

EDITORIAL

DOCTOR'S ATTIRE AND PATIENT SAFETY

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Koh and others have reported (in this issue of the MJM) the high prevalence of Methicillin resistant *Staphylococcus aureus* (MRSA) on doctors' neckties. As they have pointed out, this is nothing new, and like other studies with similar findings. They also pointed out that patient's confidence and satisfaction are not affected by doctor's not wearing neckties. They also referred to the British Department of Health decision to ban the use of neckties, long sleeve shirts and jewellery, and the Scottish government's intention to ban the wearing of white coats, including neckties, to stop the spread of infections. They support the call by the Malaysian Medical Association to avoid the use of neckties.

The doctor-patient relationship is the basic foundation for professional patient care. Wearing professional dress including a white coat may favourably influence trust and build confidence in the doctor-patient encounter and promotes the development of this relationship. Most doctors wear white coats for easy recognition by colleagues and patients and for convenience, however Psychiatrists and Paediatricians attempt to develop rapport by deliberately not wearing white coats. In studying the views of doctors and patients on the wearing of white coats, Douse *et. al.* found that doctors viewed white coats as an infection risk. However, most patients felt that doctors should wear white coats for easy identification.

The Department of Health in England had issued new guidelines on the clothing of staff, including doctors in the National Health Service (NHS). The policy suggests doctors should wear short sleeved shirts, avoid white coats and stop wearing watches. This policy was based on a scientific literature review by researchers funded by The Department of Health. Swindells and Rajan looked at the patients' perceptions with regard to their feeling of safety from infection, in relation to the NHS guidelines. They found that while a significant number of patients prefer their doctor to wear white coats, patients do not value doctor's attire highly and only a minority of patients felt safer from infection as a result of the new guidelines.

It would appear that more research need to be done on doctors' views as well as on patient's views on doctors' attire, and on whether patient education can change the patient's views, particularly in our local setting.

Despite advances in medicine and in public health, infections in hospitalized patients result in significant morbidity and mortality. Duce *et. al.* cited a prevalence survey conducted under the auspices of the WHO in 55 hospitals in 14 countries in 4 WHO Regions (Europe, Eastern Mediterranean, South East Asia and Western Pacific) which showed an average of 8.7% of hospital patients with nosocomial infections. Petroudi in a review of nosocomial infections and staff hygiene emphasized hand washing as the single most important measure to prevent nosocomial infections, and observed that compliance to this practice is unacceptably low, at less than 50% in studies over the last 20 years. The complexities of infection control are obviously very challenging. Semmelweis (1818-1865) working in the University of Vienna demonstrated the importance of hand washing in reducing mortality among his Obstetric patients. His colleagues were not impressed, and Semmelweis was even dismissed from his position.

Joseph Lister (1827-1912) worked on the antiseptic principle, showed the effectiveness of protecting open fractures from bacteria, using carbolic acid. These impressive results were published in 1867. However, his methods were very slow to be accepted, by the Germans in the 1870's and later followed by the USA, France and eventually England. This inherent conservatism and reticence to change that is often observed in the history of medicine is not consistent with our modern emphasis on evidence based medicine. However it needs to be understood and taken account of in managing the process of change, if change is to successfully occur in implementing new ideas.

The concern for patient safety, which really had been a long time in coming, despite a lot of work being published about it, had received wide attention following reports from the Institute of Medicine in the USA, which made recommendations on a comprehensive approach to improving patient safety. In May 2002, the 55th World Health Assembly adopted WHA resolution 55.18, which urged member states to improve patient safety and quality of health care. In May 2004, the 57th World Health Assembly supported the creation of an international alliance to facilitate the development of patient safety policy and practice in all member States, and to be a major force for improvement internationally.

The great concentration of attention on patient safety and the global response, initiated by the World Health Organization (WHO) call for action on Patient Safety have generated the necessary sense of urgency in improving patient safety and quality in health care. As part of this, all hospitals should have in place properly organized infection control systems, with infection control programmes, nosocomial infection surveillance, prevention of nosocomial infection, practical aspects of infection control and plans on dealing with outbreaks. A manual on the prevention of hospital acquired infections should be available as a resource for all units within a hospital. In the context of these guidelines, each hospital should have practical guidelines on the attire of doctors and other hospital staff, which is appropriate for the different work to be done in different parts of the hospital. As far as possible these guidelines should be evidence based. While enhancing the doctor-patient relationship is very important, patient safety is critically important and should be our paramount interest. More research need to be done in these areas, and the report by Koh and others is a good reminder to use all on these important and sometimes overlooked issues.

