significantly in kidney volume but the actual difference was small. In most kidney dimensions, left similar to right. Nomograms for kidney length and kidney volume versus birth weight were presented. The kidney size established from this study was relatively smaller compared to Western data.

Conclusion : There is a need to establish a set of normal standard of kidney dimension based on our local newborn population as this study suggests that the use of norms from other population may not be appropriate.

Assoc. Prof. Dr. Haji M. Abdul Kareem : Supervisor
Dr. Wan Madziah Wan Mohamad : Co-Supervisor

COMPARISON OF COLOUR MONITOR AND HIGH RESOLUTION GREYSCALE DIAGNOSTIC MONITOR USING DEDICATED PACS WORKSTATION ON COMPUTED RADIOGRAPH (CR) OF THE CHEST

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Introduction : Computers and monitors are the most important tools in digital imaging. High resolution greyscale diagnostic monitor is the current gold standard for soft copy display. However, this type of monitor is very expensive and its use in clinical practice may not be cost effective. Hence, for economical reason, a hospital-wide flimless system based on PACS equipped with workstation for viewing radiographs has not yet been accepted in HUSM. An alternative to the expensive diagnostic workstation monitor that is more cost-effective and can present comparable images must be considered. Colour monitor is considerably cheaper; however there were very few studies on the

accuracy and reliability of colour monitor in the interpretation of radiographs in comparison to that of a high resolution greyscale monitor.

Objectives : The aim of this study is to determine the diagnostic accuracy and reliability of colour monitor compared to high resolution greyscale diagnostic monitor on CR chest.

Methodology : The institutional ethics committee approved the study; informed consent was not required. This study was a comparative cross sectional study and conducted in Hospital Universiti Sains Malaysia (HUSM), Kubang Kerian, Kelantan. All computed chest radiographs from 1 June 2004 to 31 December 2005 were used as source population. A total of 136 chest images remained after the screenings. Two observers reviewed 136 CR chest images comprising of 48 normal and 88 abnormal images using colour monitor and greyscale monitor at different occasions separated between 3 — 4 weeks. The detections were scored using a scoring form. Analysis of sensitivity, specificity, accuracy and reliability were used.

Results : Combination of both observers showed sensitivity of 74.8% and specificity of 94.0% for greyscale monitor and 69.2% sensitivity with 94.1% specificity for colour monitor. There was no statistical significant different for sensitivity and specificity between the two monitors at 95% confidence interval. The calculated accuracy was 91.9% for greyscale monitor and 91.5% for colour monitor. Intraobserver agreements for all the abnormalities were substantial for observer 1, observer 2 and both observers combined together (k=0.748-0.767). Moderate agreement were demonstrated between the observers for greyscale (k=0.599) and colour monitor (k0.5 15).

Conclusion :

Colour monitor was comparable to high resolution greyscale diagnostic monitor in sensitivity, specificity, accuracy and reliability for detection of chest abnormalities.

Dr. Mohd. Ezane Aziz : Supervisor
Assoc. Prof. Dr. Ibrahim Lutfi Shuaib : Co-Supervisor

THE USE ETHYL CHLORIDE AS TOPICAL ASSESSMENT OF VOLUME REDUCTION OF UTERUS AND UTERINE FIBROIDS USING ARTERIAL EMBOLIZATION

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Objective : The objective of this study was to assess the volume reduction of the uterus and the uterine fibroid using artery embolization for patients with symptomatic fibroids. This study was also aimed to determine the complications of uterine artery embolization and to document improvement of the symptoms post UAE.

Materials and Methodology : Twelve patients had bilateral uterine artery embolization(UAE) for symptomatic uterine fibroids. This study was conducted over a period of 21 months in Hospital Universiti Sains Malaysia. All the patients had a pre-embolization Magnetic Resonance Imaging (MRI) and ten of the patients had a repeat MRI three months post uterine artery embolization. One patient developed bleeding post-embolization and had a hysterectomy done. The second patient got pregnant immediately post-embolization and delivered a healthy term baby girl by caesarean section. Volume of the uterus and the dominant fibroid was calculated pre-embolization and post-embolization. Comparison was done between the volume pre-embolization and post-embolization, to see the percentage of reduction. Symptom improvement and the complication due to uterine artery embolization were also noted.

Results : Results show fibroid volume reduction median to be 63.82% with interquartile range of 36.78 and uterine volume reduction median to be 47.85% with interquartile range of 36.99. Symptom improvement at three months was 85-100%. The complications which occurred were mostly minor complications with one major complication requiring hysterectomy.

Conclusion : UAE is an effective and a safe method of treatment for symptomatic uterine fibroids. There is significant symptom and volume reduction of both the uterus and the dominant fibroid.

Dr. Mohd. Shafie Abdullah : Supervisor
Dr. Nik Haslina Nik Hussin : Co-Supervisor

TEN YEARS REVIEW OF CANCER BLADDER IN HOSPITAL UNIVERSITI SAINS MALAYSIA, KUBANG KERIAN

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The bladder constitutes the most frequent localization of malignant tumours in the urinary tract and it is one of the common urological malignancies occurring worldwide in both sexes. Local literature on bladder cancer are rather scare and hence the need for a study of this nature. Sixty-seven patients with cancer of the bladder treated in a period of ten years from 1996 to 2005 at Hospital Universiti Sains Malaysia were studied to determine the pattern of the disease and highlight the clinical presentation, cystoscopic finding, histopathology and modalities offered for treatment of the disease. It was found that the mean age of occurrence was 64.5 years. Male to female ratio was 5.7: 1 and predominantly affecting the Malays (86.57%). Sixty-one percent smoker with significant statistical correlation to tumour grade. The most common clinical presentations were haematuria (85.1%). Transitional cell carcinoma was found in 95.5% of studied population and most patients present with invasive stage (64.2%). TUR was done for 83.6% of them while 28.4% of patients underwent systemic chemotherapy therapy and 4.5% underwent radiotherapy.

