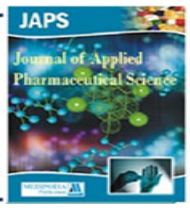
Journal of Applied Pharmaceutical Science

Available online at www.japsonline.com



ISSN: 2231-3354
Received on: 13-02-2012
Revised on: 12-03-2012
Accepted on: 18-03-2012

Selection of Proton Pump Inhibitors (PPIs) for Formulary Inclusion Using an Objective Scoring System in Malaysia

Lynette Lim and Mohamed Izham M.I

Lynette Lim
[a]*Pharmacist, Hospital Serdang, Selangor, Malaysia*
[b]*MSc. Social & Administrative Pharmacy Discipline, School of Pharmaceutical Sciences, Universiti Sains Malaysia, Penang, Malaysia*

Mohamed Izham M.I
Professor of Social & Administrative Pharmacy, Department of Pharmacy Practice, College of Pharmacy, Al Qassim University, Buraidah, Al Qassim, Saudi Arabia

For Correspondence
Lynette Lim
Pharmacist,
Hospital Serdang,Jalan Puchong,
43300 Serdang,Selangor.
H/P: 012-5899 180

ABSTRACT

The main aim of this study was to develop an objective Drug Evaluation Scoring System (DESS) by determining criteria for differentiation among 5 PPI drugs available in the market i.e. esomeprazole, lansoprazole, omeprazole, pantoprazole and rabeprazole. Secondly, was to assign weightage according to its importance of the criteria. Thirdly, was to determine the scores and rank the PPI drugs. In developing DESS, 200 points was assigned for the clinical documentation criterion, 300 points for the clinical efficacy criterion, 200 points for the safety criterion and 300 points for the cost criterion. The higher the assigned score, the higher importance the criterion is. The criteria were designed in the format of questionnaire to enable participants to allocate scores according to their perception on the importance of the criteria. Self-administered questionnaires were distributed to 165 specialists and medical officers. Study findings from the scoring system found that all PPI drugs have very negligible difference in clinical efficacy and clinical safety. Omeprazole was found to be the most cost economical PPI in the government hospitals. The DESS was able to compare and rank PPI drugs based on the scoring system and also assist in the selection of PPI drugs into the drug formulary.

Keywords: 'Drug evaluation', 'Drug formulary, 'Formulary management', 'Drug selection', 'Scoring tool'

INTRODUCTION

The cost of healthcare budget in developed countries is increasing at an alarming rate. The total value of drugs procured for the use in all hospitals and health clinics in Malaysia for 2008 was USD 490.26 million (MOH, 2008). Having a reliable yet comprehensive drug formulary is one way to promote rational prescribing and to limit costs (Schwartz *et al.*, 1984). The formulary will usually cover 80% of all prescribing decisions (Karr, 2000).

Pharmaceutical Product Drug Differential Evaluation (PPDEM), Comparative Utilisation of Resource Evaluation Model (CURE), Formulary Analysis and System of Objectified Judgement Analysis (SOJA) are all drug selection tools used for formulary purposes in which drug entity from the same therapeutic class are differentiated in terms of its efficacy, safety and price (Savelli *et al.*, 1996; Janknegt *et al.*, 1997; Karr, 2000). In this study, the criteria were adapted from various drug selection tools to develop a scoring system to evaluate the therapeutic group of PPI drugs for the treatment of gastroesophageal reflux disease (GERD). The process of drugs selection can be done in a more transparent and systematic approach by using an objective scoring system to differenciate the criteria of clinical experience, clinical efficacy, clinical safety and acquisition cost for each drugs belonging to the same therapeuctic class. As in this case, the scoring system was used to evaluate all the available PPIs and to select the most preferred PPIs which proven to have the highest clinical effectiveness with the least safety issues and lowest cost to be included in the Drug Formulary.

All PPIs that are available in Malaysia were included in the analysis i.e. esomeprazole, lansoprazole, omeprazole, pantoprazole and rabeprazole. There has been a rapid increase in PPI prescibing in Malaysia, with omeprazole ranked fourth highest expenditure among the 40 most utilised drugs. Drugs for acid related disorders ranked 6th in the ranking of expenditure on therapeutic drug groups (Goh, 2007).

AIM OF THE STUDY

The study was carried out with the following objectives:

-To determine the list of criteria that can be used as a scoring system for the inclusion and exclusion of PPIs in the National Drug Formulary for Gastroesophageal Reflux Disease (GERD).

-To determine the weightage for the selected criteria of PPIs to be used as a scoring system.

-To determine the scores obtained for each PPI and to rank these PPIs from the most preferred to the least preferred.

-To analyze and determine the most efficacy with the lowest cost PPI to be included into the Drug Formulary.

METHODOLOGY

Research Design

The study was conducted through a cross sectional survey. This study was approved and permission was granted by the Medical Registration Ethics Committee (MREC).