ORIGINAL ARTICLES

EPIDEMIOLOGY OF *HELICOBACTER PYLORI* INFECTION IN MALAYSIA – OBSERVATIONS IN A MULTIRACIAL ASIAN POPULATION

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Summary

Observations of racial differences in the prevalence of *Helicobacter pylori* in Malaysia have been intriguing. The Indians and Chinese consistently have a higher prevalence compared to the Malays. The racial cohort theory has been proposed to explain these differences where transmission and perpetuation of infection takes place within a racial group rather than between races, races being separate owing to the low rate of interracial marriages. Studies have demonstrated distinctive bacterial strains between races. Phylogenetic studies have shown that *H.pylori* isolates amongst Chinese and Indians are distinctive while Malays have Indian and other strains suggesting a more recent acquisition of the bacterium from Indians. *H.pylori* is recognized as the major causative factor in peptic ulcer disease and gastric cancer. Despite the high prevalence of *H.pylori*, Indians have a relatively low prevalence of peptic ulcer disease and a low incidence of gastric cancer. This paradox with regards to gastric cancer has been termed the “Indian enigma”. Bacterial strain differences between races may be putative but this observation may also indicate gastroprotective environmental factors or a lower genetic susceptibility to develop cancer in the Indians.

Key Words : *H.pylori, Racial cohort, Indian enigma, Gastric cancer, Peptic ulcer, Malaysia*

MOLECULAR CHARACTERIZATION AND EPIDEMIOLOGY OF ROTAVIRUS ISOLATES OBTAINED FROM CHILDREN WITH DIARRHOEA IN MALAYSIA

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Summary

This retrospective study examined the G/P type of rotavirus in RNA samples that have previously been e-typed by RNA-PAGE in 1996. The results were then compared to 2007 samples to ascertain the extent of changes that may have occurred in this 11-year time interval. The G and P genotypes were determined by hemi-nested PCR and further analyzed by phylogenetic study. In 1996, the G/P combination G1P[8], G^{UT}P[8] and G1P^{UT} prevalence rate were 81%, 9% and 7%, respectively. As expected, the G9 genotype which has already emerged worldwide was identified in 42% of the 2007 samples with the remaining 33% G1P[8] and 25% G1P^{UT}. Analysis of the RNA pattern showed that majority of the isolates were long e-type in both series, nevertheless minor differences within electropherotypes were observed. Genetic diversity in some strains of the human group A rotaviruses was analyzed by phylogenetic methods. These findings will help in the decision to introduce rotavirus vaccines within the next decade.

Key Words : Group A rotavirus, G and P genotypes, Phylogenetic study

LOW BACK PAIN AND ASSOCIATION WITH WHOLE BODY VIBRATION AMONG MILITARY ARMoured VEHICLE DRIVERS IN MALAYSIA

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Summary

A cross sectional study was conducted among military armoured vehicle drivers in the two largest mechanized battalions with the objective to determine the prevalence of low back pain (LBP), and its association with whole body vibration (WBV) and other associated factors. A self administered questionnaire and Human Vibration Meter were used in this study. A total of 159 respondents participated in this study and 102 (64.2%) of them were subjected to WBV measurement. One hundred and seventeen respondents complained of LBP for the past 12 months giving a prevalence of 73.6%. The prevalence of LBP among tracked armoured vehicle drivers was higher (81.7%) as compared to wheeled armoured vehicle drivers (67.0%). The mean acceleration at Z-axis in tracked armoured vehicles ($1.09 \pm 0.26 \text{ ms}^{-2}$) and wheeled armoured vehicles ($0.33 \pm 0.07 \text{ ms}^{-2}$) were the dominant vibration directions. The mean estimated vibration dose value (eVDV) for eight-hour daily exposure at Z-axis ($19.86 \pm 4.72 \text{ ms}^{-1.75}$) in tracked armoured vehicles showed the highest estimation. Based on the European Vibration Directive (2002), the mean exposure action value (EAV) ($> 9.1 \text{ ms}^{-1.75}$), but did not exceed exposure limit value (ELV) ($< 21.0 \text{ ms}^{-1.75}$). Logistic regression analysis revealed that only driving in forward bending sitting posture (OR = 3.63, 95% CI 1.06-12.42) and WBV exposure at X-axis (OR = 1.94, 95% CI 1.02-3.69) were significant risk factors to LBP. Preventive measures should be implemented to minimize risk of WBV and to improve ergonomic postures among drivers.