Dr. Mohd. Nor Gohar : Supervisor

CHITOSAN DERIVATIVE AS A SCAFFOLD FOR AUTOLOGOUS TISSUE ENGINEERING IN AN ISOLATED SILICONE CONSTRUCT ; UTILIZING THE DEEP INFERIOR EPIGASTRIC ARTERIOVENOUS PEDICLE. AN EXPERIMENTAL STUDY IN RATS

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Introduction : Tissue engineering is the next frontier in reconstructive surgery. The ability to create new tissue to replace defects, without the ensuing donor site deformity and disability is a problem that is being worked on by scientists the world over.

Objectives : The objective of this study is to evaluate a chitosan derivative, chitosan gel with 5% PEG (polyethylene glycol) polymer, usefulness as a scaffold for tissue engineering in a rat model, using the deep inferior epigastric arteriovenous pedicle, in an isolated silicone construct.

Methodology : A previously described in vivo tissue generation experiment involving two experimental models, that is the flow through arteriovenous bundle and the distal ligated pedicle arteriovenous

bundle, was created in the rat groin. A silicone chamber was fashioned around the vascular pedicle. Chitosan gel was inserted into the chamber to envelop the pedicle. Controls were included too. Four groups of eighteen Sprague-Dawley rats each were utilized. Six animals were sacrificed at three time points per group, that is at two, four and six weeks. Tissue generated within the construct was harvested. Volume, weight, angiogenesis and histology of tissue generated were analyzed.

Results : Both experimental models utilized were able to sustain tissue growth. Intense tissue necrosis was noted in the chitosan group. There was a linear increase in all parameter assessed in the flow through control group. In the flow through chitosan group, there was an initial decrease, followed by an increase in all parameters assessed. In the distal ligated pedicle control group, there was an initial decrease, followed by an increase in all parameters assessed, except angiogenesis, where there was a linear decrease. In the distal ligated pedicle chitosan group, there was an increase, followed by a decrease in all parameters assessed.

Conclusions : This study showed that the chitosan derivative evaluated was not a suitable scaffold to support tissue generation in the experimental models described.

Prof. Dr. Ahmad Sukari Halim : Supervisor
Prof. Dato' Dr. Ahmad Ridzwan Arshad : Co-Supervisor

FUNCTIONAL AND COSMETIC OUTCOME OF TWO-STAGE HYPOSPADIAS REPAIR: AN OBJECTIVE SCORING EVALUATION AND UROFLOWMETRY

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Introduction : Hypospadias is characterized by an abnormally located urethral opening that could occur anywhere proximal to its normal location on the ventral surface of glans penis to the perineum and usually accompanied with chordee. Distal hypospadias is including glans, coronal and distal penile hypospadias. Proximal hypospadias is including proximal penile and penoscrotal hypospadias. It is the most common congenital anomaly affecting the penis (Wilcox & Ransley, 2000) with an incidence of 0.7% of male live births (Michael *et al*., 2001). There have been many operations described for hypospadias involving many surgical subspecialties. This reflects the difficulty in getting optimum results from the surgery and implies that there is no gold standard technique for hypospadias repair (Arshad, 2005, Oztruk *et al*., 2005). There is also no standardized objective method to assess the outcome of hypospadias repair until Holland *et al*.; (2001) came with hypospadias objective scoring evaluation (HOSE).

Objective : The main objective of this study is to evaluate the functional and cosmetic outcome of patients who underwent two-stage hypospadias repair in Hospital Universiti Sains Malaysia and Hospital Raja Perempuan Zainab between January 1997 and December 2004, using HOSE (hypospadias objective scoring evaluation) and uroflowmetry and also to determine the factors that could influenced the outcome.

Methodology : This is an historical cohort study among hypospadias patients who have undergone two-stage hypospadias repair in Hospital Universiti Sains Malaysia and Hospital Raja Perempuan Zainab II between January 1997 and December 2004. Over the eight years 90 hypospadias patients underwent two-stage repair. Only 55 patients out of 90 patients (61 .1%) with complete record and agree to participate were included in the study. They were examined to evaluate the functional and cosmetic outcome using HOSE: hypospadias objective scoring evaluation and uroflowmetry (if they were able to void volitionally and had no fistula). Five factors that may have influenced the outcome of hypospadias were studied, including type of hyposapadias, age at the completion of repair, duration between the first and the second-stage repair, techniques of hypospadias repair and surgeon.

Results : 53 of the 55 patients were Malay, one Chinese and one Siamese. The age of patients at the time of the study ranged from 8 to 23 year-old (mean age 14.89 year). 35 patients (63.6%) had proximal type hypospadias (23 penoscrotal and 12 proximal penile) and 20 patients (36.4%) had distal hypospadias (12 distal penile, 7 subcoronal and one glannular) Four patients underwent circumcision in one to two years before hypospadias repair and two patients underwent previous unsuccessful hypospadias repair. The types of operations performed were Bracka's two-stage procedure (37) and Byar's two-stage procedure (18). The complications encountered were urethralcutaneous fistula 17 patients (3 0.9%), followed by meatal stenosis 2 patients (3.6%), urethtal stricture one patient (1.8%) and wide meatal opening at subcoronal one patient (1.8%). Of the 17 patients with fistula, 9 underwent fistula repair and three had recurrence. Using the assessment criteria in HOSE, 34.5% had acceptable score and 65.5% had unacceptable score. The meatal openings were located at the tip of glans penis in 17 patients (30.9%), the meatal opening were vertical slit in 12 patients (2 1.8%), single urinary stream were obtained in 50 patients (90.9%), straight penis on erection were documented in 20 patients (36.4%) and there were no fistula in 44 patients (80%). Only 43 patients who were able to underwent uroflowmetry examination, in which 36 patients (83.7.0%) were considered normal, four patients (9.3%) as equivocal and three patients (7.0%) were obstructed. Only surgeon factor was found to have statistically significant influence on the outcome.