Study Population and Sampling Method

The population of this study were consultants, specialists, clinical lecturers and medical officers of the Medical, Surgical, Nephrology and Cardiology out-patient clinics in 6 established hospitals in the Klang Valley, i.e. Serdang Hospital, Selayang Hospital, Tengku Ampuan Rahimah Hospital, Kuala Lumpur Hospital (HKL), Universiti Malaya Medical Centre (UMMC) and National Heart Institute (IJN). These hospitals are referral hospital in the state of Selangor and Kuala Lumpur. The selected hospitals are also the major user of PPIs in the Klang Valley.

A convenience sampling method was used to generate the sample size of the participants in this survey. The total numbers of doctors in out-patients clinics in six hospitals in Klang Valley were 178. The sample size was calculated for each individual hospital using the Raosoft® sample size calculator with 95% confidence level and 5% margin of error. The total numbers of samples estimated by the sampling calculator were 165.

Tools and Questionnaires Development

Studies were identified by systematic search strategy. Literature searches were performed for all available Proton Pump Inhibitors (PPIs) drugs, i.e. esomeprazole, lansoprazole, omeprazole, pantoprazole and rabeprazole. All double blind randomized studies comparing two or more PPI drugs or doses and the prospective evaluation of measurable clinical efficacy such as healing of esophagitis or symptoms resolution from Micromedex Healthcare Series drug evaluation database, Pubmed, Cochrane Library, Medscape Resource Centre, package inserts between 1988 to 2008 were obtained.

Ten important criteria were adopted and adapted from SOJA and CURE scoring tools as well as other development and maintenance of hospital drug formulary manual to evaluate PPIs for the treatment of GERD (Janknegt *et al.*, 1997; Micromedex, 2008; Karr, 2000). A weighting score was assigned to each criterion according to its importance in the evaluation process. The more important the criterion was considered, the higher the weightage. In this study, the percentage scores allocated for quality score and cost scores were 70% and 30% respectively by using the modified SOJA as a reference (Janknegt *et al.*, 1997). There will always be room for discussion whether the weightage allocated and judgment of the importance of these criteria maybe arbitrary for all criteria. The quality score were divided into clinical documentation which consist of 200 points, clinical efficacy which consists of 300 points, and safety which consists of 200 points. The cost score consists of 300 points alone. Clinical documentation consists of i) comparative double blind studies, ii) FDA approved year, iii) FDA approved indication, iv) number of strength available and v) dosage form available. Clinical efficacy consists of vi) endoscopic cure and vii) the bioavailability of drugs. Clinical safety consists of viii) drug interactions and viv) side effects. Cost has an impact especially in helping to reduce drug procurement. The total score of all the Quality Score and Cost Score were 1000 points.

Based on the data and information summarized by the researcher from literature review and the physician's own knowledge, experience and practice, the physicians were required to choose either they strongly agree (100% of the allocated scores) or moderately agree (80% of the allocated scores) or neutral (60% of the allocated scores) or moderately disagree (40% of the allocated score) or strongly disagree (20% of the allocated score) for each sub-criteria.

Ethical Approval

This study was exempted from the ethical committee and permission was granted by the Medical Registration Ethics Committee (MREC).

Data Collection Method

A pilot study was conducted among doctors of the nephrology and cardiology out-patient in Serdang Hospital and Kuala Lumpur Hospital prior to the major study and the questionnaire was rectified. The questionnaire were distributed to a total of 8 respondents of which 3 were specialists and 5 were medical officers. However, only 6 questionnaires managed to be collected back. The respondents were asked to include their comments on the allocation of the weighting scores as well as their justification or even to include new selection criteria if there is any. Problems encountered were firstly, incomplete questionnaires. Only 1 questionnaire was fully scored with justification while 5 questionnaires were scored without any justification. The questionnaire was then modified to close ended questions with 5-point Likert scale i.e. the current scoring system. Secondly, the

literature review of each drugs were simplified to bullet form and brief explanations were incorporated for every sub-criterion and instructions were added to assist the respondents to rate the given drugs. Thirdly, the respondents commented that the cost provided should be in Ringgit Malaysia (RM) instead of pounds (£) as prices of drugs in pounds do not reflect the real comparison in Malaysia. The prices in the questionnaire were changed to Ringgit Malaysia (RM) and prices were based on the government hospital's price.

Data Analysis

All responses were coded and data were analyzed by Statistical Package for Social Sciences (SPSS) program version 16. Descriptive statistics were used to calculate the total scores, mean±SD, median and inter-quartile range (IQR) for each PPI obtained by each hospital for both inclusion and exclusion of cost factor, and the most preferred rank for each drug were determined. Kolmogorov-Smirnov test was used to test for normality. ANOVA or Kruskal-Wallis tests were used for multiple comparisons between PPI drugs. Student T-test or Mann–Whitney U tests were used for any significant differences among PPI drugs between gender, school of medicine attended by the respondents and their current post. Pearson's correlation or Spearman's rho was used to obtain the relationship between PPI score and respondent's experience. All tests were carried out at alpha level of 0.05 (with 95% confidence level). Cost-outcome analysis was also calculated using the formula cost/score. The price of each PPI was based on the government hospital's price. The price of each tablet of all PPIs was obtained and simple multiplication was used to calculate the price of all the PPIs for 28 days regimen. The cost of therapeutic substitution of all PPI with omeprazole was calculated and potential savings were determined.