Key Words : *Low-back pain, Whole-body vibration, Military armoured vehicle drivers, Tracked armoured vehicles, Wheeled armoured vehicles, Estimated vibration dose value (eVDV)*

TRANSLATING KNOWLEDGE TO ATTITUDE : A SURVEY ON THE PERCEPTION OF BYSTANDER CARDIOPULMONARY RESUSCITATION AMONG DENTAL STUDENTS IN UNIVERSITI SAINS MALAYSIA AND SCHOOL TEACHERS IN KOTA BAHRU, KELANTAN

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Summary

This voluntary, anonymous questionnaire survey was performed to assess the willingness of Basic Life Support (BLS) participants to perform bystander cardiopulmonary resuscitation (CPR). A total of 55 dental students and 73 school teachers were assessed on their willingness to perform bystander CPR after completion of their BLS training. In general, only 29.0% of the total 128 participants said that they would offer to perform CPR under any cardiac arrest condition and 69.0% said that they would just offer to call the ambulance but they would not offer to perform CPR. When analyzed separately, only 16.4% of school teachers said that they would perform CPR as compared to 45.5% of dental students ($p < 0.001$). Knowing how to perform CPR does not necessarily translate into willingness to perform CPR.

Key Words : *Bystander cardiopulmonary resuscitation, Mouth-to-mouth resuscitation*

CUTANEOUS VASCULITIS : A REVIEW OF AETIOLOGY AND CLINICAL MANIFESTATIONS IN 85 PATIENTS IN MALAYSIA

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Summary

Cutaneous vasculitis presents with a variety of clinical morphologies and causes significant morbidity. A total of 85 patients with cutaneous vasculitis at Hospital Kuala Lumpur were retrospectively reviewed. Palpable purpura was seen in 49.4% and frequently involved the lower limbs (50.6%). Identifiable causes include drugs (28.2%), infections (20.0%) and connective tissue disorders (16.5%). Non steroidal anti inflammatory was the commonest group of drugs responsible for 25% of cases while β -haemolytic streptococci were the leading infectious cause (64.7%).

Key Words : Cutaneous vasculitis, Palpable purpura

ENDOSCOPIC NASOPHARYNGECTOMY : THE SARAWAK EXPERIENCE

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Summary

Shifting the paradigm of treatment of a locally recurrent nasopharyngeal carcinoma (NPC) from the non surgical management to a surgical modality has always been a challenge. However, many studies on endoscopic nasopharyngectomy have proven it to be a reliable form of treatment with an excellent outcome. Since 2007, in Sarawak General Hospital, six cases of endoscopic nasopharyngectomy for locally recurrent NPC have been performed with encouraging results.

Key Words : Endoscopic nasopharyngectomy, Nasopharyngeal tumours, Recurrent nasopharyngeal carcinoma

PROGRESSIVE FAMILIAL INTRAHEPATIC CHOLESTASIS IN MALAYSIAN PATIENTS – A REPORT OF FIVE CASES

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Summary

Progressive familial intrahepatic cholestasis (PFIC) is characterized by early onset cholestasis, progressive liver cirrhosis, pruritus, poor growth and inexorable progression to liver cirrhosis in early childhood. The serum level of gamma-glutamyl transferase is low or normal, which is discordant with severe cholestasis. Five Malaysian patients with PFIC, who all had typical features of PFIC with early onset of severe and progressive cholestasis, pruritus, cirrhosis and liver failure, were described. Three patients died as a result of the disease, while another one died due to post liver transplant complication. The only survivor has compensated liver cirrhosis. Patients with severe cholestasis but has spuriously low γ GT should be suspected of having PFIC. Liver transplant, which is life saving in a majority of patients with PFIC, should be considered in all patients with PFIC.

Key Words : Progressive familial intrahepatic cholestasis, Mortality

OUTBREAK OF CHIKUNGUNYA IN JOHOR BAHRU, MALAYSIA : CLINICAL AND LABORATORY FEATURES OF HOSPITALIZED PATIENTS

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Summary

In 2008, an outbreak of chikungunya infection occurred in Johor. We performed a retrospective review of all laboratory confirmed adult chikungunya cases admitted to Hospital Sultanah Aminah, Johor Bahru from April to August 2008, looking into clinical and laboratory features. A total of 18 laboratory confirmed cases of chikungunya were identified with patients presenting with fever, joint pain, rash and vomiting. Haemorrhagic signs were not seen. Lymphopenia, neutropenia, thrombocytopenia, raised liver enzymes and deranged coagulation profile was the prominent laboratory findings. We hope this study can help guide physician making a diagnosis of chikungunya against other arbor viruses infection.