Conclusion : In conclusion, there seem to be a higher occurrence e of penoscrotal hypospadias in the Eastern side of Peninsula of Malaysia. HOSE and uroflowmerty are important objective tools to evaluate the functional and cosmetic outcome. The only factor that had a statistically significant influence on the outcome was the surgeon factor; other factors were found to be insignificant statistically.

Dr. Mohd Nor Gohar Rahman : Supervisor
Dr. Mohd Arif Kor Abdullah : Co-Supervisor

RETROSPECTIVE ANALYSIS OF HEART VALVE REPLACEMENT SURGERY IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction : The purpose of this study is to evaluate the improvement in patient based on NYHA class, and the differences in echo finding of the patient pre and post valve replacement operation as well as the association between the age and NYHA class of the patient. It is part of our audit and the aim is to improve our service.

Methodology : and Results : The new Cardiothoracic Unit, Hospital Universiti Sains Malaysia, Kubang Kerian Kelantan performed a series of valvular heart surgery. This crossectional study on 58 patients who had undergone valve replacement surgery with or without CABG for the period of 41 months from January 2002 to May 2005. Female comprising 33(46.9%) of them and the remaining 25(43.1%) were male. The patients' age ranged from 15 to 74 years old. The mean age was 36.78 years old, median 38.5 with standard deviation of 14.0 years. Ten (17.2%) underwent AVR(aortic valve replacement), thirty (5 1.7%) underwent MVR(mitral valve replacement) and 18(3 1%) underwent DVR. Twenty eight (4.3%) required concomitant procedure i.e. tricuspid valve repair (TAP) (41%),coronary bypass grafling 2(3.4%),

aortic root repair 1(1.7%) and excision subaortic membrane 1(1.7%). Out of the 58 patients, 2(34 died within the rst postoperative month and 4(6.8°/o) died during follow up excellent. Patients in NYHA class III or IV showed distinct recovery 6 months post operation and recovered well in less than 5 years in our study. However, the follow up by the cardiologist is required to access the evolution of the valve prosthesis after surgery.

Dr. Mohd Ziyadi Ghazali : Supervisor

A REVIEW OF HIRSCHSPRUNG'S DIEASE IN HOSPITAL UNIVERSITI SAINS MALAYSIA 1999-2004

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MMed (Surgery)

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Introduction : Hirschsprung's disease is a developmental disorder of the enteric nervous system causing congenital megacolon and the commonest cause of intestinal obstruction in the neonatal period. Being the only Pediatric surgical unit until the end of 2005 Hospital USM undertook all the references for Hirschsprung's disease in the upper east coast region of Malaysia. The treatment of the disease started when a patient is suspected of having the disease clinically. The patient would receive rectal irrigation until the diagnosis is confinned by rectal biopsy. When the diagnosis is confirmed the child would have a colostomy created. When the child reached about one year old or weight of 10 kilograms, the definitive procedure would be done. Until 2004, the procedure of choice in the hospital was Duhamel procedure. After the definitive procedure, the colostomy would be closed.

Objective : The objective of the study is to review the children presenting with Hirschsprung's disease to the hospital and described the demographics, mode and age of presentations, diagnosis, operative treatment, complications and outcome of the patients.

Methodology : The study was retrospective review study of the patients who were diagnosed and had their definitive pull-through procedure in the hospital during a period of 5 years (from February 1999 — February 2004). Patients who defaulted prior to the definitive procedure were excluded.

Results : There were 94 patients whose data was available for the review. There were 4: 1 male to female ratio with age of presentation ranging from 1 day old and 13 years old with 73.4% presented within the age of 3 months. The most common of clinical presentation was abdominal distension (87.2%) followed by vomiting (61.7%), poor feeding (55.3%), delayed passage of meconium (47.9%) and chronic constipation (46.8%). Seventeen percent (17%) of patients had other associated anomalies and 3.2% had a family history. Sixty three percent (63.4%) were diagnosed with rectal suction biopsy. Ninety five percent (95.7%) of patients had Duhamel type of pull-through procedure with 3 had transanal pull-through and only one who had Soave. There was a mortality recorded for the study and it was attributed to enterocolitis. The patient was also having Down syndrome and congenital heart disease. In the follow up period an average of 74% were free of complications of constipation, enterocolitis, incontinent, redo operation. There was 10.6% reoperation rate. Five patients needed a complete redo of their definitive procedures.

Conclusion : The demographics finding of the study is quite similar to the patterns in the other parts of the world. The presenting symptoms were also quite similar to other studies. The definitive procedure of choice during the study time was Duhamel operation. The operative outcome was safe and acceptable.

Dr. Syed Hassan Syed Abdul Aziz : Supervisor

MENINGIOMAS: THE RELATIONSHIP OF P53 PROTEIN IN THE DETERMINATION OF GRADING OF MENINGJOMAS AND THE VARIOUS FACTORS INFLUENCING THEIR PREVALENCE IN MALAYSIA

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Objective : The objective of this paper was to study the relationship of p53 protein and the various grades of meningioma. Other various factors that could influence their presentation such as epidemiology, clinical features, radiological findings and surgical clearance were also studied. A database of meningiomas for future studies in Malaysia is desired to be created with the information obtained from this study.

