EVALUATION OF ANGIOTENSIN II RECEPTOR BLOCKERS (ARBS) FOR DRUG FORMULARY USING OBJECTIVE SCORING ANALYTICAL TOOL

by

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Thesis submitted in fulfillment of the requirements
for the degree of
Master of Science

JULY 2011

ACKNOWLEDGEMENTS

I am very grateful and indebted to many people who have helped me along the way to the completion of this thesis. First and foremost, I would like to thank my supervisor, Professor Mohamed Izham Mohamed Ibrahim for his kind guidance, supervision and support to complete this thesis.

I would also like to thank the directors and heads of Cardiology Department, Nephrology Department and Medical Department of Tengku Ampuan Rahimah Hospital, Selayang Hospital, Serdang Hospital, National Heart Institute, University Malaya Medical Centre and Kuala Lumpur Hospital for their approval to conduct the study among the doctors. I especially like to extend my heartfelt thanks to the staffs of Clinical Research Centre of Kuala Lumpur Hospital for their exceptional assistance with the statistical analysis of the study.

Thank you

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LIST OF ABBREVIATIONS

ACEIs	Angiotensin Converting Enzyme Inhibitors
ARBs	Angiotensin II Receptor Blockers
AT_1	Receptor Subtype 1
AUC	Area Under Curve
ATC	Anatomical Therapeutic Chemical
BNF	British National Formulary
CCBs	Calcium Channel Blockers
CHARM	Candesartan in Heart Failure Assessment of Reduction in Mortality and Morbidity
CPG	Clinical Practice Guidelines
CrCl	Creatinine Clearance
CURE	Comparative Utilisation of Resources Evaluation Model
DDD	Defined Daily Dose
DTC	Drugs and Therapeutic Committee
ELITE	Evaluation of Losartan In The Elderly
FDA	Food and Drug Administration
GPs	General Practitioners
HKL	Kuala Lumpur Hospital
HSDG	Serdang Hospital
HSLY	Selayang Hospital
HTAR	Tengku Ampuan Rahimah Hospital
IDNT	Irbesartan Diabetic Nephropathy Trial
IJN	National Heart Institute
IRMA	Irbesartan in MicroAlbuminuria
IQR	Inter-quartile Range

LIFE	Losartan Intervention For Endpoints in hypertension
MDC	Malaysian Drug Code
MIMS	Malaysia Index of Medical Specialities
MOH	Ministry of Health
MSC	Medscape Resource Centre
NICE	National Institute for Clinical Excellence
NIH	National Institute of Health
OPTIMAAL	Optimal Therapy in Myocardiac Infraction with Angiotensin II Antagonist Losartan
PH	Pharmacy Hospital
PHIS	Pharmacy Hospital Information System
PPDDEM	Pharmaceutical Product Drug Differentiation Evaluation Model
RAAS	Renin Angiotensin-Aldosterone System
RENAAL	Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan
SAT	Scoring Analytical Tool
SOJA	System of Objectified Judgment Analysis
SPSS	Statistical Package for the Social Science
UMMC	University Malaya Medical Centre
URAT1	Uric Acid Transporter
Val-HeFT	Valsartan in Heart Failure Trial
VALUE	Valsartan Antihypertensive Long Term Use Evaluation
WHO	World Health Organisation