Key Words : Chikungunya, Malaysia, Clinical features, Laboratory findings

COMBINED ASSESSMENT OF TGF-BETA-1 AND ALPHA-FETOPROTEIN VALUES IMPROVES SPECIFICITY IN THE DIAGNOSIS OF HEPATOCELLULAR CARCINOMA AND OTHER CHRONIC LIVER DISEASES IN MALAYSIA

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Summary

Transforming growth factor beta-1 (TGF- β -1) is a multifunctional cytokine involved in the regulation of growth and differentiation of both normal and transformed cells. The main aim of this study was to determine whether TGF- β -1 and AFP were measured by ELISA in 40 healthy subjects, 23 patients with hepatocellular carcinoma (HCC), 70 patients with hepatitis B, 26 patients with hepatitis C and 16 patients with liver cirrhosis (LC). Patients with liver diseases showed significantly higher serum TGF- β -1 values (> 3 fold) compared to control subjects. As for serum AFP, significant elevation was only observed for HCC cases. Serum TGF- β -1 exhibited higher percent sensitivity compared to serum AFP in all liver diseases. Combination of serum TGF- β -1 and AFP increased specificities in all cases studied. In conclusion, serum TGF- β -1 is a more sensitive marker for HCC when compared to serum AFP and its specificity is increased when combined with serum AFP.

Key Words : AFP, TGF- β -1, Hepatocellular carcinoma, Tumour marker

FACTORS INFLUENCING PHYSICAL ACTIVITY LEVEL AMONG SECONDARY SCHOOL ADOLESCENTS IN PETALING DISTRICT, SELANGOR

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Summary

Physical activity is the first line approach and one of the main factors in preventing chronic diseases. Currently there is the increasing percentage of sedentary lifestyle or lack of exercise among adolescents. The main objectives of the study were to determine the prevalence of inactivity and the factors influencing physical activity in adolescents. A cross sectional study was carried out among secondary school students aged 14 and 16 in Petaling district, Selangor, Malaysia. A total of 519 respondents participated in this study. Their physical activity level was measured using the International Physical Activity Questionnaire (IPAQ). The active group was classified as those having levels of equal or more than 600 met-min per week while less than 600 met-min per week was considered inactive. Response rate in this study was 95.4%. The prevalence of inactive in adolescents was 20.8%. Female adolescents, non working mother, time constraint, exercise only when having ample time and stretching before exercise are predictor factors for being inactive among adolescents. Steps need to be taken to persistently ensure that the physical activity among adolescents be increased continuously.

Key Words : Physical activity, Adolescents, IPAQ

HIGH PREVALENCE OF METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* (MRSA) ON DOCTORS' NECKTIES

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Summary

We set out to investigate whether neckties worn by doctors are more likely to be contaminated with Methicillin resistant *Staphylococcus aureus* (MRSA) compared to neckties worn by pre clinical medical undergraduates who have never been exposed to a hospital environment. We discovered that more than half (52%) of neckties worn by doctors were contaminated with *Staphylococcus* and out of these, 62% of them were identified as MRSA. In contrast, none of the student's ties were contaminated with MRSA. Due to the high prevalence of *Staphylococcus* detected on doctors' neckties, we recommend that health care workers do not wear neckties.

Key Words : Doctors' neckties, *Staphylococcus aureus*, MRSA

EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality throughout the world and the incidence will continue to rise especially in the developing countries as the prevalence of smoking increases. By 2020, COPD is expected to be the 3rd commonest cause of death and ranked 5th as the cause of loss of disability adjusted life years (DALYs) according to the baseline projections made in the Global Burden of Disease Study. Based on model projections the prevalence of moderate to severe COPD in Malaysia is 4.7% which translates to 448,000 cases.

COPD is defined as “A preventable and treatable disease with some significant extrapulmonary effects that may contribute to the severity in individual patients. Its pulmonary component is characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases”.