Methodology : All patients with a histological confirmation of meningioma and underwent surgery in HKL between January 2002 and 2006 who fulfilled the inclusion and exclusion criteria of the study were included in this cross sectional study. A total number of 77 patients,67 patients with benign meningiomas and 10 patients with atypical meningioma who fulifiled this criteria were studied where Immunohistochemistry test was carded out to determine the expression of p53 protein in these samples. Other parameters such as dinical presentation, imaging findings, operative clearance and demographic studies were also studied. Chi square test was used to determine the significance of the various parameters.

Results : There were 141 patients admitted and operated with the of meningioma between January 2002 and January 2006, of whom only 77 patients full filled the criteria of this study. The reaction of p53 was graded as -ve for no reaction 1+ve for mild reaction, 2+ for moderate reaction and +3 for severe reaction for Monoclonal Mouse Anti-Human p53 protein (Clone DO-7). In our study, 80% of the patients with-atypical meningioma a reaction of 2+ Wand above as opposed to 0% who had 2+ and above in the benign group. 100% of patients with benign meningiomas had reaction of -ve and 1+ of p53 protein compared to 20% in the atypical group. The anaplastic meningioma however was unrepresented due to lack of specimen. We studied the significance of grading of meningiomas with immunohistochemistry reaction p53 and compared them. Using Pearson's Chi Square test we found a Fair(r and significant correlation ($p<0.001$) with increasing grades of meningioma and p53 reaction. Sample size was calculated and achieved for our primary objective that was to study the relationship between p53 and grades of meningiomas but we could not analyze association between other variables and the two meningioma groups due to the the small sample size of our study. We also checked for the differences in the proportions of variables using Chi Square test. We however did not find any significance in the two meningioma groups with regard to the population of all the variables. Other variables that were associated with meningiomas were also studied in the benign meningioma group and the atypical meningioma group. This included epidemiology factors such as sex ($p=0.765$), ethnic groups ($p=0.960$), age ($p=0.337$), dermological location ($p=0.727$), clinical features like headache ($p=0.644$) seizures ($p=0.924$), vomiting (0.555), paresis (0.153) and visual disturbance (0.918), radiological findings like location of tumor (0.591), contrast enhancement (0.514) and midline shift (0.799) and surgical clearance Based on Simpson's grading (0.909).

Conclusion : This study concluded that there was a direct relationship between the expressions of p53 protein with higher grades of meningiomas, with higher expression of p53 protein in atypical meningiomas as compared to benign meningiomas This has been found to be atistical1y significant in our study ($p<0.001$), which coincides with various studies conducted both regionally and internationally We also studied other parameters such as epidemiology, clinical features, radiological features and surgical clearance which we felt correlated

with meningioma presentation and compared them in both groups of benign meningioma and atypical meningioma. We however, found no correlation or statistical significance between these variables and the grades of meningiomas.

Supervisor : Dr.Mahammad Saffari bin Haspani
Co-Supervisor : Dr. Suriati Md Jusoh

EFFECTS OF HIGH BODY MASS INDEX ON PATIENTS WHO UNDERWENT ISOLATED CORONARY ARTERY BYPASS GRAFTING (CAB6) AT HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction : The published articles examining obesity and CABG surgery contain conflicting results about the role of body mass index (BMI) as a risk factor for in-hospital mortality.

Methodology : This study was conducted on 141 patients who underwent isolated CABG in Cardiothoracic Unit, Hospital Universiti Sains Malaysia, Kubang Kerian Kelantan from November 2001 to October 2004. The effect of BMI operative procedures, post operative complications, length of cardiac intensive care unit (CICU) stay, length of postoperative hospital stay postoperative complications and in hospital mortality were assessed by dividing patients into non overweight (BMI = or < 25 kg/m^2) and overweight (BMI> 25 kg/ m^2) group.

Results : There were 80 patients with BMI < or = 25 kg/ m^2 and 61 patients with BMI of >25 kg/ m^2 Being overweight and obese was not a statistically significant risk factor for morbidity and mortality in any of these assessments. However, we found that there were significant differences in peroperative data in CABG between the two groups.

Conclusions : In conclusions, the body size was not a significant risk factor morbidity and mortality for CABG.

Dr. Ziyadi Ghazali : Supervisor
Dr. Mohd.Nor Gohar Rahman : Co-Supervisor

THE ROLE OF PERIOPERATIVE ANALGESIA IN DECREASING THE INCIDENCE AND/OR SEVERITY OF PHANTOM LIMB PAIN (INTRAVENOUS MORPHINE VERSUS INTRAMUSCULAR DICLOFENATE)

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Purpose of The Study : To evaluate the perioperative intravenous morphine and intramuscular diclofenate in reducing the incidence of phantom limb pain as well as the seventy of phantom pain following lower limb amputation. In addition, to evaluate the association between phantom limb pain and the pain suffered before the amputation, the duration of diabetic mellitus and the duration of various feet or legs problems prior to amputation.

Methodology : This was a non-randomsed observational study involving a total 55 patients. 27 patients were selected for intravenous morphine infusion. The patients' blood pressure, heart rate, respiratory rate, sedation score, blood oxygen saturation were monitored closely. The other 28 patients were selected for intramuscular diclofenate. The drug was given to those patient who had pain score at 2 or more before operation and at regular dose after amputation. The rescue intramuscular tramadol was added if the pain was not adequately controlled in diclofenate group. Both medications were continued till day-3 post-amputation. The characteristic, intensity and location of pain encountered before analgesia, after analgesia and after amputation was documented. The modified numerical pain score was used to quantify the intensity of pain. The phantom sensation, phantom pain and stump pain following lower limb amputation was identified in both groups. The patients were followed up at one week, 1, 3 and 6 months after amputation via phone.

