Research Article

PATTERN OF ANTIDEPRESSANT UTILIZATION AT A TERTIARY HOSPITAL IN MALAYSIA (2009-2011)

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ABSTRACT

The specific goals of this study are to determine trends in the usage and comparison of clinical patterns of antidepressant treatment modality in a tertiary hospital between year 2009-2011. We retrospectively reviewed prescription records in the Outpatient Pharmacy Department (OPD) of a tertiary hospital in central Malaysia from 2009 to 2011. About 3000 prescriptions, containing at least one anti-depressant drug, were systematically sampled and evaluated. Malay patients had a decreasing trend of 3% in anti-depressant usage over the study. Escitaloprom (SSRI) group was found to be the most widely utilized antidepressant with a steady increase of 9% while usage of Fluvoxamine was found to show a decreasing trend over the three years. The overall pattern profoundly favoured monotherapy modality rather than combination therapy among practitioners. This study also found an increasing pattern in the use of antidepressants with antianxiety and antipsychotic. In general, this study has contributed additional information regarding the prescribing pattern of anti-depressants in Malaysia at the current moment.

Keywords: Antidepressants, depression, prescription pattern, Malaysia

INTRODUCTION

Depression is rapidly becoming a major global burden in the recent years with many victims becoming more vulnerable to major social and environmental factors[1]. According to the World Health Organisation (WHO) and the World Bank, depression is the fourth most disabling disease in the world. It is perceived to be an illness that potentially can overtake chronic diseases such hypertension and diabetes [2, 3]. In this context, anti-depressants play a major role in managing depression and are considered as the first line therapy for depression management in many countries. Over the years antidepressant prescribing patterns have undergone revolution with rational prescribing practice being implemented globally, resulting in conventional drugs like tricyclic antidepressant (TCA) and mono-amine oxidase inhibitors (MAOI) being gradually replaced by selective serotonin reuptake inhibitors (SSRI), serotonin–norepinephrine reuptake inhibitor (SNRI) and novel antidepressants.

In Malaysia, almost 10% of the population are believed to be suffering from this disease and practitioners rely heavily on the use of anti-depressant in disease management [4]. However, there has been very little studies involving anti-depressant usage in Malaysia. Thus, an investigation into the prescribing pattern of anti-depressants is warranted to determine the changes that have occurred in this practice. To our knowledge, this study is a pioneer study aimed at assessing the use of different classes of antidepressants in Malaysia by comparing the clinical patterns of anti-depressant medication treatment in a tertiary hospital between the years 2009-2011.

METHOD

This study was carried out as a retrospective study reviewing 3000 prescriptions from the Outpatient Pharmacy Department (OPD) of Hospital Klang , Selangor. Permission to conduct the study was obtained from the hospital ethics committees. Targeted data for the study were prescriptions available at the OPD from the year 2009 to 2011 containing one or more antidepressant drugs. Prescriptions from the OPD which fulfill these criteria will be included in the study:

a) Prescriptions used from the year 2009 to 2011
b) Has one or more anti-depressant given for indication of depression

A randomized systematic sampling method will be used, whereby anti-depressant prescriptions that satisfy the study criteria will be identified from the main study population (sampling frame). Subsequently, for every 2 anti-depressant prescriptions fulfilling the criteria, one will be randomly picked to be utilized in the study [5].

Data Collection

A data collection form was used to compile information from eligible prescriptions. Documentation of the data included demographic characteristics, pattern of drug use, duration) and trends in treatment modality (monotherapy versus combination therapy and types of combination).

Statistical Analysis

The data collected will be analyzed using SPSS version 12.0 (SPSS Inc., Chicago, IL) and Microsoft Excel. Continuous data were presented as mean values + standard deviation while categorical data were presented as percentages. Descriptive statistics were used to analyze the data and results were represented in tabular form or graphically. Cross tabulation using Chi-square tests were used to evaluate the pattern of drug use. The level of significance (*p*-value) was set at = 0.05.

RESULTS

A total of 3000 prescriptions were randomly selected for this study averaging around 1000 prescriptions for each year. As shown in Table 1, male and female had almost equal incidences of anti-depressant prescribing. Looking into ethnic differences, the Malays has the highest proportion of receiving depression treatment though the percentage has reduced from 38.9% in 2009 to 35.3% in 2011, whereas the depression medications prescribed among the Chinese have increased slightly from 2009 to 2010 (2.5%) and then small reduction was observed in 2011 (0.08%). Meanwhile, the number of depression prescriptions among the Indians reduced from 2009 to 2010 and then increased slightly in year 2011. Table-1 provides a summary of the demographic data obtained from the prescriptions The prescribing pattern of anti-depressants over the 3-year study period is shown in Table-2. SSRI is the most widely used class of anti-depressant drugs in this study. Fluvoxamine turned out to be the most frequently prescribed antidepressant and sertraline ranked second in the hierarchy of prescriptions followed by venlafaxine from SNRI class. But these SSRIs were upstaged by escitalopram in the study duration. Venlafaxine however recorded a decreasing trend over the study period. Therapeutic pattern (monotherapy vs combination therapy) in the use of depression is showed in Figure 2.