PENILAIAN PENGHALANG RESEPTOR ANGIOTENSIN II UNTUK FORMULARI UBAT MENGGUNAKAN ALAT ANALITIKAL PENSKORAN OBJEKTIF

ABSTRAK

Satu kajian menilai ubat Penghalang Reseptor Angiotensin II (ARBs) untuk formulari ubat-ubatan dengan menggunakan Alat Analitikal Pengukur Penskoran Objektif (SAT) untuk memilih ARBs secara rasional supaya ubat dapat dimasukkan atau dikecualikan daripada formulari ubat-ubatan Kementerian Kesihatan Malaysia. Lazimnya, sekumpulan doktor pakar yang berpengalaman akan dilantik oleh Kementerian Kesihatan Malaysia untuk mengendalikan pilihan ubat dalam suatu masa yang tertentu. Akan tetapi, SAT yang dicadangkan menilai ubat secara objektif berdasarkan kriteria dan pemberat relatif supaya dapat disesuaikan dengan kepentingan relatif sub-kriteria. Cara peruntukan skor yang digunakan dalam SAT membuatkannya amat objektif dan konsisten. Banyak langkah dan perancangan telah dilakukan untuk menetapkan kriteria dan sub-kriteria yang bersesuaian dengan penyakit berkenaan dan menentukan skor berdasarkan kepentingan relatif. Kriteria utama yang dipertimbangkan adalah keselamatan, kualiti, efikasi dan penjimatan kos. Semua ini ditukarkan kepada format kajian soal selidik. Semua maklumat dan data dikumpulkan melalui kaji soal selidik yang diedarkan dengan sendiri kepada pegawai perubatan dan doktor pakar dari hospital kerajaan iaitu Hospital Tengku Ampuan Rahimah, Hospital Kuala Lumpur, Hospital Selayang, Hospital Serdang, Pusat Perubatan Universiti Malaya dan Institusi Jantung Negara. Analisis statistik data ARBs yang dikendalikan menunjukkan terdapat beberapa ubat ARBs dalam urutan pemilihan ARBs oleh para doktor mungkin dipengaruhi oleh bidang

kepakaran, kelulusan tempatan atau luar negara, dan jantina. Susunan urutan pemilihan ubat ARBs berdasarkan skor mengikut keutamaan dari atas ke bawah adalah seperti berikut: Telmisartan (802.2±76.7) ≈ Irbesartan (796.5±65.0) ≈ Losartan (792.9±66.6), Valsartan (719.2±80.5) ≈ Candesartan (734.8±82.5), Olmesartan (671.0±74.6) dan Eprosartan (600.0 [63.0]). Walau bagaimanapun, urutan pemilihan ubat ARBs yang diperolehi daripada SAT adalah berbeza dengan data penggunaan ubat ARBs di Hospital Serdang. Urutan menurun mengikut keutamaan pemilihan ubat ARBs di Hospital Serdang adalah Losartan, Telmisartan, Valsartan dan Irbesartan. Perbezaan urutan pemilihan ini adalah disebabkan oleh batasan tempatan yang diimplimentasikan oleh hospital masing-masing. Penjimatan kos ARBs yang paling tinggi di hospital kerajaan ialah Irbesartan dan dituruti oleh Losartan dan Telmisartan. Kajian ini menekankan penggunaan SAT untuk mengurangkan jumlah ubat-ubatan yang harus dimasukkan dalam formulari ubat, menilai penjimatan kos ubat-ubatan, memudahkan keputusan dibuat melalui peruntukan skor untuk kriteria tertentu dan membantu membezakan ubat-ubatan yang mempunyai ciri-ciri yang sama. Secara keseluruhannya, SAT mempunyai potensi untuk melengkapkan kaedah tradisional formulari ubat-ubatan kerana SAT berkesan untuk membantu membuat keputusan yang cepat terutamanya dalam kecemasan dan untuk mengurangkan inventori ubat-ubatan.

EVALUATION OF ANGIOTENSIN II RECEPTOR BLOCKERS (ARBS) FOR DRUG FORMULARY USING OBJECTIVE SCORING ANALYTICAL TOOL

ABSTRACT

A study into the evaluation of Angiotensin II Receptor Blockers (ARBs) for drug formulary using an objective Scoring Analytical Tool (SAT) was conducted to assess and carry out rational selection of the ARBs to be included or omitted in the Malaysian Ministry of Health (MOH) Drug Formulary. Traditional MOH Drug Formulary usually conducts drug selection employing a small group of senior who are very experienced specialists to conduct this drug selection over a period of time. In contrast, the proposed SAT evaluated the drugs objectively according to criteria and relative weightage to match the relative importance of the sub-criteria. The allocation of scores made the method very objective and consistent. Much preparatory work was carried out to pre-set the criteria and sub-criteria to match the diseases concerned and to assign scores based on the relative importance. The main criteria under consideration were safety, quality, cost and efficacy. All these were converted to questionnaires format. Data and information were collected through self administered questionnaires that were distributed to pre-qualified medical doctors and specialists from the established government hospitals namely Tengku Ampuan Rahimah Hospital, Kuala Lumpur Hospital, Selayang Hospital, Serdang Hospital, University Malaya Medical Centre and National Heart Institute. Statistical analysis of the data carried out showed certain ARBs order of preference trend of the participants which may be influenced by field of specialisation, whether local or overseas graduate and even gender. Descending order of preference based on scores

