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Trends in the Utilization of Psychotropic Drugs in Serdang Hospital

Pei Yean Soo[1]*, Atiqah Hanis Mustapa[1], Hui Peng Lim[1], Chen Yuan Lee[1], Wen Suen Goh[1]

ABSTRACT

Introduction: The prevalence of mental health issues in Malaysia has tripled from 10.7 % in 1996 to 29.2 % in 2015. This was reflected by an increasing usage of psychotropic drugs over the past two decades. Thus, this study was carried out to explore the utilization trends of psychotropic drugs prescribed in Serdang Hospital. **Method:** This observational retrospective quantitative study was conducted using 11-year data from January 2008 to December 2018. Dispensing data was obtained using the electronic hospital information system (eHIS) in Serdang Hospital. Defined daily doses per 1000 populations per year metric (DDDs / 1000 / year) were used to compare the popularity of psychotropic classes and individual drugs. A comparison of the frequency and distribution of the drugs over time was made using Microsoft Office Excel 2013. **Result:** Total utilization of psychotropic drugs increased markedly by 859.2 % (from 75.9 to 727.8 DDDs / 1000 / year) from 2008 to 2018. Antidepressants were the most frequently dispensed class, with a significant increase by 1828.6 % (from 20 to 385.9 DDDs / 1000 / year). On the other hand, attention deficit hyperactivity disorder (ADHD) medication was the least dispensed class, from no usage in 2008 to 4.3 DDDs / 1000 / year in 2018. In 2018, out of 27 psychotropic drugs, sertraline (26.4 %) was the most frequently dispensed drug with 192.3 DDDs/1000/year. Conversely, clobazam (0.2 %) was the least dispensed drug with 1.2 DDDs / 1000 / year. **Conclusion:** Psychotropic drug utilization in Serdang Hospital increased markedly over the study period. All six classes contributed to the increment. Appropriate use of psychotropic drugs should be investigated in future.

INTRODUCTION

Psychiatric disorders are a growing public health concern worldwide. They affected more than 1 billion people globally in 2016 [1]. Approximately 80% arise from low and middle-income countries [2]. In Malaysia, the prevalence of psychiatric disorders among adults increased from 10.7 % in 1966, to 11.2 % in 2006, and to 29.2 % in 2015 [3]. Among all types of psychiatric disorders, depression was known to occur most commonly in Malaysia, affecting nearly 2.3 million people in Malaysia [4].

Psychiatric disorders cause significant burden on societies globally [5]. Approximately a third of those with major psychiatric disorders developed into long term disability and

dependency [6]. The 2010 Global Burden of Disease study concluded that psychiatric disorders were the fifth leading cause of burden worldwide (equivalent to 7.4 % of all disability-adjusted life years (DALYs)) and the leading cause of disability (equivalent to 22.9 % of all years lived with disability (YLDs)) [7]. They also imposed additional burden associated with suicide and ischemic heart disease [8,9]. By the year 2030, it is predicted that the most burdening illness globally will be depression [10]. In Malaysia, psychiatric disorders accounted for 8.6 % of total DALYs in 2016 [11].

Psychotropic drugs remain a mainstay in the treatment of psychiatric disorders. Data from previous studies indicated increasing utilization of drugs for psychiatric disorders in different parts of the world over the past two decades [12-19].

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*Correspondence: peiyeansoo@gmail.com

[1]Department of Pharmacy, Serdang Hospital, Ministry of Health Malaysia, Jalan Puchong 43000 Kajang, Selangor, Malaysia.

This increase was also evident in the children and adolescent population [20,21]. In a developing country like Malaysia, a wide array of psychotropic drugs is available. With the development of newer drugs such as selective serotonin reuptake inhibitors (SSRIs) and atypical antipsychotics, more treatment options are available, including augmentation therapy with these newer drugs for patients with treatment-resistant psychiatric disorders. Various factors such as efficacy, safety, cost of drugs and local paradigms may change the drug prescribing habits, and thus affect the outcome. With this backdrop in mind, this study is conducted to investigate how the utilization trend of psychotropic drugs has been changing over time. Such understanding could yield invaluable insights which could be utilized for optimization of psychotropic drug prescribing patterns.

METHOD

This observational retrospective quantitative study was conducted using 11-year data from January 2008 to December 2018. This study was registered with the National Medical Research Register, Ministry of Health Malaysia (NMRR ID-NMRR-19-788-45961).