Sensitivity Test

A sensitivity analysis was carried out to add confidence in the methodology. The rescoring was done by first removing the number of strength sub-criteria; score 30. All PPI drugs were rescored at a total score of 970. Next was rescoring by removing the dosage form sub-criteria; score 30. Both the above sub-criteria (number of strength and dosage form; score 60) were removed and rescored.

RESULTS

There were a total number of 178 specialists / clinical lecturers and medical officers available in the out-patient clinics of various departments in each respective hospital. The numbers of questionnaires distributed were based on 95% confidence level and 5% margin of error. 165 questionnaires were distributed to the respondents. The response rate was 44.2% or 73 questionnaires were returned and usable.

Figure 1 shows the mean scores and rank of each PPI with and without the inclusion of cost criteria. The full score for quality score criteria alone was 700. Esomeprazole took the first place with a score of 590.71, followed by pantoprazole, omeprazole, lansoprazole and rabeprazole. The full score for the quality criteria and cost criteria were 1000. Omeprazole scored the highest with 861.48, followed by lansoprazole, pantoprazole, esomeprazole and rabeprazole.

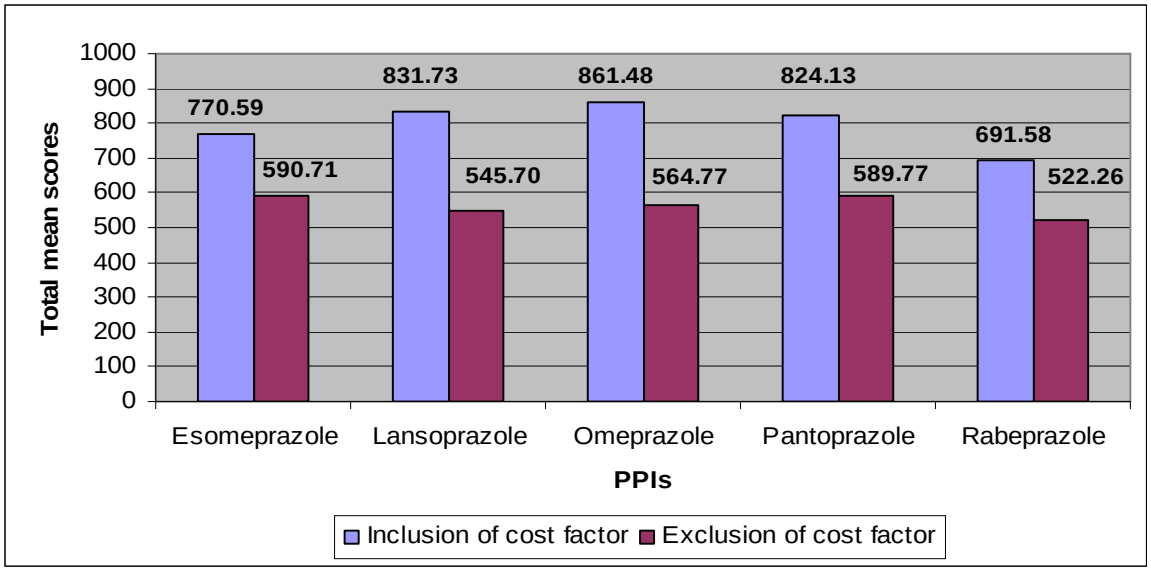


Fig. 1: Mean scores of Proton Pump Inhibitors with the inclusion and exclusion of cost criteria.

Table 1 summarized the mean scores, SD, median and IQR obtained for each drugs by specific sub-criteria.

Table 2 showed multiple comparisons between PPI drugs. For the quality scores alone, all PPIs showed significant difference ($p<0.05$) except for pair–wise esomeprazole and pantoprazole, lansoprazole and rabeprazole which showed no significant difference ($p>0.05$). There were significant differences between PPIs ($p<0.05$) except for lansoprazole and pantoprazole ($p>0.05$) for the total mean scores for both quality criteria and cost criteria.

Tables 3 and 4 showed the total mean scores based on the demographic data of the respondents. For the quality scores, no significant differences were found between the scores obtained between male and female respondents ($p>0.05$), except for lansoprazole and rabeprazole. There were also no significant difference ($p>0.05$) found between the current post held by the respondents and the school of medicine which were attended by the respondents for all PPIs except for omeprazole ($p<0.05$).

There were no significant differences ($p>0.05$) between the mean scores obtained between male and female respondents, the current posts held by the respondents and the school of medicine attended by the respondents for all PPIs except for omeprazole ($p>0.05$) for both the quality and cost scores.

Table 5 showed the relationship between PPI scores and the respondent's experience. No significant correlation between the respondent's experience (number of years a doctor practice) with the total mean scores obtained, for both inclusion and exclusion of the cost criteria ($p>0.05$).