COPD remains a disease which is often neglected and many doctors feel little can be done or indeed need to be done for the COPD patient. The disease is grossly undiagnosed as the availability of spirometry in Malaysia is limited to the major hospitals. Doctors may also miss the opportunity to make the diagnosis when the smoking individual with a “smokers cough” presents with other illnesses such as chest infection. Patients with mild COPD may already have symptoms such as cough with sputum production and by making the diagnosis early, steps can be taken to prevent further accelerated decline in lung function which is the characteristic hallmark of the disease. Without intervention, patients typically seek medical case when the disease is advanced and they are already disabled.

Exacerbation of COPD is defined as *“An event in the natural course of the disease characterized by a change in the patient’s baseline dyspnoea, cough and/or sputum that is beyond normal day to day variations, is acute in onset, and may warrant a change in regular medication in a patient with underlying COPD”.*

The most common cause of exacerbations is infection of the tracheobronchial tree and air pollution, but in one third the cause of severe exacerbations cannot be identified. The cause of exacerbation may be multifactorial, so that viral infection or air pollution may amplify the existing inflammation of the airways and in turn may predispose to secondary bacterial infections.

Guidelines for the diagnosis, management and prevention of COPD have been published by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) and various regional bodies such as the American Thoracic Society and the European Respiratory Society (ATS/ERS), the British Thoracic Society (BTS) and the Canadian Thoracic Society. The Malaysian Clinical Practice Guidelines (CPG) on Management of COPD was published in 1998 and is currently being updated to include many new developments in COPD. This article will address the impact, management and prevention of exacerbations based on the current available evidence.

Impact of Exacerbations

COPD exacerbation is one of the greatest burdens associated with this condition. It is associated with significant economic burden as exacerbations account for two thirds of the direct cost of COPD care. Patients with frequent exacerbations have significantly worse exercise capacity and greater decline in health status compared than those with infrequent exacerbations. Exacerbations are also associated with an accelerated rate of decline in lung function. Patients with poorer lung function are more likely to have exacerbations as there is a positive correlation between the severity of lung function and the frequency of exacerbations.

Severe exacerbations have a direct and independent effect on mortality. Mortality is increased when COPD exacerbation is associated with hospitalization. Connors *et al* showed that patients hospitalized with an acute exacerbation of severe COPD had an inpatient mortality of 11% and the 60 day, 180 days, 1 year and 2 year mortality was high at 20%, 33%, 43% and 49% respectively. This is comparable to myocardial infarction and the prognosis is poorer than many other cancers.

Management of Exacerbations

The aims of management in exacerbations of COPD are to relieve symptoms and airflow obstruction, maintaining adequate oxygenation, treat any co morbid conditions that may contribute to respiratory deterioration or any precipitating factors such as infection.

The majority of patients with acute exacerbations of COPD are treated in primary care. However, a minority of patients will require hospital admissions to treat the exacerbations. The GOLD guidelines have suggested indicators for hospital assessment or admission for acute exacerbations of COPD (Table I).

Table I : Indications for hospital assessment or admission for acute exacerbations of COPD

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- Marked increase in intensity of symptoms such as sudden development of dyspnoea
 - Underlying severe COPD
 - Development of new physical signs e.g. cyanosis, peripheral oedema
 - Failure of exacerbation to respond to initial medical management
 - Significant co morbidities
 - Newly occurring arrhythmias
 - Older age
 - Insufficient home support
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Home Management

Bronchodilator Therapy

The dosage and frequency of existing short acting β_2 -agonists therapy should be increased, e.g. salbutamol 2-4 puffs every 3-4 hours. Short acting anticholinergic therapy (ipratropium bromide) may be added until the symptoms improved. If the inhalers are inadequate to relieve the acute symptoms, nebulizers can be given on as 'needed basis' for several days if a nebulizer is available e.g. short acting β_2 -agonists (salbutamol 2.5mg or terbutaline 5mg) or combination of short acting β_2 -agonists and short acting anticholinergics (combivent 2.5 mls or duovent 4 mls). There is evidence that the use of spacer device with metered dose inhaler has a similar effect as nebulised bronchodilators for exacerbations of COPD.

Glucocorticosteroids

Systemic glucocorticosteroids should be used in an acute exacerbation of COPD with significant increase in breathlessness as it has been shown to shorten recovery time, improve oxygenation and lung function and reduce treatment failure. A dose of 30-40mg prednisolone per day for 7-10 days is appropriate for most patients. The beneficial short term effects of

glucocorticosteroids should be balanced against the potential risk of short term and long term side effects in the individual patients as many are often elderly with associated co morbid conditions.

