BY INVITATION

CARDIOVASCULAR RESEARCH IN THE UNIVERSITY DEPARTMENT OF MEDICINE OVER THE LAST TWO DECADES

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SYNOPSIS

During the past two decades, much progress has been made in the specialty of cardiology in the University Department of Medicine. This paper describes the research work that has been done in cardiovascular diseases in the department.

INTRODUCTION

During the last 2 decades, significant progress has been achieved in the specialty of cardiology in the department of medicine of the University of Singapore. This progress has been in the areas of innovation of new techniques, service to the community, teaching of medical students, post-graduate doctors and nursing personnel, education of the public and lastly medical research. It is timely at this seventy-fifth jubilee anniversary of the medical school to pause and reflect on what has been achieved in the past and to plan for what lies ahead. This paper examines one aspect of this achievement viz. the research of cardiovascular diseases that has been done and its contribution to medical progress and to society.

Medical research can take many different forms and is done with varying objectives. Many medical scientists all over the world are today engaged in esoteric research, much of which have little relevance to existing health problems. Such research usually take many years to complete and are frequently unfruitful in terms of cost effectiveness with regard to the improvement of the health care of the community. Such academic luxury may perhaps be justified in more affluent Western countries such as the United States of America, Australia and Sweden, where there is an abundance of wealth and personnel, but is hardly appropriate for a country like Singapore, with its limited resources and talent. It is gratifying to note therefore that the majority of the research in cardiovascular diseases which has been accomplished so far in the University Department of Medicine has been done bearing in mind the relevant health problems of our country. A chronicle of this research provides a panoramic view of some aspect of the progress in medical care and the changing spectrum of disease patterns in Singapore over the past 2 decades.

CORONARY CARE UNIT

The coronary care unit (CCU) in the University Department of Medicine (II), (then known as Medical Unit II), Singapore General Hospital was started by Professor Charles Toh in 1967. By that time,

it was apparent from research done elsewhere that approximately half of the deaths in acute myocardial infarction are due to electrical causes such as ventricular fibrillation and are potentially salvageable if the patients are monitored in an intensive care environment. The inception of this CCU provided an unparallelled opportunity for the study of coronary artery disease, cardiac arrhythmias, newer modalities of treatment etc, and was a fore-runner of several other intensive care units in Singapore.

In the past decade, several publications arose from work done in the CCU. In 1971, Lim and co-workers[1] reported on the results of treatment of atrioventricular blocks in acute myocardial infarction in the CCU and the role of temporary cardiac pacing. These early observations confirmed work done elsewhere that temporary cardiac pacing was a useful, safe and simple procedure and frequently was life saving. Today, this procedure is done routinely in patients where it is indicated and the total number of cases who have had temporary cardiac pacing in the CCU number approximately 450. The importance of digitalis toxicity as a cause of paroxysmal atrial tachycardia with atrio-ventricular block was emphasized in another communication in 1974[2]. This study showed that this ominous arrhythmia usually occurs in the background of chronic lung disease and is frequently fatal. With advances in knowledge of pharmacokinetics, the importance of preventing digitalis toxicity and digitalis induced arrhythmias is today well recognised in Singapore.[3]

In 1972, Wan and associates[4] described 15 cases of sick sinus syndrome seen in this department and postulated that in the Singapore context, thyrotoxicosis was an important aetiological cause. At that time, the sick sinus syndrome was just beginning to be recognised as an important cardiac arrhythmia and the Singapore observations were commented upon in an editorial in the Lancet.[5] Today, the sick sinus syndrome has taken its rightful place in the list of potentially lethal arrhythmias and is routinely diagnosed and recognised in clinical practice in this country. Indeed, its importance is highlighted in a subsequent publication by Low and co-workers where it was found that of the 29 cases who had permanent pacemaker implantations in Singapore up to the year 1975, 6 were for the sick sinus syndrome.[6]

Although it was earlier reported in other parts of the world that acute viral myocarditis very seldom caused complete heart block and Stokes Adams Attacks, it was for many years realised that experience in Singapore was at variance with these findings. In 1975, Lim and co-workers[7] reported a study of 10 cases presenting with Stokes Adams attacks due to complete heart block arising from acute non-specific myocarditis, and this series has remained the largest reported so far. It was also pointed out in this study that cardiac pacing was frequently a life saving procedure in cases of acute myocarditis complicated by complete heart block.