Table 6 showed the cost analysis of all PPIs. Omeprazole was found to be the cheapest PPI available in government hospitals with the lowest cost/score ratio, followed by lansoprazole.

Table 7 showed all PPI drugs still scored and ranked the same as Figure 1 in the sensitivity tests.

Figure 2 showed the comparison and cost savings through therapeutic substitution of omeprazole. Further analysis were undertaken to estimate the potential savings that could be achieved by replacing all PPI drugs with omeprazole. Therapeutic substitution with omeprazole (100% adoption) would produce a significant savings of 44.4% or USD 23,941.71 a year.

Table. 1: Summary of criteria and mean scores.

Criteria	PPIs	Mean(±SD)	Median	IQR
Question 1: Number of double comparative studies	Esomeprazole	23.01(±5.10)	24	18 – 24
	Lansoprazole	27.12(±4.01)	24	18 – 24
	Omeprazole	27.12(±4.01)	30	18 – 24
	Pantoprazole	23.59(±4.40)	24	18 – 24
	Rabeprazole	20.88(±4.01)	18	18 – 24
Question 2: FDA approved year	Esomeprazole	24.00(±4.58)	24	24 – 30
	Lansoprazole	25.15(±4.43)	24	24 – 30
	Omeprazole	26.38(±4.21)	30	24 – 30
	Pantoprazole	25.40(±4.30)	24	24 – 30
	Rabeprazole	23.84(±4.60)	24	21 – 27
Question 3: FDA approved indication	Esomeprazole	75.40(±7.77)	80	64 – 80
	Lansoprazole	74.52(±8.52)	80	64 – 80
	Omeprazole	74.52(±8.52)	80	64 – 80
	Pantoprazole	66.63(±11.31)	64	64 – 80
	Rabeprazole	62.47(±9.30)	64	64 – 64
Question 4: Number of strength available	Esomeprazole	23.01(±2.83)	24	24 – 24
	Lansoprazole	23.01(±2.83)	24	24 – 24
	Omeprazole	28.52(±2.79)	30	30 – 30
	Pantoprazole	23.26(±2.99)	24	24 – 24
	Rabeprazole	22.60(±2.74)	24	21 – 24
Question 5 Dosage form available	Esomeprazole	27.37(±3.16)	30	24 – 30
	Lansoprazole	27.95(±2.87)	30	24 – 30
	Omeprazole	27.95(±2.87)	30	24 – 30
	Pantoprazole	27.45(±2.99)	30	24 – 30
	Rabeprazole	18.49(±4.87)	18	16 – 20
Question 6: Endoscopic cure	Esomeprazole	195.46(±13.85)	200	200 – 200
	Lansoprazole	126.58(±28.30)	120	120 – 160
	Omeprazole	166.58(±22.12)	160	160 – 180
	Pantoprazole	170.02(±21.35)	160	160 – 200
	Rabeprazole	150.14(±22.88)	160	120 – 160
Question 7: Bioavailability	Esomeprazole	82.19(±13.15)	80	80 – 100
	Lansoprazole	76.44(±15.03)	80	60 – 80
	Omeprazole	65.48(±15.37)	60	60 – 80
	Pantoprazole	82.19(±13.15)	80	80 -100
	Rabeprazole	58.36(±13.64)	60	40 – 60
Question 8: Drug interaction	Esomeprazole	60.00(±11.55)	60	60 -60
	Lansoprazole	83.56(±11.23)	80	80 -100
	Omeprazole	63.56(±12.62)	60	60 – 70
	Pantoprazole	85.48(±11.67)	80	80 – 100
	Rabeprazole	81.64(±13.23)	80	80 – 90
Question 9: Side effects	Esomeprazole	80.27(±11.78)	80	80 – 80
	Lansoprazole	81.37(±12.17)	80	80 – 80
	Omeprazole	84.66(±11.31)	80	80 – 100
	Pantoprazole	85.75(±11.29)	80	80 – 100
	Rabeprazole	83.84(±14.01)	80	80 – 100

		Esomeprazole	180.82(±32.39)	180	180 – 180
		Lansoprazole	286.03(±25.54)	300	300 – 300
Question 10:	Acquisition cost	Omeprazole	296.71(±13.75)	300	300 – 300
		Pantoprazole	233.42(±27.50)	240	240 – 240
		Rabeprazole	169.32(±40.43)	180	180 – 180

Table. 2: Multiple comparison between PPIs .