Antibiotics

The use of antibiotics in exacerbations of COPD is discussed in the hospital management section.

Hospital Management

The initial action in treating a patient with an exacerbation of COPD in emergency department is to provide controlled oxygen therapy and assessing the patient to determine if the exacerbation is life threatening requiring admission to high dependency unit or ICU. Guidelines have suggested indications for invasive mechanical ventilation in patients admitted with severe acute exacerbations of COPD (Table II). Otherwise, the patient may be managed in the emergency department or general wards (Table III).

Table II : Indications for invasive mechanical ventilation

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- Life threatening hypoxaemia despite maximal therapy ($P_aO_2 < 5.3\text{kPa}$, 40 mmHg)
 - Severe acidosis despite maximal treatment ($\text{pH} < 7.25$ and/or hypercapnia ($P_aO_2 > 8\text{kPa}$, 60 mmHg)
 - Respiratory arrest
 - Severe breathlessness with use of accessory muscles
 - Respiratory rate > 35 breaths per minute
 - Impaired mental status
 - Inability to protect airways
 - Haemodynamic instability (hypotension, shock)
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Controlled Oxygen Therapy

Oxygen is considered the cornerstone of hospital treatment for an acute exacerbation of COPD. The aim of oxygen therapy during an acute exacerbation of COPD is to correct or prevent life threatening hypoxaemia. The potential benefits of oxygen are reduction of pulmonary vasoconstriction, decrease in right heart strain and improvement of cardiac output and oxygen

delivery to the vital organs. Oxygen therapy is given to maintain adequate oxygenation ($P_aO_2 > 8$ kPa, 60 mmHg or saturation $> 90\%$) without worsening hypercapnia.

Controlled oxygen therapy is given in the form of 24-28% oxygen via venturi mask in the first instance, delivering the required fraction of inspired oxygen and reducing the complications of inadequate oxygenation and/or hypercapnia. If venturi masks are not available or tolerated, nasal prongs with 1-2 litres oxygen are an alternative. Arterial blood gases should be checked 30-60 minutes later to ensure adequate oxygenation without CO_2 retention or acidosis.

Bronchodilator Therapy

The relief of airflow obstruction by bronchodilator therapy is the major goal in the treatment of acute exacerbation of COPD. Short acting inhaled β_2 -agonists are the preferred initial bronchodilator for the treatment of acute exacerbations of COPD. It is usually given in the nebulised form although there is evidence that administration of short acting inhaled β_2 -agonists via metered dose inhaler and spacer device has equal efficacy to nebulised treatment. If there is no prompt response to these drugs or if the patient has a very severe exacerbation, short acting anticholinergic (ipratropium bromide) treatment is recommended, although the evidence concerning the combination of these two drugs is controversial. When prescribing nebulised therapy, the driving gas (air or oxygen) must be stipulated, as some COPD patients may have background chronic type 2 respiratory failures.

Despite the widespread use, the role of methylxanthines (theophylline or aminophylline), in the treatment of acute exacerbations of COPD remains controversial. In severe exacerbations, intravenous methylxanthines can be considered with close monitoring if there is inadequate response to short acting inhaled β_2 -agonists and anticholinergics. Patients not previously treated with theophylline can be given a loading dose of slow intravenous aminophylline 250-500 mg (5 mg/kg) over at least 20 minutes with close monitoring followed by maintenance dose of 0.5 mg/kg/hour.

Glucocorticosteroids

Oral or intravenous corticosteroids are effective treatment for acute exacerbations of COPD and are recommended as an addition to other forms of therapy in hospital management of exacerbations of all COPD patients in the absence of significant contraindications. The use of oral or intravenous corticosteroids improves lung function over the first 72 hours, shortens

hospital stay and reduces treatment failure over the subsequent 30 days. Additional studies are required to determine the optimal dose and duration of corticosteroid therapy during acute exacerbations of COPD but a dose of 30-40 mg of oral prednisolone daily for 7-10 days appears to be safe and effective. A study has shown that nebulised corticosteroids may also be beneficial during acute exacerbations of COPD as an alternative to oral prednisolone in the treatment of non acidotic exacerbations of COPD. Intravenous corticosteroids should be reserved for patients who are unable to take oral therapy or have potential malabsorption problems. Systemic corticosteroids should be discontinued after the acute episode as it is associated with significant side effects such as hyperglycaemia and osteoporosis.