Results : Patients in both groups experienced comparable pain intensity before and after the operation ($p > 0.05$). However, two patients in diclofenate group required rescue i/m tramadol 50 mg for post-amputation pain control. Overall, 50 out of 55 patients (90%) experienced phantom limb sensation and 33 patients (60%) encountered phantom pain after amputation. Twenty one patients (75%) out of 28 in diclofenate group had phantom limb pain compared with 12 patients (44%) out of 27 in morphine group. The phantom sensation in diclofenate and morphine group was 89% and 92% respectively. In 16 patients with phantom limb pain (48%), the symptom subsided within 6 months. Most of the phantom pain encountered was low pain score and only 2 patients required medical treatment. Patients in morphine group was 0.176 time (odd-ratio) less likely to develop phantom limb pain as compared to diclofenate group ($p < 0.05$). Intravenous morphine significantly reduced the severity of phantom limb pain after adjusting possible confounding factors like sex, age, race and presence or absence of diabetic mellitus ($p < 0.05$). The maximal phantom pain score in morphine and diclofenate groups was 1.57 and 2.37 respectively. The severity pf pre-analgesia pain and the duration of various leg and food problem encountered prior to amputation did not significantly relate to phantom pain. However, the longer history of diabetic mellitus had less risk or incidence of phantom pain (p=0.03)

Conclusions : This study showed perioperative intravenous morphine infusion reduced the incidence and severity pf phantom linb pain as compare to

Prof. Zulmi Wan : Supervisor
Dr. Mohd. Iskandar Mohd Amin : Co-Supervisor
Dr. T. Vishvanathan : Co-Supervisor
Dr. Mohd Anuar Han Abdullah : Co-Supervisor

ANGIOTENSIN II TYPE I RECEPTOR GENE A ^{1166}C POLYMORPHISM IN HYPERTENSION ; A STUDY ON ITS INFLUENCE ON AORTIC STIFFNESS AND RESPONSE TO ANTIHYPERTENSIVE THERAPY AMONG MALAYS

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Introduction : Hypertension is a major contributor to cardiovascular disease (CVD) which is the leading cause of death in Malaysia. Aortic stiffness (AS) is an independent marker of cardiovascular (CV) morbidity and mortality in these patients. Angiotensin II type I receptor (ATIR) gene A polymorphism has been shown to be associated both with essential hypertension and AS measured as pulse wave velocity (PWV). Treatment with angiotensin converting enzyme inhibitor (ACEI) perindopril has been shown to reduce PWJ among hypertensive patients carrying C allele. Data on association of AT1 R gene A allele

with hypertension among Asians is controversial, while little is known about its association with PWV and its influence on response to antihypertensive treatment.

Objectives : Studies in this thesis were done to determine (1) the association between C polymorphism of ATIR gene with hypertension and PWV among Malay hypertensive and normotensive subjects and (2) to study its influence on reduction in PWJ comparing two blockers of the renin angiotensin aldosterone system.

Methodology : Two hundred and one hypertensive without evidence of CV complication and 201 age and sex matched normotensive subjects were studied in a cross sectional design. Blood pressure (BP), PWV, anthropometric measurements (height, weight, hip and waist circumference), were recorded and waist hip ratio and body mass index (BMI) were calculated. Venous blood samples were obtained for routine laboratory investigations and genetic analysis. A polymorphism was detected by polymerase chain reaction followed by restriction endonuclease digestion. In a second study 46 hypertensive subjects without C polymorphism of AT1R gene and without evidence of target organ damage, were randomly assigned to receive either perindopril or losartan in a double blind parallel fashion for 4 months after a washout period of two weeks. During the study, dose was adjusted to achieve target blood pressure (<140/90 mmHg) and if required indapamide 1.5 mg was added to the study medication. Heart rate, systolic and diastolic blood pressure (SBP and DBP) and PWV were measured at the baseline, one month and 4 months after treatment. In both studies PWV was measured using automated Complior® machine. Data from both studies was analyzed using statistical software (SPSS 11.0) using appropriate tests.

Results : Results from study I showed that C ^{1166} allele frequency was 7.96% among hypertensive patients and 7.73% among the normotensive subjects. There was therefore a slightly higher C allele frequency in the hypertensive population which was of borderline significance (p = 0.091). There was no significant difference in SBP and DBP between carriers and non carriers of C allele in hypertensive group (p=0.09 and p=0.161, respectively). Likewise there was not significant difference in SBP and DBP in the normotensive group (p=0.708 and p=0.838, respectively) and in the overall study population (p=0.174 and p=0.431, for SBP and DBP respectively). Subjects carrying C allele had slightly higher PWV as compared to non carriers in the hypertensive group (11.09 ± 2.08 vs. 10.72 ± 1.80; p = 0.093) which was also of borderline significance. No difference in PWV was seen among carriers and non carriers in the normotensive group (9.86 ± 1.18 vs. 9.53 ± 1.54, p = 0.440). However when both normotensives and hypertensives were analyzed together, 01166 polymorphism carriers had significantly higher PWV as compared to those without this polymorphism (10.52±1.82 vs. 10.15±1.80, p= 0.040). In study Il, a total of 19 hypertensive patients on losartan and 20 on perindopril completed the study. In both the groups patients had similar age, anthropometric measurements and sex distribution. There was no significant difference in baseline BP (150.89 ± 13.91/ 93.68 ± 10.37 vs. 151.85 ± 12.21/ 91.65 ± 7.54, p = 0.821 and 0.486) and PWV (11.63 ± 1.75 vs.10.97 ± 1.69, p =0.293) between the groups. After 4 months treatment there was a significant reduction from baseline in SBP (13.57 ± 15.97, p = 0.002), DBP (8.26 ± 8.54, p = 0.001) and PWV (0.83 ± 1.19, p=0.007) in the losartan group and SBP (17.95 ± 12.26, p <0.001), DBP (9.25 ± 6.23, p <0.001) and PWV (0.57 ± 1.22, p = 0.047) in the perindopril group. However there was no significant difference in reduction in SBP (p=0.342), DBP (p = 0.681) and PWV (p = 0.521) between the two groups among Malay hypertensive subjects without C polymorphism. Regression analysis showed that reduction in PWV by losartan and perindopril group was independent of reduction in BP by these drugs and reduction in BP explained about 22 % (r = 0.221) in losartan group and 21% (r = 0.209) in perindopril groups, of the total change in PWV.