was Telmisartan (802.2±76.7) ≈ Irbesartan (796.5±65.0) ≈ Losartan (792.9±66.6), Valsartan (719.2±80.5) ≈ Candesartan (734.8±82.5), Olmesartan (671.0±74.6) and lastly Eprosartan (600.0 [63.0]). Even equating the drug preference trending data obtained from SAT to the hospital usage database in Serdang Hospital did show that there were differences in trending of drug preference which in descending order were Losartan, Telmisartan, Valsartan and Irbesartan. Differences occurred due to localised restriction imposed by the respective hospitals. The most cost saving ARBs for hypertension in government hospitals was Irbesartan and followed by Losartan and Telmisartan. This study emphasises the usefulness of SAT which included reducing the number of drugs to be kept in the formulary, assessing cost saving of drugs, score allocation of criteria helped decision making easier and helping to differentiate drugs where the properties of the drugs were quite similar. On the whole SAT has the potential to complement the traditional or conventional method as it is effective in aiding decision making especially in reducing the inventory and urgent drug decision.

CHAPTER ONE

INTRODUCTION

1.1 Background

A formulary system is a process whereby the medical staff of an institution, working through a Drug and Therapeutics Committee, evaluates and selects the numerous available drug products that are considered most efficacious, safe and cost effective. A good formulary system not only involves selection of appropriate drugs but also provides drug use evaluation to enhance quality of care for patients, ensures treatment protocol and procedures are up to date and consistent with optimal therapeutics and continuously improve quality of care through monitoring, reporting and analysis of adverse results of drug therapy (Laing & Tisocki, 2004; Savelli et al., 1996). Woodhouse (1994) defined main aims of a formulary are to encourage clinically effective and cost-effective prescribing that restrict the range of medicines, allow prescribers to increase their familiarity with a smaller number of choices, favor generic substitution, prevent relatively untried medicines from getting into uncontrolled widespread use and aid in cost containment.

A drug formulary is a manual containing clinically oriented summaries of pharmacological information of selected drugs, administrative and regulatory information pertaining to the prescribing and dispensing of drugs (Savelli et al., 1996; Quick et al., 1997). As a matter of fact, the World Health Organisation (WHO) Model Formulary (Laing & Tisocki, 2004) has already made available a practical guide on how to develop a national formulary so as to provide objective unbiased

information to health workers in a country and to promote safe, effective and rational use of medicines.

The main reason for developing a formulary is to promote rational prescribing and to limit costs (Duerden & Walley, 1999; Avery et al., 1997). However, it should be noted here that rational prescribing might even lead to increased drug costs. Furthermore, the cheapest drug doesn't always become the drug of choice. On the other hand, there is a myth indicating that expensive drug is more superior to its competitor and therefore, the newer and expensive drug is always been pushed into the formulary by the pharmaceutical industries as well as the prescribers. Evidence that introduction of formulary improves quality of prescribing is limited but a few number of cases do show cost savings (Duerden & Walley, 1999). Rational drug use was defined by World Health Organisation (WHO, 1985), as "patients receive medication appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community". Irrational or non rational use is the use of medicines in a way that is not compliant with rational use as defined. One of the core interventions to promote rational drug use is through implementing Drugs and Therapeutic Committee (DTC) in districts and hospitals. The DTC should represent all the major specialists and be independent and must declare any conflict of interest, to be free from biasness (WHO, 2002).