Table 1: Demographic characteristic of outpatients' prescriptions for anti-depressant therapy at a tertiary hospital in peninsular Malaysia (2009-2011)

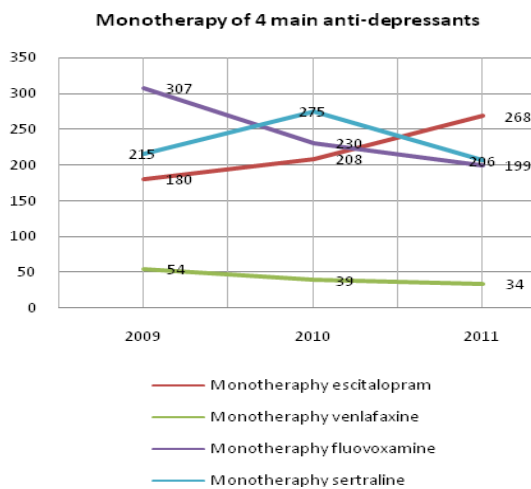| Characteristic	2009	2010	2011	p-value
Gender				
Female	477 (47.7%)	439 (43.9%)	492 (49.2%)	<0.05 (S)
Male	523 (52.3%)	561 (56.1%)	508 (50.8%)	
Mean	42.41	43.21	44.17	<0.05
Race				
Malay	389 (38.9%)	376 (37.6%)	353 (35.3%)	
Chinese	314 (31.4%)	339 (33.9)%	331 (33.1%)	0.06 (NS)
Indian	237 (23.7%)	20 (20.3%)	226 (22.6%)	
Others	60 (6%)	82 (8.2%)	90 (9%)	

S = Significant; NS=Non significant

Figure 1: Trends in monotherapy of anti-depressant agents for outpatients receiving depression prescriptions at a tertiary hospital in Peninsular Malaysia (2009-2011)

Generally, combination therapy is not practiced in Malaysia as we can see the number of prescriptions being very low while monotherapy is strongly favoured registering high number of prescriptions each year. The monotherapy category was initially largely dominated by fluvoxamine in 2009 but then a significant downward trend was observed where the usage dropped from 37.7% in 2009 to 20.9% in 2011. However, this drift was in contrast to the pattern seen in escitalopram where a tremendous increase can be seen, about 9% over the 2 years period as shown in Figure 1.

Monotherapy antidepressant drugs are concomitantly prescribed with antianxiety and anti-pscyhotic drugs, which is displayed in Figure 3 and Figure 4. A tremendous increase in co-precribing anti-depressant drug with clonazepam was recorded, with increases amounting to 19% from the year 2009 till 2011. On the other hand, lorazepam which was initally the highest anti-anxiety drug prescribed illustrated a downward trend from 13.9% in 2009 to 5.4% in 2011. Diazepam also showed a drop in usage ,around 2.5%, although it was not as popular as the other anti-anxiety drugs. Similarly, Figure 4 shows that risperidone and sulpride are the most common anti-psychotics prescribed together with anti-depressant drugs. There was a continuous increase in usage of risperidone with anti-depressants from year 2009 to 2011 while sulpride had fluctuating usage over the years.

Table 2: Trends in the usage of anti-depressants among outpatients receiving antidepressants prescriptions at a tertiary hospital in Peninsular Malaysia (2009-2011)

| Agent	2009	2010	2011	p-value
Selective Serotonin Receptor Inhibitor (SSRI)				
Escitalaprom	193 (19.3%)	227 (22.7%)	228 (22.8%)	<0.001
Fluvoxamine	377 (37.7%)	245 (24.5%)	209 (20.9%)	<0.002
Sertraline	223 (22.3%)	290 (29.0%)	215 (21.5%)	<0.001
Selective Norephineprine Reuptake Inhibitor (SNRI)				<0.05
Venlafaxine	54 (5.4%)	42 (4.2%)	39 (3.9%)	
TricyclicAntidepressants (TCA)				
Mirtazapine	43 (4.3%)	54 (5.4%)	53 (5.3%)	<0.001
Total	890 (89%)	858 (85.8%)	744 (74.4%)	