Other publications on cardiac arrhythmias included studies in the Wolff-Parkinson White Syndrome[8,9] and repetitive tachycardia in normal individuals.[10]

Although the concept of intensive care for the treatment of acute myocardial infarction was mooted as early as 1963[11] doubts about its value in terms of lowering mortality still lingers. There is a school of thought which believes that the final outcome is similar whether the patients are treated in a CCU or at home.[12]

The existence of the CCU for more than a decade offers an excellent opportunity for the assessment of the value of such a unit in the treatment of myocardial infarction in our local setting.

In 1980, Chia[13] compared the results of treatment of myocardial infarction patients in the CCU when it first started in 1967[14] to those obtained about 1 decade later. It was found that there has been a significant fall in mortality in Grade I (uncomplicated) and Grade II (complicated) cases but not those in the Grade III category (cardiogenic shock). For example, in the initial experience, the mortality for Grade I and II cases were 3% and 25% respectively and these fell in the subsequent series to 0.5% and 8% respectively. However, the mortality rate for cardiogenic shock cases remained high at 84%. It was concluded that in grade I and II cases, improvement in mortality was due primarily to advances in treatment of potentially lethal cardiac arrhythmias such as ventricular tachyarrhythmias and in particular, ventricular fibrillation. In general, the mortality rate for cardiogenic shock cases still remain dismally high and there has been no major advances in the treatment. The search for better methods of preserving ischaemic myocardium and treatment of cardiogenic shock remains the greatest challenge in the present and future management of acute mycardial infarction.

INVASIVE CARDIOVASCULAR LABORATORY

The cardiovascular laboratory in the Singapore General Hospital was started by the University of Singapore in 1964 with the help of Professor Sujoy Roy, who was then a WHO visiting professor to Singapore. Its inception provided an excellent opportunity for haemodynamic investigations and research hitherto not possible before its existence. The development of invasive haemodynamic cardiovascular studies and angiography was an essential pre-requisite in the establishment of open heart surgery in Singapore which began in 1967.

Many papers were published in the last two decades stemming from work done in the cardiovascular laboratory. In 1965, Ghosh[15] published the initial experience of the cardiac team on various cardiovascular haemodynamic investigations which were performed for the first time in Singapore. This was followed in 1969 by a report on clinical and haemodynamic studies of mitral stenosis patients before and after mitral valvotomy.[16] Subsequently, studies on more complicated subjects such as coronary artery fistula,[17] ruptured aneurysms of the aortic sinus of valsalva[18], ventricular septal defect with aortic incompetence[19] and non specific aorto-arteritis[20] were published. A doctoral thesis on atrial septal defect based on haemodynamic studies done in the cardiovascular laboratory was obtained by Ghosh from the University of Singapore in 1970. During the past two decades, a tremendous amount of cardiovascular investigations in paediatric patients were also carried out and this was highlighted by Loh in his Haridas memorial[21] lecture in 1969, and his M.D. thesis in 1968 on ventricular septal defect.

Since 1974, the administration and running of the cardiovascular laboratory has been taken over by the Ministry of Health. However, University cardiologists continue to participate fully in haemodynamic investigations. The cardiovascular laboratory at present is fully

equipped to perform all forms of haemodynamic and angiographic procedures. During the past few years, coronary angiography has been started and the initial experience of the first 100 cases performed was presented by Ng and co-workers at the twelfth Singapore Malaysia Congress of Medicine.[22] This paper shows that coronary angiography can be accomplished safely in Singapore with minimal morbidity and mortality and is frequently extremely useful in providing important information which is necessary for the management of the patient. Coronary artery surgery is currently being launched in Singapore and coronary angiography is a prerequisite before this surgical procedure can be performed.

NON-INVASIVE CARDIAC INVESTIGATIONS

The early fifties saw tremendous progress in cardiology in terms of invasive cardiac investigations such as cardiac catheterization and angiography and treatment. Those were indeed the golden years of cardiology.