Antibiotics

Primary bacterial infection is the commonest cause in the development of exacerbations of COPD or represents a secondary infection following an initial viral infection. However, bacteria are present in the cultured secretions of 30-40% of patients with chronic sputum expectoration and COPD even in the stable state. Meta analysis indicates the benefits of using antibiotics during acute exacerbations of COPD, but no benefit is derived if used to prevent exacerbations. There is a clear relationship between sputum purulence, bacterial isolation and increased bacterial load, therefore antibiotics should be given to patients with purulent sputum with one more cardinal symptoms of dyspnoea or increased sputum. Patients with a severe exacerbation of COPD that requires mechanical ventilation should also be covered with antibiotics as it has been shown to reduce mortality, shortened ventilator days and hospital days compared to placebo. Simple first line antibiotics should be used and the choice of antibiotics should depend on local antibiotic policy and the pattern of local pathogens. The common pathogens isolated in patients hospitalized for pneumonia in Malaysia are *Klebsiella pneumonia*, *Streptococcus pneumonia*, *Haemophilus influenza*, *Mycoplasma pneumonia* and *Pseudomonas aeruginosa*.

Assisted Ventilation

Some patients may show deterioration despite aggressive pharmacological and controlled oxygen therapy. These patients will require some form of ventilator support during this phase to maintain oxygenation. Ventilatory support can be instituted non invasively via facial mask (NIV) or invasively via an endotracheal tube.

Non Invasive Ventilation (NIV)

Many studies have shown the benefits of NIV in acute COPD exacerbations with early correction of acidosis and respiratory rate, reducing the intubation rates and mortality compared to those on conventional therapy. Complications associated with endotracheal intubation and mechanical ventilation such as nosocomial pneumonia and length of hospital stay were also reduced. Another advantage of NIV is that it can be applied outside the intensive care unit such as high dependency ward or in general ward with experienced staff using NIV. Clinical practice guidelines for the use of NIV in acute exacerbations of COPD have been published. Generally, patients admitted with an acute exacerbation of COPD with the following features should be considered for NIV :

- Respiratory distress with moderate or severe dyspnoea with use of accessory muscles.
- pH < 7.35 or pCO₂ > 6kPa or 45mmHg
- respiratory rate of > 25 breaths per minute

NIV may not be appropriate for all patients and there are several contraindications such as the presence of respiratory arrest, haemodynamic instability, inability to protect airways, uncooperative patient and inability to clear secretions. Currently NIV is only available in some hospitals in Malaysia with specialist facilities such as ICU, HDU and wards with trained nurses to handle NIV.

Other Therapies

There is no convincing evidence to support the routine use of pharmacological mucus clearance strategies in acute exacerbations of COPD. Chest physiotherapy has no proven value during exacerbations unless a large amount of sputum is produced (> 25mls per day) or there is mucus plugging with lobar atelectasis. Fluid balance and nutrition should be monitored. Diuretics are indicated if there is evidence of peripheral oedema or increased jugular venous pressure. Prophylactic subcutaneous heparin should be used in immobile patients and those with acute or chronic respiratory failure if there are no contraindications.

Hospital Discharge and Follow Up

The median length of hospital stay for an exacerbation of COPD is 9 days (5-15 days). Patients should be clinically stable with acceptable oxygen saturation prior to discharge. Discharge criteria have been suggested by the GOLD guidelines (Table IV). Follow up clinic visit is recommended 4-6 weeks after discharge from hospital. If the patient remains hypoxemic on air (oxygen saturation < 90%), supplemental oxygen therapy at this stage may be required and this

should be reassessed at the first follow up clinical visit (4-6 weeks) and a decision is made on whether the patient requires long term oxygen therapy (Table V) with an oxygen concentrator. Long term oxygen therapy has been shown to improve survival in patients whom fit the criteria when used more than 15 hours per day.