This study included data on oral psychotropic drugs dispensed in emergency pharmacy, in-patient pharmacy, out-patient pharmacy and ward floor stock. Data on patients from other Ministry of Health (MOH) facilities who were referred to Serdang Hospital solely for the collection of medication as well as medication loaned to other facilities were excluded from this study. Dispensing data was obtained using the electronic hospital information system (eHIS) in Serdang Hospital. Defined daily doses per 1000 populations per year metric (DDDs / 1000 / year) were used to compare the usage of psychotropic classes and individual drugs. A comparison of the frequency and distribution of the medications over time was made using Microsoft Office Excel 2013.

RESULT AND DISCUSSION

Overall dispensing for the six major classes of psychotropic drugs (anxiolytics and sedatives, antidementia, attention deficit hyperactivity disorder (ADHD) medication, mood stabilizers, antidepressants and antipsychotics) is shown in Figure I. When all the psychotropic classes were considered, the total DDDs / 1000 / year increased markedly by 859.2 % (from 75.9 to 727.8 DDDs / 1000 / year). This notable increase was driven by increases in all psychotropic classes, with antidepressants contributing the most increase by 1828.6% (from 20.01 to 385.92 DDDs / 1000 / year). This is because depression was the most widely treated psychiatric disease in Malaysia [4]. A previous study conducted in Australia also concluded that the increase in psychotropic dispensing was majorly driven by increases in antidepressants (95.3 %) [17].

Comparison of the contribution of each psychotropic class to total psychotropic dispensing in 2008 and 2018 is shown in Figure II. Our findings illustrated that the most frequently dispensed class was mood stabilizers (48.3 %) in 2008 and antidepressants (53 %) in 2018. This is in tune with data from several studies which reported that antidepressant were the most popular psychotropic class of late [15,17,22,23]. As for the least dispensed psychotropic class, our results revealed that ADHD medication was the least dispensed in 2008 (no usage) and 2018 (0.6 %). This may be attributable to the reluctance of parents to allow their children to take medications for long term [16]. Parents are concerned about their children's treatment options. They believe that a prolonged use of stimulants can result in increased risk of drug addiction [24]. They also have the misconception that the cause of ADHD symptoms is associated with sugar intake, and thus they are not keen to start their children with medication as the first option [25].

Comparison of the list of psychotropic drugs available in Serdang Hospital in 2008 and 2018 is shown in Table I. There were a number of new psychotropic drugs being added into the drug formulary, with 14 drugs in 2008 versus 27 drugs in 2018. This could explain the significant increase in drug utilization from 2008 to 2018 because these drugs are known to have clinical superiority relative to the first-generation drugs.

Of the 27 psychotropic drugs in 2018, sertraline (26.4 %) was the most popular dispensed drug with 192.3 DDDs / 1000 / year. In contrast, clobazam (0.2 %) was the least dispensed drug with 1.2 DDDs / 1000 / year. Data from the Malaysian Statistics on Medicines found a similar trend, which documented that sertraline was among the top three most dispensed drugs in public sectors in 2014, while clobazam was the least popular drug [16]. An overseas study conducted in Iran also reported that sertraline (12.4 %) was the most commonly used psychotropic drug between 2012 and 2013 [23].

Anxiolytics and sedatives

We observed a remarkable 305.6 % increase in anxiolytics and sedatives dispensing (from 14.8 to 60.2 DDDs / 1000 / year) from 2008 to 2018. However, our findings are in contrast to several recent local and global studies. Data from Malaysian Statistics on Medicines indicated a drop of 5.8 % in the overall usage of anxiolytics and sedatives from 2011 to 2014 [16]. An overseas study carried out in Australia found that dispensing of anxiolytics remained unchanged, while sedatives decreased by 26.4 % [17]. Hence, results of our study should raise awareness regarding appropriate prescribing practices for anxiolytics and sedatives. This includes strategies to discontinue long-term prescribing of benzodiazepine. Benzodiazepines are recommended to be tapered down slowly, with psychological support emphasized during the tapering process. Basic approaches include the use of the same medication for tapering,