Pair – wise PPIs	Drugs	Inclusion of cost criteria		Exclusion of cost criteria	
		Mean scores	p-value	Mean scores	p-value
Esomeprazole & Lansoprazole	Esomeprazole	770.59±48.81	0.000	590.71±35.35	0.000
	Lansoprazole	831.73±61.17		545.70±51.80	
Esomeprazole & Omeprazole	Esomeprazole	770.59±48.81	0.000	590.71±35.35	0.006
	Omeprazole	861.48±45.16		564.77±42.57	
Esomeprazole & Pantoprazole	Esomeprazole	770.59±48.81	0.000*	590.71±35.35	**1.000**
	Pantoprazole	824.13±58.29		589.77±44.75	
Esomeprazole & Rabeprazole	Esomeprazole	770.59±48.81	0.000*	590.71±35.35	0.000
	Rabeprazole	691.58±65.77		522.26±45.34	
Lansoprazole & Omeprazole	Lansoprazole	831.73±61.17	0.002	545.70±51.80	0.011
	Omeprazole	861.48±45.16		564.77±42.57	
Lansoprazole & Pantoprazole	Lansoprazole	831.73±61.17	**0.852***	545.70±51.80	0.000
	Pantoprazole	824.13±58.29		589.77±44.75	
Lansoprazole & Rabeprazole	Lansoprazole	831.73±61.17	0.000*	545.70±51.80	**0.082**
	Rabeprazole	691.58±65.77		522.26±45.34	
Omeprazole & Pantoprazole	Omeprazole	861.48±45.16	0.000*	564.77±42.57	0.004
	Pantoprazole	824.13±58.29		589.77±44.75	
Omeprazole & Rabeprazole	Omeprazole	861.48±45.16	0.000*	564.77±42.57	0.000
	Rabeprazole	691.58±65.77		522.26±45.34	
Pantoprazole & Rabeprazole	Pantoprazole	824.13±58.29	0.000*	589.77±44.75	0.000
	Rabeprazole	691.58±65.77		522.26±45.34	

* Kruskal-Wallis test

Table. 3: Total mean scores according to respondent's demographic (inclusion of cost factor).

Drugs	Total Mean Scores with inclusion of cost criteria								
	Gender[a]			School of medicine[b]			Current Post[c]		
	Total Mean Scores with the inclusion of cost criteria		p-value	Total Mean Scores with the inclusion of cost criteria		p-value	Total Mean Scores with the inclusion of cost criteria		p-value
	Male	Female		Local	Overseas		Specialist	MO	
Esomeprazole	589.78	777.86	0.38	732.55	777	0.22	767.27	772.93	0.451
Lansoprazole	540.93	837.77	0.093	826.73	827.15	0.977	820.07	831.77	0.466
Omeprazole	564.77	866.74	0.51	874.55	850.7	**0.024**	863.33	860.19	0.762
Pantoprazole	590.71	830.23	0.323*	834.79	815.35	0.478*	816.73	829.3	0.739*
Rabeprazole	522.25	703.16	0.174*	703.39	681.8	0.244*	682.87	697.63	0.350*

Note: Gender[a] :male vs female
School of medicine[b]: local vs overseas
Current Post[c]: specialist/lecturers vs medical officers
*Mann - Whitney U test

Table 4: Total mean scores according to respondent's demographic (exclusion of cost factor).

Drugs	Total Mean Scores with exclusion of cost criteria								
	Gender[a]			School of medicine[b]			Current Post[c]		
	Total Mean Scores with the exclusion of cost criteria		p-value	Total Mean Scores with the exclusion of cost criteria		p-value	Total Mean Scores with the exclusion of cost criteria		p-value
	Male	Female		Local	Overseas		Specialist	MO	
Esomeprazole	595.40	581.73	0.287	585.15	593.60	0.54	581.03	597.00	0.386
Lansoprazole	551.67	525.53	**0.038**	533.70	546.90	0.447	535.81	545.15	0.325
Omeprazole	566.56	562.60	0.854	565.39	564.25	**0.034**	576.36	555.20	0.941
Pantoprazole	596.65	582.20	0.522	583.88	596.35	0.484	594.79	587.35	0.289
Rabeprazole	531.07	509.60	**0.029**	516.61	526.90	0.846	523.39	514.55	0.327

Note: Gender[a] :male vs female
School of medicine[b]: local vs overseas
Current Post[c]: specialist/lecturers vs medical officers

Table 5: Relationship between PPI scores with respondent's experience.

	Esomeprazole	Lansoprazole	Omeprazole	Pantoprazole	Rabeprazole
Experience (inclusion of cost factor) (p-value)	0.270	0.563	0.505	0.650*	0.124*
Experience (exclusion of cost factor) (p-value)	0.886	0.679	0.531	0.683	0.383

* Spearman's rho

Table 6: Cost analysis of PPIs.

Drugs	Esomeprazole	Lansoprazole	Omeprazole	Pantoprazole	Rabeprazole
Cost / 28 tab	USD 17.27	USD 7.18	USD 4.45	USD 17.36	USD 18.18
Score	589.78±35.35	540.93±51.80	564.77 ±42.57	590.71±44.75	522.25±45.34
Cost/ Score ratio	0.029	0.013	0.008	0.029	0.035
Rank	3	2	1	3	4

'Note: USD 1 = RM 3.08 (for the year 2008)'

Table. 7: Sensitivity test.