Developing of drug formulary is a continuous and on-going process due to constant changes in information about drugs and pharmacological practice. It is an important

process especially updating and monitoring but it is time consuming. The Malaysian MOH Formulary is an example of such a slow traditional process that generally employs the seniority and expertise of just a handful of specialists to oversee the tasks of evaluating the drugs to be approved or omitted from the common lists. Over recent years many tools have been developed and nowadays, there are many decision making tools available which can help to speed up the process of evaluation and selection of drug in the formulary. It is not practical for those involved in the drug evaluation and selection to delay important decision making especially on life saving drugs. The decision making tool must enable drugs to be assessed in a more consistent and reproducible manner. The tool should be objective and exclude subjective factors such as emotional factors, commercial influence or financial interest in seeing a drug included or be excluded as much as possible and be transparent especially on criteria and weighting decisions.

A few drug selection methods with scores have been developed and used worldwide for formulary purposes such as Comparative Utilisation of Resources Evaluation Model or CURE Model (Karr, 2000), System of Objectified Judgment Analysis or SOJA (Janknergt & Steenhoek 1997), Pharmaceutical Product Drug Differentiation Evaluation Model or PPDDEM (Karr, 1994) and Ranking Model (Bochner et al., 1994). PPDDEM, CURE and SOJA models of drug selection focus on the way in which the products are differentiated from each other within the same therapeutic class such as efficacy, safety, side effect, patient compliance, outcome data, duration of effects, price or route of administration. The development of the Scoring Analytical Tool (SAT) which is the main focus of this paper, will involve essentially selection of group of drugs which requires evaluation, identification of the relevant

criteria for that group of drugs which can be used to compare competing or similar drugs, assigning a weighting score to each criteria according to its degree of importance in the evaluation process. The more important criteria will have a higher relative weight. Scores for each drug are added up and drugs with the highest total score will be the preferred drugs for formulary inclusion.

The group of drugs to be focused for the development of the scoring tool for evaluating or selection of drugs is Angiotensin II Receptor Blockers (ARBs), hypertensive drugs. ARBs were introduced in the market in 1995 as a new drug class for hypertension after proving efficacy in lowering blood pressure. ARBs work by targeting the Renin Angiotensin-Aldosterone System (RAAS) which is the regulator of blood pressure homeostasis. Activation of RAAS will result in the release of renin from the juxtaglomerular complex of the nephron which converts Angiotensinogen into Angiotensin I. Next, either Angiotensin Converting Enzyme or a non-specific chymase generates Angiotensin II from Angiotesin I. Angiotensin II increases the blood pressure by three distinct mechanisms i.e. a) increases peripheral vascular resistance; b) stimulates release of Aldosterone from the adrenal medulla which induces sodium and water retention; c) causes smooth muscle cell proliferation and hypertrophy, further enhancing vascular tone. ARBs interfere with the RAAS by selectively blocking the binding of Angiotensin II to its receptor subtype 1 (AT_1). This selective blockage antagonises the effects of Angiotensin II at the target site, regardless of the pathway through which it was formed (Givertz, 2001; Rodger & Patterson, 2001; Burnier, 2001).

Table 1.1: Pharmacokinetic parameters of ARBs

Drug	Pro-drug	Maximal Onset (week)	$T_{1/2}$ (hr)	Bioavailability (%)	Food Effect (AUC %)	P450 Metabolism	Route of Elimination (%)		Trough: Peak Ratio %
							Renal	Hepatic	
Candesartan	Yes	2-4	9	15	No	No	33	67	80
Eprosartan	No	3	5-9	13	Yes	No	7	90	67
Irbesartan	No	2	12-20	60-80	No	No	20	80	>60
Losartan	Yes	2-3	2	33	No	Yes	35	60	58-78
Olmesartan	Yes	2	13	26	No	No	35-50	50-65	51.8-79.1
Telmisartan	No	3	24	42-58	No	No	0.5	98	>97
Valsartan	No	2	6	40-50	Yes	No	13	83	69-76