S = Significant; NS=Non significant
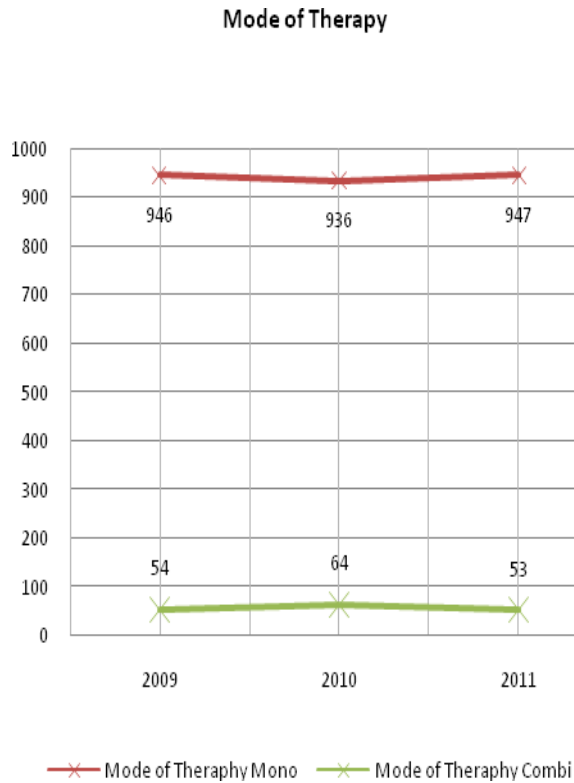
Figure 2: Trends in therapy modalities for anti-depressants amongst outpatients receiving depression prescriptions at a tertiary hospital in peninsular Malaysia (2009-2011)
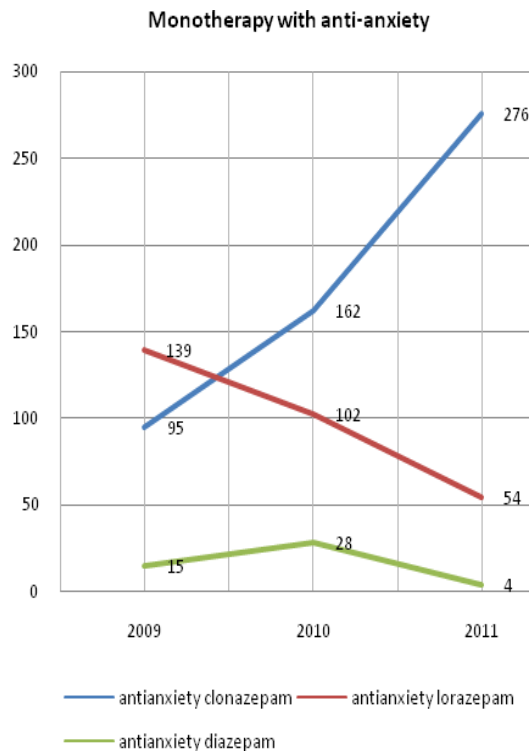

Figure 3 : Trends in monotherapy of anti-depressants with anti-anxiety agents for outpatients receiving depression prescriptions at a tertiary hospital in Peninsular Malaysia (2009-2011)
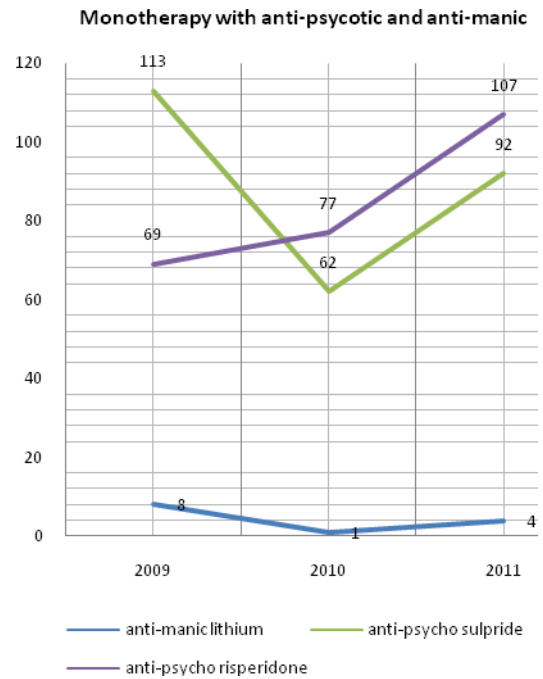