Table IV : Discharge criteria for patients with exacerbations of COPD

- Inhaled β_2 -agonist therapy is required no more frequently than every 4 hours
 - If previously ambulatory, able to work across room
 - Able to eat and sleep without frequent awakening by dyspnoea
 - Clinically stable for 24 hours
 - Oxygen saturation has been stable for 24 hours
 - Able to use medications correctly
 - Follow up arranged at hospital or clinic
 - Patient, family and doctor are confident patient can manage successfully at home
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Table V : Indications for long term oxygen therapy

- PaO₂ at or below 7.3 kPa (55mmHg) or SaO₂ at or below 88%
OR
 - PaO₂ between 7.3 kPa (55mmHg) and 8.0 kPa (60mmHg) or SaO₂ of 88%, if there is evidence of pulmonary hypertension, peripheral oedema suggesting congestive cardiac failure, or polycythemia (hematocrit > 55%)
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Prevention of Exacerbations

In view of the significant impact of exacerbations on the patient and the healthcare system, efforts should also be directed in preventing exacerbations. Several risk factors for frequent exacerbations (> 2 exacerbations/year) have been identified which includes increased age, severity of forced expiratory volume in one second (FEV1) impairment, chronic bronchial mucus hypersecretion, frequent exacerbations, daily cough and wheeze and persistent symptoms of chronic bronchitis.

Smoking cessation has been shown to reduce the rate of decline in lung function in patients with COPD and may reduce the risk of acute exacerbations of COPD. Since tracheobronchial infection is the commonest cause of exacerbation of COPD, improving the immune system may reduce the rate of exacerbation. Although there is little data available in COPD patients per se, influenza vaccination have been shown to reduce pneumonia and cardiac hospitalizations in the elderly population. Since most COPD patients are elderly with cardiac co morbidities, influenza vaccination should be given to most COPD patients. The use of pneumococcal vaccination is recommended in the guidelines since *Streptococcus pneumonia* is one of the most frequently identified bacterial pathogen in COPD exacerbations.

Chronic maintenance pharmacotherapy has been shown to reduce the exacerbation rates of COPD. There is evidence that inhaled corticosteroid, long acting β_2 -agonist (salmeterol, formoterol), long acting anticholinergics (tiotropium) and combination inhaled therapy (symbicort, seretide), reduces the rate of exacerbations. In the ISOLDE study, the inhaled corticosteroid fluticasone group had a 25% reduction in exacerbation rate (1.32 v 0.99/years) and slower decline in health status compared to placebo. The long acting β_2 -agonist salmeterol treatment limb of the TRISTAN study was associated with reduction in exacerbation rate of around 20% compared to those randomized to placebo. Trials with the long acting anticholinergic, tiotropium have shown a significant reduction in exacerbations of approximately 20-25% when tiotropium is added to the usual therapy. Combination therapy of inhaled corticosteroids and long acting β_2 -agonists have been known to produce greater improvement in lung function compared to either drug alone and studies now have shown that both combination inhalers reduces exacerbation rates by approximately 25%. These studies demonstrated that the reductions in exacerbations results in decreased hospitalizations and health care utilizations.

Some of these medications are not available at many health centers in the country or only accessible by respiratory physicians, therefore patients who experiences recurrent exacerbations of COPD should be referred to the nearby centers with respiratory services as these patients are most likely to benefit from these medications.

Pulmonary rehabilitation is an effective non pharmacological treatment in stable COPD. Unfortunately only a few centers in Malaysia provide this service because of the lack of physiotherapist support although there is overwhelming evidence of its benefits in improving

patients' quality of life, exercise tolerance and symptoms. Pulmonary rehabilitation has also been shown to reduce exacerbation rates and duration of hospitalizations. If pulmonary rehabilitation is not available, patients should be encouraged to exercise at home and maintain an active lifestyle as much as possible. Self management education including managing an exacerbation can be recommended for suitable patients by providing a supply of antibiotics and steroids (provided patient understands when to take them) to be started at the beginning of an exacerbation. This may shorten and reduce the severity of the exacerbation, reducing unscheduled doctor visits and hospital admission.

CONCLUSIONS

Exacerbations of COPD are important events for the patient and expensive for the healthcare system. Patients with frequent exacerbations have poorer health status, greater decline in lung function and higher mortality compared to those spared the events. The immediate management is assessing the patient whether the exacerbation can be treated at home or requires hospital admission and if life threatening, high dependency unit or ICU admission.

The initial treatment includes regular inhaled short acting bronchodilators and corticosteroids. Antibiotics are indicated if purulent sputum is present with increased breathlessness or increased sputum volume and in severe exacerbations requiring mechanical ventilation.

Controlled oxygen therapy and non invasive ventilation improve gas exchange and decrease muscle fatigue. Failure to improve with treatment is an indication for invasive ventilation. Preventive strategies including smoking cessation, vaccinations, pulmonary rehabilitation, chronic maintenance pharmacotherapy and self management education may prevent exacerbations but the optimum combination remains to be established.