Conclusions : Work from this thesis shows that the frequency of C ^{1166} polymorphism is similar among Malay hypertensive and normotensive subjects and it is not associated with hypertension. A polymorphism is not associated with PWV in hypertensive patients and normotensive subjects but is significantly associated with PWJ in the overall Malay population.

Prof. Dr. Abdul Rashid Abdul Rahman : Supervisor

CONSTRUCTION OF GENETICALLY ENGINEERED LIVE ATTENUATED NON TOXIGENIC, AUXOTROPHIC VIBRIO CHOLERAE

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Introduction : Cholera is an epidemic, endemic and the only pandemic bacterial disease known till now. This thesis reflects the construction of genetically engineered live attenuated non toxigenic auxotrophic Vibrio cholerae vaccine candidates, VCUSM5 and VCUSM6.

Methodology : These vaccine strains are metabolic auxotrophs of amino levulinic acid (ALA) because of the mutation in hemA gene This auxotrophy in VCUSM5 was achieved by insertion mutation of aphA cassette into hemA that codes for gutamyl tRNA reductase, an important enzyme of 05 pathway of ALA biosynthesis. in case of VCUSM6 auxotrophy was achieved by frame shift mutation in *hem*A.

Results : Experiments with infant mice reflects the vaccine candidates are good colonizers of small intestine with a least toxigenicity in rabbit ileal loop experiments which was confirmed by histopathological examination of ileal loops. These vaccine candidates are environmentally safe as they can not survive longer than 4-5 days in environmental waters as compared to wild type which survive more than 15 days in water samples.

Conclusions : All the above results show that VCUSM5 and VCUSM6 are promising least toxic and safe vaccine candidates.

Assoc. Prof. Dr. M Ravichandran : Supervisor
Prof. Zainul F. Zainuddin : Co-Supervisor

MOLECULAR GENETIC ANALYSIS OF FRAGILE X SYNDROME PATIENTS IN HOSPITAL UNIVERSITI SAINS MALAYSIA (HUSM)

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Introduction : Fragile X syndrome is one of the most common inherited genetic disorders that cause mental retardation. This disease results from the expansion of a trinucleotide repeat (CGG)n sequences, located in the 5' UTR of FMR1 gene, that further inactivate the normal function of this gene. It is also associated with the expression of folate sensitive fragile site at the q arm of chromosome X, at locus Xq27.3 or FRAXA.

Objectives : This study was done to analyze the distribution of FRAXA alleles in Kelantan's Malay population consist of normal male, fragile X patients and their family members.

Methodology : The distribution of FRAXA alleles was studied and compared with other population. Analysis of trinucleotide repeats (CGG)n structure and microsatellite loci located nearby were done. A total of 142 samples were analyzed. The samples were obtained from 69 normal males as normal control, and 73 samples which consist of 48 fragile X syndrome patient's and 25 family members were analyzed.

In order to analyze the existence of fragile site at the q arm of chromosome X (Xq27.3), cytogenetics analysis were done on samples obtained from individuals whom were clinically confirmed of Fragile X syndrome. Molecular genetics tests were done on all samples.

Results : Results of cytogenetics test showed that only 2 (4.17%) out of 48 samples studied have the fragile site. 73 samples from fragile X syndrome patients and their family members were tested using PCR to determine the repeat number of trinucleotide repeat (CGG)n sequence. 18 samples (3 7.50% of patients) were failed to be amplified, suggested that the samples may have a full mutation allele, and 55 remaining samples (75.34% of 73 samples studied) showed variable number of (CGG)n repeats. The distribution of trinucleotide (CGG)n repeat sequences among normal male in this study was found to be difference from several findings in other populations, and this may suggest the occurrence of new mutation in this population. Analysis of RFAXAC1 and DXS548 alleles distribution showed no significant difference between normal and fragile X samples. This may suggest that no founder effect was found in this population. The haplotypes analysis (DXS548-FRAXAC1) showed significant difference between normal and fragile X samples and also suggested the existence of protector haplotypes or founder haplotypes in this population. Results obtained from this study demonstrated that the molecular genetic test is suitable and possible to be used in the diagnosis of Fragile X syndrome in Hospital Universiti Sains Malaysia (HUSM).

Conclusions : We would also like to suggest that a screening program to study the causes of mental retardation among patients in HIJSM as well as to help their family members or hospital to plan suitable effective patient management system, need to be established. The results of this study also will enable us to establish the diagnosis method for Fragile X syndrome as well as to compensate the genetic counseling process.

Prof. Mohd Nizam Hj. Isa : Supervisor
Dr. Wan Asma Wan Ismail : Co-Supervisor

POLYMORPHISM OF 13 RECEPTOR, LEPTIN RECEPTOR, GLUCOCORTICOID RECEPTOR AND TUMOUR NECROSIS FACTOR-A GENE AMONG PATEENTS WITH TYPE 2 DIABETES MELLITUS

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Introduction : Type 2 diabetes (T2D) is a common complex disorder that develops from changing of human nutrition and life styles. The etiology of T2D includes genetic mutations that disturb lipid and glucose metabolism, insulin resistance, obesity and deficiency in insulin secretion. However, major differences of genes mutations occur among various populations with different origin and geographical backgrounds.