PPIs	Mean Scores exclusion of number of strength criteria	Mean Scores exclusion of dosage form criteria	Mean Scores exclusion of number of strength criteria and dosage form criteria
Esomeprazole	747.59±47.58	743.23±48.38	720.22±47.17
Lansoprazole	803.95±60.26	799.01±60.55	776.00±59.66
Omeprazole	832.96±45.15	833.53±44.30	805.01±44.29
Pantoprazole	800.88±57.49	796.68±58.23	773.42±57.42
Rabeprazole	668.96±65.14	673.07±64.75	650.47±64.08

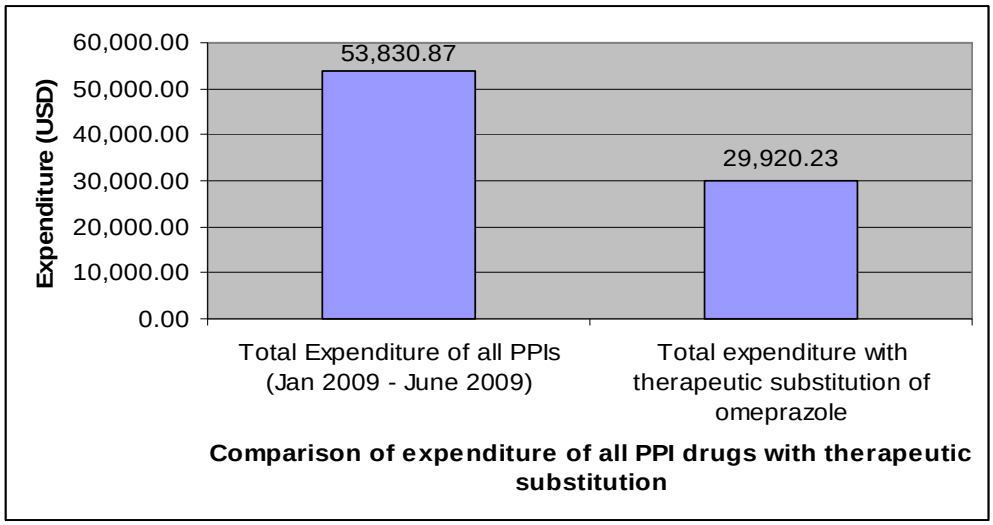


Fig. 2: Comparison and cost savings through therapeutic substitution.
'Note: USD 1 = RM 3.08 (for the year 2008)'

DISCUSSION

The scores obtained from DESS showed that omeprazole scored the highest scores and would be the preferred choice of PPI in the government hospitals. The results was supported by one survey done on PPI prescribing in an Irish general hospital where omeprazole was the most prescribed PPI while rabeprazole was the least prescribed PPI (Mat Saad *et al.,* 2005). Omeprazole being the choice of PPIs was the first PPI to be approved by FDA and was first marketed in 1989. The number of years a drug is marketed is an indicative of clinical experience with the drugs, thus giving physicians more confident in prescribing it. A PPI drug which is long enough in the market is unlikely to cause any serious side effects that have not been seen in the first few years of its introduction through post marketing surveillance. Omeprazole has the most double blind comparative studies, again is an indicative of its efficacy and safety for the treatment of GERD as compared to other PPIs (Micromedex, 2008). Having the most number of approved indications for management of GERD, duodenal ulcers, gastric ulcers and pathologic hypersecretory conditions evidently gives omeprazole an added advantage. Omeprazole which is the only PPI that have 3 strengths clearly was the choice of the respondents when the patients have the flexibility of adjusting the dose without having to split the tablets or to take more than one tablets for their prescribed dose. The more dosage form a drug has, the more convenient it is for the physician to individualize the patient's dose. PPIs that have more than one dosage form (tablet / suspension) will be an advantage for children as well as in hospitalized patients with difficulties in swallowing or those on tube feeding. The delayed release esomeprazole tablets cannot be crush but must be left disperse in water before administering through gastric tube (Nexium® Package Insert, 2008).

The bioavailability of omeprazole, pantoprazole and rabeprazole were not affected by food (Radhofer-Welte, 1999; Swan *et al.,* 1999; Geus *et al.,* 2000; Warrington *et al.,* 2002) which again gives omeprazole the added advantage of the flexibility on the administration time, thus increased patients compliance.

Direct comparisons between PPI drugs in double blind randomized controlled trial have consistently found the safety and tolerability of all PPIs to be similar (Holtmann *et al.,* 2002; Lauritsen *et al.,* 2003). Diarrhea, abdominal pain and headache were usually the most common side effects (Bianchi *et al.,* 2002), regardless of the dose (Castell *et al.*; 1996; Sontag *et al.,* 1997).