The pharmacokinetics of ARBs (Drug Facts and Comparisons, 2001; Rodger & Patterson, 2001; Schwocho & Mansonson, 2001) are listed in Table 1.1. All the ARBs exhibit distinctive pharmacokinetics profiles (Song & White, 2001). Losartan and Candesartan are pro-drugs and their antihypertensive activities are due to their metabolites. Candesartan is activated in the small intestine while Losartan is being biotransformed in the liver by cytochrome P450 enzymes. Drugs that inhibit the cytochrome P450 enzymes may interfere with the conversion of Losartan to its metabolite, possibly decreasing its effectiveness. The systemic bioavailability varies widely from a low of 13% for Eprosartan to as high as 80% for Irbesartan. Food alters the bioavailability of both Eprosartan and Valsartan. There is a large variation in plasma elimination half-life ($t_{1/2}$) of ARBs where Losartan has a short half-life of 2 hours while Telmisartan has extremely long-half of 24 hours. The antihypertensive is consistent across ARBs drugs and is within two to four weeks after initiation of therapy. The mode of elimination of ARBs is predominantly by hepatic route (Unger, 1999; Parnell et al., 2000; Drug Facts and Comparisons, 2001; Rodger & Patterson, 2001; Schwocho & Masonson, 2001).

Several clinical trials have shown the beneficial effects of ARBs therapy that goes beyond blood pressure control. Firstly, in renal disease, ARBs reduce progression of proteinuria and the development of end-stage renal disease in patient with hypertension and renal insufficiency (Brenner & Cooper, 2001; Lewis, 2002; Berl et al., 2003; Viberti & Wheeldon, 2002). Secondly, ARBs therapy reduces left ventricular mass and cardiovascular morbidity and mortality in patients with left ventricular hypertrophy and hypertension (Dahlof et al., 2002). Thirdly, ARBs protect against stroke (Dahlof et al., 2002; Lithell et al., 2003; Hankey, 2004).

Fourthly, ARBs play significant role in the treatment of heart failure (Konstam et al., 2005; Young et al., 2004; Maggioni et al., 2002). Most recently, ARBs have shown to delay the development of hypertension in prehypertension (Vasan, 2002). The therapeutic uses of ARBs and dosage adjustments in renal or hepatic impairment patients (Malaysia Index of Medical Specialities (MIMS) Annual, 2009) are as summarised in Table 1.2

Table 1.2: Therapeutic Uses of ARBs

Drug	Therapeutic Uses					Use in	
	Diabetic Nephropathy	Heart Failure and Left Ventricular Dysfunction	Hypertension	Hypertension and Left Ventricular Dysfunction	Post Myocardiac Infraction with / without Left Ventricular Dysfunction	Renal Impairment	Hepatic Impairment
Candesartan		Yes	Yes	Yes		Adjust dose (CrCl<30ml/min)	Adjust dose. Avoid in severe impairment
Eprosartan			Yes			No Adjustment	Adjust dose. Avoid in severe impairment
Irbesartan	Yes		Yes			Adjust dose (Undergoing haemodialysis)	No clinical experience in severe impairment
Losartan	Yes		Yes	Yes		Adjust dose (CrCl<20ml/min)	Adjust dose

Table 1.2 (Continued)

Drug	Therapeutic Uses					Use in	
	Diabetic Nephropathy	Heart Failure and Left Ventricular Dysfunction	Hypertension	Hypertension and Left Ventricular Dysfunction	Post Myocardiac Infraction with / without Left Ventricular Dysfunction	Renal Impairment	Hepatic Impairment
Olmesartan			Yes			Not recommended if CrCl<20ml/min	Avoid use
Telmisartan			Yes			Not recommended if CrCl<30ml/min)	Adjust dose. Avoid in severe impairment
Valsartan		Yes	Yes		Yes	Adjust dose (CrCl<20ml/min)	Adjust dose. Avoid in severe impairment

In this study, hypertensive drugs were chosen because hypertension is one of the most prevalent chronic disorders in the country (Lim et al., 2004). The prevalence of hypertension is high but the level of awareness, treatment and control are low. A national study on the prevalence, awareness, treatment and control of hypertension which involved 16,440 subjects and conducted in 2004 (Rampal et al., 2008) revealed that the prevalence of hypertension among those age 30 years has increased from 32.9% in 1996 to 40.5% in 2004. Only 34.6% of the hypertensive patients were aware of their hypertensive status and 32.4% were taking antihypertensive drugs. Many patients were not on drug treatment at all and of those treated, their drug treatment are likely to be inadequate as reflected by the study that only about 26.5% of those on antihypertensive drugs had their blood pressure under control. The Mortality Country Fact Sheet (World Health Statistics, 2006) showed that hypertensive heart disease is one of the top ten causes of death, all ages in Malaysia in year 2002. These results indicate that there is an urgent need to address this growing problem of hypertension among the Malaysians.