Figure 4: Trends in monotherapy of anti-depressants with anti-psychotic and anti-manic agents for outpatients receiving depression prescriptions at a tertiary hospital in Peninsular Malaysia (2009-2011)

DISCUSSION

This was a retrospective study through prescriptions evaluation, detailing on the epidemiology of depression in a tertiary hospital in Malaysia. Three main groups of antidepressant drugs comprising of the (SSRI), (SNRI) and (TCA) were identified and pattern of their usage were evaluated. Results of the demographic data reveal that ethnic differences occur in the prevalence of anti-depressant prescribing whereby there is a continuous decrease in among Malay patients and increase in the number of Chinese patients. This can be explained by the vulnerability of the Chinese community towards stress and mental health problems. A study by Tahir Mehmood Khan et al [6] revealed that the Chinese in Malaysia display high priority in matters relating to emotions and due to increase of divorce rate and relationship breakdown among Chinese, a higher risk of depression is inevitable.

This study revealed that the primary anti-depressants used by practitioners in Malaysia are SSRI as regulated by the Clinical Practice Guidelines 2007 [7, 8]. As shown by Figure 1, the findings also imply that escitalopram is the most widely used SSRI agent with a gradual increase from 2009 to 2011. This is an interesting finding as escitalopram was not a very popular drug initially. But recent studies have shown that escitalopram has the potential to deliver superior benefits compared to traditional SSRI [9, 10] and might have caused the surge in usage. Venlafaxine, a SNRI agent, proved to be another widely used anti-depressant although its use illustrates a downward trend while TCA seems to have regained popularity and has an increasing trend by the year 2011. Practitioners in Malaysia may have reduced venlafaxine use and turned towards TCA due to the adverse effects and the high cost of venlafaxine. SNRI has a higher affinity towards serotonin toxicity and can lead to tolerability issues with patients along with increased health cost burden [11, 12].

Generally in Malaysia, monotherapy of antidepressant is the main mode of therapy utilized by practitioners in tertiary hospital nationwide. Figure 2 suggests a similar trend was discovered in this study that shows combination therapy is very rarely used practice. According to JK Trivedi (2011) dual or triple medications for is associated with higher frequency of adverse effects without any additional benefits [13] .Rather than utilizing multiple anti-

depressants, physicians in Malaysia prefer to combine benzodiazepines (anti-anxiety) with anti-depressants for optimum health outcome. The administration of benzodiazepines in suicidal, anxious or agitated patients with depression is common international practice [14, 15, and 16]. Furukawa et al. (2001) analysed nine studies with a total of 679 patients to determine benefits of adding benzodiazepines to antidepressants in patients with major depression. The intent-to-treat analysis (with drop-outs assigned the least favourable outcome) showed that patients allocated to the combination therapy were less likely to drop out of study and were more likely to show improvement of depression[15].

Based on our finding in Figure 3, clonazepam is the most used widely benzodiazepine agent registering an increase of 15% each year compared to lorazepam and alprazolam. This is probably due to the augmentation effect demonstrated by clonazepam when combined with SSRI. Clonazepam has potential to increase the effects of SSRI and also partially suppress the adverse effects of SSRI [15, 16, and 17]. Although these properties are minimally present in lorazepam and alprazolam, but clonazepam exhibits the highest degree of these beneficial effects. Figure 4 shows the analysis on usage of anti depressants with antipsychotic drugs and anti-manic drugs. Risperidone shows a gradual increase from year 2009 to 2011 which implies that practitioners have found beneficial effects utilizing this agent for depression management. A study done by Ostroff & Nelson reported on eight patients with non-psychotic depression who failed to respond to an SSRI, but responded when risperidone was added. Similarly, practitioners believe that patient also benefit from addition of lithium to anti-depressant therapy. This is due to the increase in serotonin (5-HT) neurotransmission, possibly through a synergistic action of lithium and the antidepressant on brain 5-HT pathways. But lithium is reserved primarily for refractory depression, hence the low number of usage shown in Figure 4.

CONCLUSION

Our study shows that the appearance of novel therapeutic agents and new clinical evidences in the management of depression has initiated a revolution in anti-depressant drugs utilization among practitioners. SSRIs are widely acknowledged to have fewer side effects and a more tolerable pharmacological profile making them more 'user friendly'. Escitaloprom is gradually replacing Fluvoxamine as the first line therapy among the physicians in Malaysia. The prescribing mode of therapy still remains favourable for monotherapy. Studying the prescription patterns can help the practitioners to adopt rational prescribing practice in a better manner throughout Malaysia.

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