Omeprazole and lansoprazole which are available in the generic form were the cheapest PPI, while esomeprazole, pantoprazole and rabeprazole which are still available in the original brand were the most expensive PPIs. The price of each PPI was based on the price which was offered to government hospitals. The cost analysis of PPIs in this study was based only on acquisition cost without taking into consideration of any direct and indirect costs that could possibly be incurred. The scoring of PPIs showed the same sequence as the main study when the number of strength available and dosage form sub-criterion were removed. This adds confidence to the methodology and findings. In another analysis where the cost criterion was excluded, esomeprazole scored the highest. This proved that cost does make a difference when evaluating the choice of PPIs for formulary management. The rationale for the preference for esomeprazole is that the S-isomer of omeprazole which was claimed to have greater activity than omeprazole. This is consistent with a systematic review which showed esomeprazole was slightly more effective than the other PPIs (Vakil *et al.,* 2003). Another study concluded that the superiority of esomeprazole 40mg is probably related to the higher dose compared with omeprazole 20mg rather than the clinically significant improvement of the S-isomer as a racemic mixture and therefore cannot be considered a true comparison of effectiveness (Klok *et al.,* 2003) In a smaller direct comparative study between esomeprazole 40mg and pantoprazole 40mg, the results showed no significant difference between these two drugs (Gillessen *et al.,* 2004).

Systematic review of this class of drugs concluded very little difference that gives no important difference in the effectiveness of all PPIs in the general population (McDonagh *et al.,* 2009). A few randomized controlled clinical trials have also proven the healing rate in patients with erosive esophagitis were similar with all PPIs when given in equivalent doses; esomeprazole 20mg ~ lansoprazole 30mg ~ omeprazole 20mg ~ pantoprazole 40mg ~ rabeprazole 20mg (Hughes *et al.,* 2005; Schneiweis, 2008). A meta-analysis comparing lansoprazole 30mg and omeprazole 20mg showed no significant difference in healing rates at 4 and 8 weeks (Sharma *et al.,* 2001). Additional studies showed the same conclusion (Caro *et al.,* 2001; Edwards *et al.;* 2002).

Limitations of study

In this survey, convenience sampling method was used to generate the required sample size and therefore the respondents may not represent all specialists and medical officers in Malaysia. The scoring system can only objectively access a particular therapeutic group of drugs for one indication at a time, when in actual practice, a single drug is used for more than one indication. There will be a certain level of subjectivity in the scoring system as new data on existing drugs were reported.

Study Recommendations

DESS can be introduced at the hospital level as well as the national level P&T committees to assist in decision making of drugs to be included into the drug formulary and at a quicker process. The scoring system though developed for PPI drug class can be used as a comparison framework and extended to other therapeutic class of drugs.

CONCLUSIONS

Study outcomes from the scoring system have demonstrated that the most preferred PPIs at government hospitals level were omeprazole followed by lansoprazole, panoprazole, esomeprazole and rabeprazole. Cost analysis of the PPI therapeutic class found omeprazole to be the cheapest PPI available in government hospitals at 0.78 cents / 1 point. Drug Evaluation

Scoring System is a scoring system which can assist the P&T committee in making better and rational drug decision to restrict the number of PPI drugs which were considered to be therapeutically equivalent with only marginal differences in efficacy and pharmacokinetics with the lowest cost to be selected and included into the Drug Formulary. Potential savings for the expenditure of PPIs from therapeutic substitution (100% adoption) were estimated to be 44.4% or USD 23,941.71 per year if esomeprazole, lansoprazole, pantoprazole and rabeprazole were substituted with omeprazole.

ACKNOWLEDGEMENT

The author would like to thank the specialists, medical doctors, institutions and all those who have participated in this survey.

FUNDING

None Declared.

CONFLICT OF INTEREST

The authors have no conflict of interest matter to declare.

REFERENCES

Alabbadi, I., McElnay, J., Crealey, G., Scott, M., Baird, S., Trouton, T., Mairs, J. Impact of Modified System of Objectified Judgement Analysis (SOJA) Methodology on Prescribing costs of ACE Inhibitors. *Clin Drug Invest*. 2006; 26 (9):485-494.

Bianchi, P.G., Lazzaroni, M., Imbesi, V., Montrone, F., Santagada, T. Efficacy of pantoprazole in the prevention of peptic ulcers, induced by non-steroidal anti-inflammatory drugs: a prospective, placebo-controlled, double-blind, parallel group study. *Dig Liver Dis*. 2002; 32:201- 8.

Caro, J.J., Salas, M., Ward, A. Healing and relapse rates in gastro-oesophageal reflux disease treated with the newer proton-pump inhibitors lansoprazole, rabeprazole, and pantoprazole compared with omeprazole, ranitidine and placebo: evidence from randomized clinical trials. *Clin Ther*. 2001; 23:998-1017.

Castell, D.O., Richter, J.E., Robinson, M., Sontag, S.J., Haber, M.M. Efficacy and safety of lansoprazole in the treatment of erosive reflux disease. *Am J Gastroenterol*. 1996; 91:1749-57.

Edwards, S.J., Lind, T., Lundell, L. Systematic review of proton pump inhibitors for the acute treatment of reflux oesophagitis. *Aliment Pharmacol Ther*. 2002; 16:1729.

Geus, W.P., Mathot, R.A.A., Mulder, P.G., Lamers, C.B. Pharmacodynamics and kinetics of omeprazole MUPS 20mg and pantoprazole 40mg during repeated oral administration in Helicobacter pylori-negative subjects. *Aliment Pharmacol Ther*. 2000; 14:1057-64.