Based on Malaysian Statistics on Medicine (Sameerah & Sarojini, 2005), Malaysia is third in the top 30 list based on the therapeutic group by utilisation in DDD/1000 population/day 2005 for antihypertensive drugs acting on the renin-angiotensin system.The total utilisation of antihypertensive was 73.5 DDD/1000 population/day and Angiotensin II Receptor Blockers (ARBs) was 4.6 DDD/1000 population/day which worked out to be 22% of the agent acting on renin-angiotensin system. The low utilisation of ARBs could be due to higher cost and fewer trials supporting a mortality reduction as compared to Angiotensin Converting Enzyme Inhibitors (ACEIs) and the availability of alternatives with proven effectiveness.

Over the years, most national and international guidelines have not recommended ARBs as first-line treatment for hypertension as evidence on hard endpoints such as cardiovascular morbidity and mortality in patients with hypertension was not available until 2002 (Dahlof et al., 2002). In Malaysia, the Clinical Practice Guideline (CPG) for the management of hypertension (2008) recommended ARBs in patients with newly diagnosed uncomplicated hypertension and with no compelling indications as one of the choices of first-line monotherapy. Beta Blockers are no longer recommended for first-line monotherapy as it is not as effective in lowering blood pressure and in the prevention of stroke compared to other antihypertensive drugs (Lindholm et al., 2005). This updated CPG for the management of hypertension (2008) also supported the use of ARBs as the first-line therapy for hypertension in patient with concomitant condition such as diabetes mellitus with nephropathy, non-diabiatic renal disease, cardiovascular disease and stroke. This was due to the accumulated evidences of ARBs in reducing the cardiovascular morbidity and mortality (Hansson et al., 1999; Brown et al., 1999; Wing et al., 2003; Davis et al., 2002) and also significantly lower morbidity and mortality from further strokes (Schrader et al., 2005) in addition to effectiveness, tolerability, adherence profiles and demonstrated benefits in organ protection. Also, there have been no reports of adverse effects on carbohydrate and lipid metabolism (Parving, 2001; Brenner, 2001; Lewis, 2001). The utilisation rate of ARBs is expected to increase with these evidences supporting beneficial effects that extend beyond blood pressure reduction alone.

This paper will discuss and highlight in sequence the evaluation of Angiotensin II Receptor Blockers (ARBs) for drug formulary using an objective Scoring Analytical Tool (SAT). Generally, the development of the scores allocation for safety, efficacy and cost criteria and sub-criteria for the ARBs for hypertension leading to the full questionnaire format and the feedback from selected specialists and non-specialists participants from selected government hospitals, including complete analysis of results, discussion and recommendations will be described in detail.

1.2 Problem statement

Currently, there is no scoring tool that has been developed or even used in Malaysia which can assist decision-makers at all levels (national, regional, hospital, primary care) faced with difficult choices about which drugs to make available to their patients especially those new drugs which offer marginal improvement over existing therapies but at substantially increased costs. The Ministry of Health (MOH) Drug List Review Panel will review and update the drug listed in the formulary from time to time to ensure that a comprehensive, evidence based and dynamic list of drugs is available for prevention and treatment of patients. They will meet two to three times per year to evaluate the proposal or requests for addition or deletion of drugs to the formulary (Malaysian MOH Drug Formulary Manual, 2008). Here, the process of screening or evaluating the drugs for inclusion or exclusion into the formulary will take long period depending on the expertise of a handful of senior specialists. A scoring tool will be a great help as it will enable drugs to be assessed in a more structured, consistent and reproducible manner and hopefully to overcome biasness in terms of main drug supplier influence and emotional aspects.