switching to a longer-acting equivalent and the use of adjunctive medications to mitigate the withdrawal symptoms. The recommended initial dose reduction ranges between 5 % and 25 % of the starting dose, followed by further reduction of 5 % to 25 % every one to four weeks as tolerated [26].
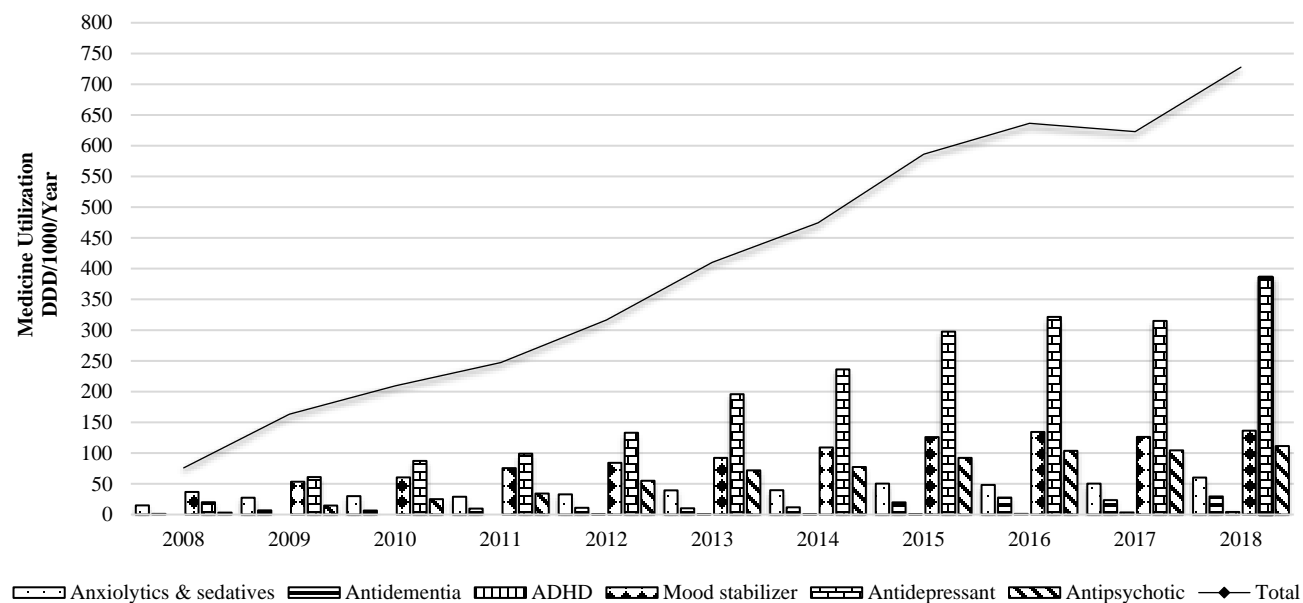

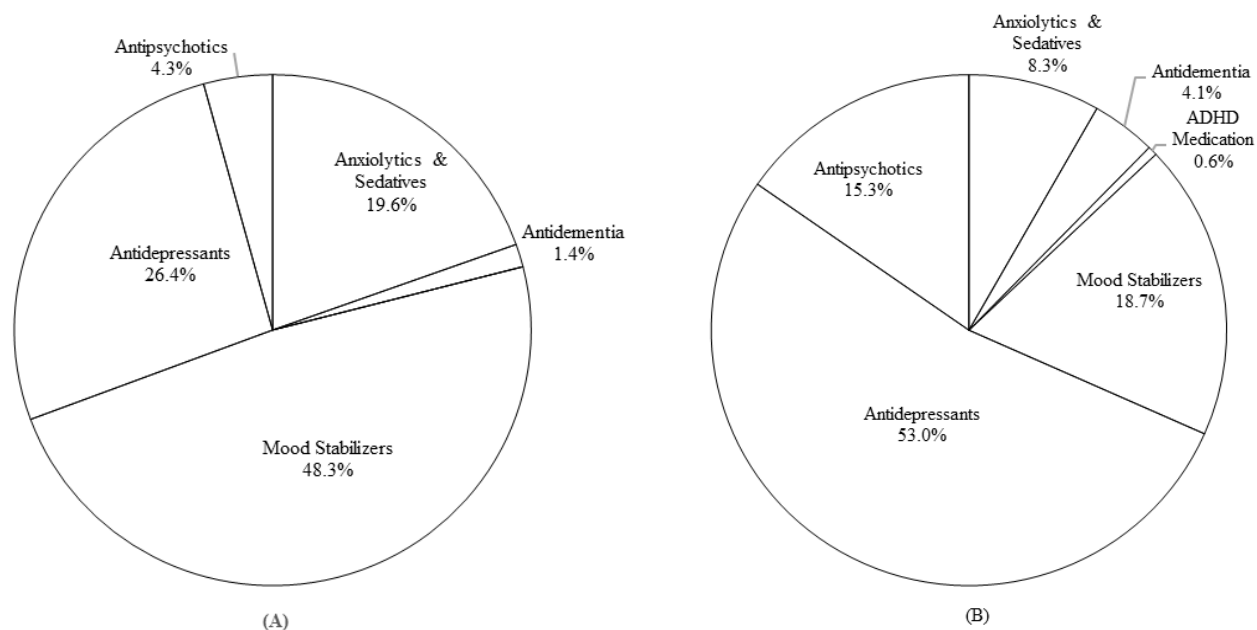**Figure I: Overall Dispensing for the Six Main Psychotropic Classes from 2008 to 2018**