Objectives : This study was performed to determine the incidence and pattern of b_3-AR, LEPR, Tnf-a and GRL gene polymorphisms in T2D Malay patients attending Klinik Rawatan Keluarga, HUSM, Kelantan.

Methodology : A total number of 116 T2D patients and 84 normal healthy controls were involved in this study. Mutation analysis using PCR-RFLP procedures were used to study missense mutation in the polymorphism of $Trp^{64}Arg$ of the b_3-AR $G^{308}A$of the Tnf-a and $Asn^{363}Ser$ of the GRL genes polymorphisms. PCR-PAGE was used to analyze the insertion/deletion polymorphism of 3'-UTR of the LEPR gene. Then, DNA sequencing was carried out to confirm the insertion sequence.

Results : The results showed no significant different of genotype frequencies in the polymorphisms of Trp^{64} Arg, insertion/deletion of 3 '-UTR, G^{308} and $Asn^{363}Ser$ occurred between T2D patients and controls, with 0.099, 0.164, 0.026 and 0.047 compared to 0.098, 0.131, 0.071 and 0.036 respectively (p= 0.646, 0.701, 0.090 and 0.656). LEPR gene was the most common polymorphism appearing in T2D patients (16.4%), followed by b_3-AR gene (9.9%), GRL gene (4.7%) and Tnf-a gene (2.6%). The controls showed almost similar pattern for the LEPR gene (13.3%) and b_3-ARgene (9.8%), but Tnf-a gene polymorphism was found to be higher than GRL (Tnf-a gene, 7.1% and GRL gene, 3.6%). Most of the T2D patients and controls that have the mutation alleles (59.0% and controls 90.0% respectively) have single gene mutation, followed by the combination of 2-genes mutation in 20.7% of patients and 10.0% of controls. The most common combinations are polymorphism of LEPR and GRL gene and also and GRL gene in T2D patients. Whereas the combination of LEPR and GRL gene and also b_3-AR and GRL gene in control subjects. Only one patient had the combination of 3-gene mutations and none of the studied samples had all 4-gene mutations. Patients showed significant association between all mutant genotypes studied with gender and positive family history. Patients also revealed the contribution of heterozygous $Trp^{64}Arg$ with higher min age, BMI and SBP, G^{308} with longer duration of diabetes, and heterozygous Asn^{363} with obesity as compared to controls.

Conclusions : In conclusion, the analysis of the polymorphism of $Trp^{64}Arg$ of the b_3-AR, insertion/deletion of 3'-UTR of the LEPR gene, $G^{308}A$ of the Tnf-a gene and Asn^{363} of GRL gene suggest that these polymorphisms do not directly contribute to the development of T2D when functioning individually in these subjects. However, they may contribute to the pathogenesis of T2D when function synergistically with several other genes.

Prof. Mohd Nizam Hj. Isa : Supervisor
Prof. Madya Ab. Aziz Al-Safi Ismail : Co-Supervisor

EFFECT OF P-GLYCOPROTEIN INHIBITORS ON MEFLOQUINE RESISTANT MALARIA MODEL SYSTEM IN VITRO AND IN VIVO : TOWARDS IDENTIFYING CHEMOSENSITIZERS FOR MALARIA

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Introduction : Drug resistance is a common feature in malaria, caused by Plasmodium falciparum. Mefloquine (MQ) resistance is a worldwide problem and is invariably associated with the pfmdrl gene.

Objectives : The objective of this study is to find out the effective chemosensitizers to prevent or reverse MQ resistance, by using Dd2, clone of *P. falciparum, an in vitro* malaria parasite model, followed by using *Plasmodium berghei* (*P. berghei*)-N1100, an *in vivo* malarial parasite model.

Methodology : Molecular studies were done before *in vitro* studies, the extracted genomic DNA of Dd2 clone was amplified and sequenced. Point mutation at position 86 (86-Tyr changed to 86-Phe) revealed the vital role of its contribution in MQ resistance. *In vitro* study, MQ was tested in combination with 10 drugs against two P. falciparum clones (Dd2 and W2). Drug assays were carried out with a modification of the semi-automated microdilution technique. Radiolabeled ^{3}H-hypoxanthine was added to the parasite suspension at 48 h and the microtiter plates were incubated for another 24 h before harvesting. The 50 % inhibitory concentration (IC was determined by using SPSS software for each of the drugs and for drugs in various fixed concentration. Then, the fractional 50 % inhibitory concentration index (FIC index) was calculated. Isobolograms and growth curves were constructed from the FIC_{50} indices and percentages of parasite growth respectively.