Gillessen, A., Beil, W., Modlin, I.M., Gatz, G., Hole, U. 40 mg Pantoprazole and 40 mg esomeprazole are equivalent in the healing of esophageal lesions and relief from gastro-oesophageal reflux disease-related symptoms. *J Clin Gastroenterol*. 2004; 38:332-40.

Goh, K.L. Gastroesophageal Reflux Disease (GERD) in the East – Same as the West. *J Clin Gastroenterol*. 2007; 41:S54-S58.

Holtmann, G., Bytzer, P., Metz, M., Loeffer, V., Blum, A.L. A randomised, double-blind, comparative study of standard-dose rabeprazole and high-dose omeprazole in gastro-oesophageal reflux disease. *Aliment Pharmaol Ther*. 2002; 16:479-85.

Hughes, D.A., Bytzer, P. Economic Analysis of on demand maintenance therapy with proton pump inhibitors in patients with non erosive reflux disease. *Pharmacoeconomics*. 2005; 23(10):1031-1041.

Janknegt, R., Steenhoek, A. The System of Objectified Judgement Analysis. A tool in rational drug selection for formulary inclusion. *Drugs* 1997; 53:551-62.

Karr, A. The comparative utilization of resources evaluation model: a cure for all diseases. *Pharm. J*. 2000; 265 (7119): 619-621.

Klok, R.M., Postma, M.J., van Hout, B.A., Brouwers, J.R. Meta-analysis: comparing the efficacy of proton pump inhibitors in short term use. *Aliment Pharmacol Ther*. 2003; 17:1237-457.

Lauritsen, K., Deviere, J., Bigard, M.A., Bayerdorffer, E., Mozsik, G., Murray, F., *et al*. Esomeprazole 20 mg and lansoprazole 15 mg in maintaining healed reflux oesophagitis: Metropole study results. *Aliment Pharmacol Ther*. 2003; 17:333-41.

Mat Saad, A.Z., Collins, N., Lobo, M.M.H.J. Proton Pump Inhibitors: a survey of prescribing in an Irish general hospital, *Int J Clin Pract*. 2005; 59(1):31-34.

McDonagh, M.S., Carson, S. Drug class review on Proton Pump Inhibitors. 2006. [cited 2009 Aug 18]. Available at: http://www.ohsu.edu/drugeffectiveness/reports/final.cfm.

Micromedex ® Healthcare Series [database on CD-ROM]. Version 5.1. Greenwood Village, Colo: Thomson Reuters (Healthcare) Inc; 2008.

Ministry of Health (MOH). *Pharmaceutical Services Division Annual Report*. Kuala Lumpur: MOH; 2008.

Nexium [package insert online]. Wilmington, DE: AstraZeneca LP; 2008. [cited 2009 Aug 19]. Available at: http://www.astrazenecaus.com/pi/Nexium.pdf.

Radhofer-Welte S. Pharmacokinetics and metabolism of the proton pump inhibitor pantoprazole in man. *Drugs Today*. 1999; 35:765-72.

Savelli, A., Schwarz, H., Zagorski, A., Bykov, A. Manual for the development and maintenance of Hospital Drug Formulary 1996. Arlington; Management Sciences of Health.

Schneiweis, S. Proton Pump Inhibitors: Evidence for Concern. Independent Drug Information Service. 2008. [cited 2009 Aug 16]. Available at http://www.rxfacts.org.

Schwartz, W.B., Aeron, H.J. Rationing hospital care. Lessons from Britain. *N Engl J Med*. 1984; 310:52-56.

Sharma, V.K., Leontiadis, G.I., Howden, C.W. Meta-analysis of randomized controlled trials comparing standard clinical doses of omeprazole and lansoprazole in erosive oesophagitis. *Aliment Pharmacol Ther*. 2001; 15:227-31.

Sontag, S.J., Kogut, D.G., Fleiscman, R. Campbell, D.R., Richter, J., Robinson, M., *et al*. Lansoprazole heals erosive reflux oesophagitis resistant to histamine H2-receptor antagonist therapy. *Am J Gastroenterol*. 1997; 52:429-37.

Swan, S.K., Hoyumpa A.M., Merritt G.J. Review article: the pharmacokinetics of rabeprazole in health and disease. *Aliment Pharmacol Ther*. 1999; 13 suppl. 3:11-7.

Vakil, N., Fennerty, M.B. Systematic review: direct comparative trials of the efficacy of proton pump inhibitors in the management of gastro-oesophageal reflux disease and peptic ulcer disease. *Aliment Pharmacol Ther*. 2003; 18:559-68.

Warrington, S., Baisley, K., Boyce, M., Tejura, B., Morocutti, A., Miller, N. Effects of rabeprazole 20mg or esomeprazole 20mg, on 24-h intragastric pH and serum gastrin in healthy subjects. *Aliment Pharmacol Ther*. 2002; 16:1301-7.