Figure II. Contribution of each Psychotropic Class in (A) 2008 and (B) 2018

Table I. Dispensing Data for each Individual Psychotropic Drugs in 2008 and 2018

Drug	DDDs/1000/year	
	2008	2018
Anxiolytics and Sedatives		
Midazolam	3.9 (5.14)	1.56 (0.21)
Clonazepam	1.46 (1.92)	20.52 (2.82)
Phenobarbitone	3.03 (3.99)	1.99 (0.27)
Alprazolam	2.71 (3.57)	11.72 (1.61)
Diazepam	0.44 (0.58)	2.05 (0.28)
Lorazepam	3.3 (4.35)	12.82 (1.76)
Clobazam		1.18 (0.16)
Zolpidem		8.35 (1.15)
Antidementia		
Donepezil	1.1 (1.45)	27.25 (3.74)
Memantine		2.26 (0.31)
ADHD		
Methylphenidate		4.3 (0.59)
Mood Stabilizers		
Carbamazepine	18 (23.72)	32.53 (4.47)
Lamotrigine	1.05 (1.38)	15.23 (2.09)
Sodium Valproate	17.6 (23.2)	88.58 (12.17)
Antidepressants		
Tricyclic Antidepressant (TCA)		
Amitriptyline	18.51 (24.4)	15.83 (2.18)
Selective Serotonin Reuptake Inhibitors (SSRIs)		
Fluvoxamine	1.5 (1.98)	81.59 (11.21)
Escitalopram		52.32 (7.19)
Fluoxetine		33.27 (4.57)
Setraline		192.29 (26.42)
Others		
Duloxetine		7.99 (1.1)
Mirtazapine		2.63 (0.36)
Antipsychotics		
Typical antipsychotics		
Haloperidol	3.08 (4.06)	5.67 (0.78)
Sulpiride	0.19 (0.25)	9.14 (1.26)
Atypical antipsychotics		
Aripiprazole		7.34 (1.01)
Olanzapine		25.27 (3.47)
Quetiapine		12.76 (1.75)
Risperidone		51.34 (7.05)
Total	**75.87 (100)**	**727.78 (100)**

Of the 8 anxiolytics and sedatives, clonazepam was the most widely dispensed drug. Use of clonazepam increased markedly by 1305.5 % (from 1.46 to 20.52 DDDs / 1000 / year). The findings are consistent with several drug utilization studies conducted in tertiary care hospitals in India [27,28]. Benzodiazepines are known to have differences in distribution, elimination half-life and rate of absorption. Clonazepam is a long-acting and high-potency benzodiazepine, having lower lipid solubility and longer elimination half-life, as compared to lorazepam and alprazolam. Thus, it has a lower incidence of adverse events, drug abuse and interdose withdrawal symptoms [29]. Moreover, it has no drug interaction with antidepressants,

and thus, favouring its use over other benzodiazepines [30,31].

Antidementia

Our study's result showed that donepezil was the most preferred drug for dementia over memantine. According to the Malaysia Clinical Practice Guidelines on Management of Dementia, donepezil has been approved for mild to severe dementia. As for memantine, it is approved to be used only for moderately severe to severe dementia and in patients who are unable to tolerate acetylcholinesterase inhibitors such as donepezil [32].

ADHD medication

Our study revealed that methylphenidate was the only psychiatrist-prescribed stimulant for the treatment of ADHD in children. A study conducted in Iran also reported similar practice in ADHD prescription [23]. In terms of drug efficacy, it reduces core symptoms of ADHD such as poor concentration and hyperactivity by 70 % as compared to placebo [33]. It is being recommended by the National Institute for Health and Clinical Excellence (NICE), the Scottish Intercollegiate Guidelines Network (SIGN) and the American Academy of Pediatrics (AAP) as the first line drug in treating ADHD [34-36]. In terms of drug safety, it generally has a favourable side effect profile which is mild and of short duration. The most common side effect is appetite suppression which can be overcome by taking the drug after meal.