Results : Verapamil (VRP), a potent P-gp inhibitor (as a positive

control for the drug assay *in vitro*) had a significant synergistic response when it is combined with MQ. The effect of MQ/ Fluoxetine (F LX) combination was synergistic on both of the clones (Dd2 and W2) with an average FIC of 0.77 and 0.79. The effect of MQ/Roxithromycin (ROM) combination was synergistic on clone Dd2 (average FIC of 0.86) and additive on clone W2 (average FIC of 1 .02). The average FIC indices of Clotrimazole (CLT), Simvastatin (SV), Glibenclamide (GB) and VRP were 0.88, 0.82, 0.81 and 0.60, respectively. The average FIC indices of Itraconazole (ITZ), Albendazole (ABZ), Ciprofloxacin (CPL) and Clarithromycin (CLR) were 1.31, 1.04, 1.18 and 1.02, respectively. ROM, FLX, CLT, SV, GB and VRP were Synergistic with MQ, while ITZ, ABZ, CPL and CLR were additive or slightly antagonistic with MQ. On the basis of the *in vitro* results, there was a need to evaluate the combination of MQ and (ROM, FLX, CLT, SV and GB) in experimental animals before considering for clinical trials. However, only the effects of FLX and ROM, the two effective chemosensitizers were accessed in vivo against MO resistance clone of P. berghei N1100. Mice were infected intra-peritoneally with 10^6 parasitizied erythrocytes. The infected mice of the treatment groups were treated for 4 days either with MQ alone or with various combinations of MQ/ ROX or MQ/FLX. All drugs were given orally; whereas the control groups were given either DMSO or tap water for 4 days according to the Peters test. The asexual stages of P. berghei were eliminated with the combination of MQ (200 mg/kg) and FLX (20 mg/kg) at cure rate of 57.14 % [survival time (MST) >47.714 days], while the combination of MQ (200 mg/kg/day) and ROM (80 mg/kg/day) achieved the cure rate at 50 % (MST >39.67 days). Both chemosensitizers exerted obvious suppressive effect when combined with higher concentration of MQ. The cure rates of MQ (100 mg/kg/day)/ROM (80 mg/kg/day) and MQ (100 mg/kg!day)/FLX (20mg/kg/day) are 30 %. However, none of the infected mice from drug alone group (MQ, FLX, ROM) were survived beyond 7 days post infection. Both chemosensitizers exhibited significantly higher cure rates and prolonged (MST) when they were combined with MQ. Our results indicate that only FLX, ROM, SV, GB and CLT could potentiate the effect of MO on MQ resistant P. falciparum clone in in vitro. Among them FLX and ROM were evaluated and exhibited a potentiating effect in vivo studies.

Conclusions : We conclude that FLX and ROM are very promising drugs to reverse or prevent MQ resistance and should be evaluated further.

Assoc. Prof. Dr. S. Sivachandran Raju : Supervisor
Assoc. Prof. M. Ravichandran : Co-Supervisor
Prof. Norazmi Mohd Nor : Co-Supervisor

AN IMMUNOHLSTOCHEMICAL STUDY OF SURVIVIN EXPRESSION IN NORMAL AND IN TRANSFORMED CELLS

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Introduction : Survivin is a new member of the inhibitors of apoptosis protein (lAP) family, selectively over-expressed in common human cancers but not in normal adult tissues. It is also expressed in cancer cell lines. The study was performed generally to investigate the basic and clinical roles of survivin in nonnal and transformed cells. Rabbits were immunized with two synthetic oligopeptides, MGAPTLPPAWQP and KEFEETAKKVRRAIEQLAAMD amino acids sequences of the survivin molecule. Serum antibodies were purified by ammonium sulphate and caprilic acid and their specificities were confirmed by immunoblotting and pre-absorption tests against survivin positive tissues or synthetic survivin oligopeptides. These antibodies were used to detect survivin in normal and transformed cells by immunohistochemistry in formalin-fixed paraffin embedded tissue sections, evaluated by a standard scoring system and chequerboard analysis. Normal cells were obtained from fetal and adult tissues of mouse and rat whilst the transformed cells were obtained from the human breast cancer cell line MCF-7 and the infiltrating ductal carcinoma (IDC) of the breast patients. In the MCF-7 cell line experiment, the effects of chemotherapeutic drugs namely doxorubicin, 5-fluorouracil, cyclophosphamide, and tamoxifen on the apoptosis index measured by propidium iodide and acridine orange dyes. The relative cell viability was measured by an MTT assay and survivin expression was measured by immunocytochemistry. In IDC patients (n=382), survivin expression in tissues was analyzed for its correlation with clinicalpathological factors, hormonal status, p53, bcl-2 and the survival rate. Patients and their tissue blocks were obtained from three general hospitals in The East Coast of Malaysia, Autoantibodies to survivin were also investigated in the sera of the same IDC patients population (n57) and were compared to the control population (n=44). For the immunohistochemistry assay, four rabbit antiserum were produced and tested against survivin.

Results : The results of this study indicated that the antigen retrieval buffer, pH 9 was superior than pH 6 and optimization immunohistochemistry was obtained by chequerboard analysis. Furthermore, it was found that survivin is expressed abundantly in normal growing fetal cells but not in normal differentiated adult tissues of mouse and rat. In the MCF-7 cell line, the cell viability was reduced in a dose-dependent pattern when incubated with the drugs. The IC_{50} estimation in MCF-7 cell line for doxorubicin was 6.0 μg/ml, cyclophosphamide μg/ml, 5-fluorouracil 0.61 μg/ml, and tamoxifen 0.7 μg/ml respectively. It was found that most of the MCF-7 cells expressed survivin, predominantly in the cytoplasm. The percentages of apoptotic cells were increased with the increased concentrations of the drugs. Among the IDC patients, the expression of survivin was 68.1%, p 53 29.6%, and bcl-2 43.7%, respectively. There was a significant correlation ($p<0.05$) between survivin expression and lymph node involvement, tumour sizes, p53, bcl-2 expression, and survival rate among the IDC patients. Anti-survivin autoantibodies reactivities were detected in 7% of the sera of IDC patients but not in normal sera. These autoantibodies correlated with the positivity of survivin expression, and with advanced breast cancer.

Results : It was concluded that suryivin was abundantly and prominently expressed during fetal development of rat and mouse. The polyclonal antibody SUR12A-CFI recognized rat and mouse survivin. It was also concluded that survivin is frequently over-expressed in IDC patients, and in most MCF-7 cells. Survivin expression has a predictive value in predicting the aggressiveness of the tumour cells suggesting that survivin may be a useful tool in assessing a prognosis.

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