Scoring tool with cut off point score for inclusion of drugs in the drug formulary will be able to reduce the number of drugs of the same therapeutic class and subsequently a decrease in hospital inventory. Reducing number of drugs of the same therapeutic class with only slight differences in clinical effectiveness, adverse effect or price could be one of the options to lower the overall expenditure. This is because the cost of all aspects of health care is increasing at an alarming rate. For example, in Malaysia, the drug expenditure had increase from RM346 million in year 2000 to RM915 million in 2005. Based on the Annual Report by Malaysian

Ministry of Health Pharmaceutical Services Division (2005), in year 2004 to 2005, an increase of 13.3% of drug expenditure was recorded. In Malaysia, the public health facilities support 80% of the country's patient population and the drugs made available for use in the public health care are controlled through the Malaysian MOH Drug Formulary. It is important that the Malaysian MOH Drug Formulary have the strategies involving formulary management so as to curb the high drug expenditure and ensure efficient allocation.

In short, the main problem at large is the insufficient and lacking of available simplified easy-to-use method to evaluate and carry out rationalised drug selection which can replace the existing more time consuming conventional or traditional method like the one being used by the MOH Drug Formulary. Here, it can be seen that the application of SAT can potentially or prospectively fill this gap. As an example, SAT can be used to establish whether it is justified to select members of the drugs belonging to the same therapeutic group. For example, these four ARBs (Losartan, Telmisartan, Irbesartan and Valsartan) which were selected by our Drug and Therapeutic Committee can be determined from the order of preference based on the Final Score of each ARB using SAT. SAT can also be used to determine the trend of drug use and also whether there is any discrepancy between pattern of drug use and local clinical guideline recommendation by the drug usage as a means of relating to the order of preference of the drugs concerned.

1.3 Rationale of the study

The rationale of this study is to enable drugs for inclusion or exclusion into a formulary to be assessed in a more objective, free from biasness, consistent and reproducible manner. The nature of the SAT which is essentially a score allocating method of evaluating drugs will hasten the whole drug approval or disapproval process as it is not practical for those involved in the drug evaluation and selection to delay important decision making especially on life saving drugs. By virtue of this fact, it will tremendously assist decision-makers at all levels (national, regional, hospital, primary care) faced with difficult choices about which drugs to make available to their patients. In fact, it can also help to simplify the whole process.

SAT can also reduce the number of drugs of the same efficacy and safety within the same therapeutic class as there is no need to include all members of a particular drug class in a drug formulary especially those new drugs which offer only marginal improvements over existing therapies but at substantially increased costs (Kessler et al., 1994).

This scoring tool can be used as a template to evaluate and re-evaluate when the need for re-assessment arises and also be extended to other classes of drugs. Thus, this study is justified in that if the tool can be effectively developed, it can be very useful in improving and speeding up the formulary inclusion or exclusion process in Malaysia.

1.4 Research objectives

1.4.1 General objective

The general objective is to develop an objective scoring tool for rational drug selection into the national drug formulary.

1.4.2 Specific objectives

The specific objectives of this study are:

a) to determine the list of relevant criteria and sub-criteria that can be used to evaluate the selection of Angiotensin II Receptor Blockers (ARBs) to be included in the drug formulary

b) to determine the scores for each selected criteria/sub-criteria of Angiotensin II Receptor Blockers (ARBs) for evaluation

c) to determine the cut off point for selection of Angiotensin II Receptor Blockers (ARBs) into drug formulary

d) to evaluate cost analysis of Angiotensin II Receptor Blockers (ARBs) by using ratio of drug acquisition cost to score of quality criteria

e) to compare the prescribing pattern of Angiotensin II Receptor Blockers (ARBs) in Serdang Hospital, Selangor with the order of preference of ARBs based on Final Score of ARBs using Scoring Analytical Tool (SAT)

f) to examine the prescribing pattern of Angiotensin II Receptor Blockers (ARBs) in Serdang Hospital, Selangor as first-line and second-line treatment of hypertension.