Mood stabilizers

Our study showed that the drugs used in the treatment of bipolar disorders consist of anticonvulsant drugs only, namely sodium valproate, carbamazepine and lamotrigine. Anticonvulsants exhibit their acute antimanic response and prophylactic efficacy in bipolar disorders in various ways, which include blockage of the voltage-gated ion channels (sodium valproate, carbamazepine and lamotrigine), enhancement of gamma aminobutyric acid (GABA) inhibition (sodium valproate), and reduction of glutamate release (lamotrigine) [37]. Their role in the treatment of bipolar disorders was evident in many recent studies despite lithium being the mainstay of treatment for many years [38]. This is because lithium has a narrow therapeutic index of safety, thus requiring frequent blood monitoring as per recommendations by the National Patient Safety Agency [39]. In Serdang Hospital, the lithium blood monitoring test is not available, therefore discouraging its use for bipolar disorders.

Among the anticonvulsants, sodium valproate was the most commonly dispensed mood stabilizer, which is in line with the findings from several overseas studies [18,27]. It has been recommended as the first line drug for bipolar patients because it demonstrates efficacy in the treatment of a broad spectrum of bipolar conditions, including as augmentation therapy in schizophrenia, as augmentation with SSRI in depression, organic brain syndrome and dementia with behavioural symptoms [40,41].

Antidepressants

Our results showed that the use of SSRIs spiked notably, while tricyclic antidepressants (TCAs) dropped gradually over the study period. This finding is comparable to both local and overseas studies in which SSRIs were the preferred prescribed antidepressant class [13,17,18,19,42]. Considering efficacy

and safety profiles, SSRIs are recommended as the initial treatment of depression, while conventional antidepressants (TCAs) are considered as second line treatment [43]. SSRIs have high affinity to serotonin reuptake receptors but little blocking activities at the histaminic, cholinergic, and alpha-adrenergic receptors. For these reasons, they have a superior safety profile relative to TCAs.

Our study showed that sertraline was the most widely used SSRI drug. This finding is in agreement with several similar studies done in other countries [17,44]. One of the reasons is that, sertraline has the most favourable balance between effectiveness, side effects, and cost [45]. It only produces mild inhibition on cytochrome P450 2D6 and has little effect on other cytochrome P450 isoenyzmes as compared to other SSRIs. Therefore, in patients at risk for drug interactions, sertraline is considered as a first line treatment option [46,47]. Additionally, it is relatively safe in overdose [47].

Antipsychotics

Our findings showed a paradigm shift from typical antipsychotics to atypical antipsychotics. In 2008, only typical antipsychotics were used for treatment of schizophrenia. However, over the years, there was a surge in atypical antipsychotics usage, overtaking typical drugs. This finding is in tune with several drug utilization studies [14,17,28]. This may be explained by their role in the treatment of negative symptoms, lesser extrapyramidal side effects and lower treatment discontinuation rate [48]. Besides, they have been used as adjunctive therapy to mood stabilizers, providing faster and more notable symptom improvement compared to conventional monotherapy with mood stabilizer [49].

Our results reported that risperidone was the most preferred antipsychotics, with a tremendous rise by 3300% (from 1.51 to 51.34 DDDs / 1000 / year) from 2009 to 2018. This is significantly higher when compared to data from the Malaysian Statistics on Medicines, which reported 34.3% increase from 2011 to 2014 [16]. Risperidone was extensively prescribed most likely because it is the only atypical antipsychotic drug with prescriber category B as listed in the MOH drug formulary. All medical officers, including consultants and specialists, can start patients on this drug when indicated. In terms of weight gain and metabolic abnormalities, it is better tolerated than olanzapine and quetiapine [50].

CONCLUSION

Psychotropic dispensing in Serdang Hospital increased markedly from 2008 to 2018, with major increases contributed by antidepressant use. Growing increase in anxiolytics and sedatives usage should raise awareness on appropriate benzodiazepine prescribing. The inclusion of newer drugs such

as SSRIs and atypical antipsychotics has altered the treatment paradigms.

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CONFLICT OF INTEREST

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