The last decade has however witnessed a resurgence of interest in non-invasive cardiac investigative techniques such as exercise stress testing, continuous Holter ambulatory monitoring of the cardiac rhythm, nuclear cardiac imaging and echocardiography. Echocardiography in particular has made much progress in the last decade because it is relatively cheap, easy to perform, repeatable and completely non invasive, posing no danger to the patients at all. In addition, it is capable of providing important information, some of which cannot be obtained by any other techniques, invasive or non invasive. With the state of the art, echocardiography at the present point of time cannot entirely replace cardiac catherization and angiography in every case. However, because of its ability to confirm the clinical diagnosis in many instances, it can frequently obviate the need for invasive studies in cases which do not require cardiac surgery. For example, echocardiography has shown that the prolapsing mitral valve syndrome is a common disease in Singapore and we have confirmed this diagnosis using echocardiography alone without cardiac catheterization in many instances. The advent of echocardiography also has revolutionised the management of pericardial effusion because currently this is the most sensitive technique for the diagnosis of fluid in the pericardial sac. Prior to echocardiography, many patients required cardiac catheterization because of uncertainty of diagnosis before pericardiocentesis, but this is almost never done today. Apart from its great value in diagnosing various cardiovascular disease, echocardiography is also an excellent tool for research. In 1978, we published our first paper on a study of the mitral echogram in 72 patients with various cardiac diseases.[23] Currently, we are using echocardiography to study cardiac involvement in thyroid diseases, acromegaly, infective endocarditis and the various haemoglobinopathies.[24] [25] So far, we have been using one dimensional or M mode echocardiography. With 2-dimensional echocardiography or cross sectional scanning, tomographic sections of the heart can be obtained and the heart can be studied in real time motion. The images of the heart beating in real time are truely spectacular and much more information can be obtained than one dimensional echocardiography. We hope to embark on 2 dimensional echocardiography sometime this year.

Treadmill exercise stress testing began in this department in 1974 and was a fore-runner to numerous other exercise testing laboratories all over Singapore. This test is invaluable for the diagnosis of coronary artery disease and for the assessment of cardiopulmonary fitness.

PREVENTIVE CARDIOLOGY

Despite major advances in the field of therapy in cardiovascular diseases, it has long been realised that significant improvement in morbidity and mortality can only be achieved if there is greater emphasis on preventive measures. Because of the astronomical costs of curative medicine as a result of advancing technology, no country in the world can afford to provide every form of sophisticated treatment to all its citizens. It is much cheaper, and indeed more logical to prevent diseases, whereever this is possible, rather than to have to treat them.

Cardiovascular diseases have assumed major importance as health problems in Singapore. For the past decade, cardiovascular disease such as hypertension and coronary artery disease have competed notoriously with cancer for the dubious honour of being the biggest killer in our society. With improvement in our standards of living, our disease patterns have become those seen in the more affluent Western countries, rather than those occurring in developing countries. For example, in nation wide surveys conducted by the Ministry of Health, hypertension was found to be present in 14% and diabetes mellitus in 2% of our adult population.[26] [27]

In 1960, Muir[28] studied necropsy material of patients dying from coronary artery disease in Singapore and noticed that the Indians have the highest propensity to suffer from this condition. This finding was subsequently confirmed in clinical studies done by Wan and co-workers[14] and Chia. [13] In a study of risk factors seen in survivors of myocardial infarction in Singapore, Lim and co-workers[29] found that the most commonly encountered risk factor was cigarette smoking, this being present in 67% of our patients. Hypertension and diabetes mellitus were present in 23% and 25% of cases respectively. Significant hyperlipidaemia was not common in our patients. In a multicentre study of risk factors in young myocardial infarction patients which we participated, it was found that whereas hyperlipidaemia and cigarette smoking were the most common risk factors in patients from Auckland, Melbourne, Los Angeles, Atlanta, Cape Town, Tel Aviv, Heidelberg and Edinburgh, the most common risk factor in the Singapore patients was cigarette smoking.[30]

The great value of treating hypertension to increase lifespan and prevent complications such as heart failure and strokes has been amply confirmed in the last decade. During this period of time, significant advances in pharmacological therapy was also achieved. The introduction of beta blockers as hypotensive agents in 1964 marked a milestone in anti-hypertensive therapy. In 1974, we reported on the efficacy of Propranolol for the treatment of hypertension in Asians.[31] Subsequently, we also found that other beta blockers such as Atenolol[32] and Metoprolol[33] were equally effective for controlling hypertension in our patients.

It is clear that control of hypertension and other risk factors for coronary artery disease such as cigarette smoking, diabetes mellitus, hyperlipidaemia and physical

inactivity is of paramount importance if cardiovascular mortality and morbidity in SIngapore is to be lowered in the future.

CONCLUSION

Much has been accomplished in the University Department of Medicine in the research of cardiovascular diseases over the past two decades. More research, which are meaningful and relevant to the health problems of our society, will continue to be done in the coming years.

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