1.5 Significance of the study findings

The study on utilising SAT involved essentially developing relevant criteria and sub-criteria pertinent to individual specific Angiotensin II Receptor Blockers (ARBs) and correspondingly allocating the scores for each selected criteria and sub-criteria of the ARBs concerned and eventually subjecting for evaluation via statistical means. The results so obtained strongly showed that SAT is indeed a very useful tool which just employs scores to evaluate and simplify evaluation of drugs for decision making. It is clear that the existing ways of decision making is more qualitative and experiential-based and time consuming. Taking MOH for instance which a handful of senior expert specialists presides periodically to decide what drugs to select or omit for drug formulary inclusion. Envisaging using SAT, the decision process would be reduced tremendously. The Drug and Therapeutics Committee at hospital level can use SAT as a guide for selection of drug for hospital formulary. The data collected from SAT can be used to identify general prescribing and design appropriate interventions and to measure the impact of these interventions on the drugs use. The doctors especially the non-specialists who are not involved in the decision making in the Drug and Therapeutics Committee have the opportunity to evaluate the selected drug for the hospital formulary and voiced their opinions. SAT can also reduce the number of drugs of the same efficacy and safety within the same therapeutic class in our MOH Drug Formulary. This will enable the Pharmacy Store to reduce drug inventory or reduction in the number of drugs purchased and hence results in lower overall expenditures. The drug allocation or fund can be used to buy other safe and effective drugs. Here, the patients also benefit in terms of lower medication costs and drugs available are more safe and effective. Healthcare professionals can by using such tool to evaluate drugs and the results thus obtained

can be used to advise the patients on the side effects, effectiveness, etc. Even insurance companies, for example, can be specific about what drugs or medication that when prescribed may incur higher premiums by merely having more side effects.

CHAPTER TWO

LITERATURE REVIEW ON THE SCORING ANALYTICAL TOOLS

2.1 Introduction

Development of a Scoring Analytical Tool or SAT to rationalise a large number of drugs available with a view to shortlist essential medicines, control costs and improve prescribing practices requires essentially an objective, transparent and free-from external influence environment. This tool that is so developed would be re-evaluated or re-assessed from time to time and made available for use to the medical community in general. This tool is essentially being formulated with a main purpose of fine-tuning the means of evaluating drugs in a manner that is not biased. Generally, many countries are using formularies principle for drugs selection. According to Woodhouse (1994), the main aims of a formulary are to encourage clinically effective and cost effective prescribing, to restrict the range of medicines, allowing prescribers to increase their familiarity with a smaller number of medicines, encourage generic substitution, prevent relatively untried medicines getting into widespread use and aid cost containment. Woodhouse also suggested that medicines should be chosen for inclusion in a formulary on the basis of their relative proven efficacy, favorable risk-benefit ratio and cost. Some conventional formulary models that will be touched on like Malaysian Ministry of Health (MOH) Drug Formulary and World Health Organisation (WHO) Drug Formulary as well as other recent methods which include Pharmaceutical Product Drug Differentiation Evaluation Model or PPDDEM (Karr, 1994), Comparative Utilisation of Resources Evaluation Model or CURE Model (Karr, 2000), System of Objectified Judgment Analysis or SOJA (Janknegt & Steenhoek, 1997) and Ranking Model (Bochner et al., 1994).

The main purpose of this literature review is to critically evaluate the proposed developed scoring tool by comparing similarities and differences among the available established methods. Each of the published methods will be discussed in detail and the similarities and differences will also be dealt with and eventually leading to the justification of the development of SAT and the scope of its application.

2.2 Drug formulary

The traditional and conventional as mentioned earlier generally employs formulary system involving such a method whereby the medical staff of an institution, working through a Drug and Therapeutics Committee, manages, evaluates and selects from the numerous available drug products that are considered most efficacious, safe, and cost effective (Savelli et al., 1996). Initially, at the health facility level usually ministerial, an authoritative body, known as the Drug and Therapeutics Committee, must be established to be held responsible for all aspects of the formulary system, including drawing up policies and procedures for selection and use of drugs, compiling drug information, designing and conducting on-going monitoring and evaluation programs that ensure proper use of drugs in the facility. The result of such drug selection process is a drug formulary list. The list contains all drugs approved for procurement and used in a given health facility.

Well established formularies are useful reference or tools in helping solve problems of drug therapy, namely providing impartial drug information to counteract biased promotional activities. At present, as many as 70% of the pharmaceuticals on the