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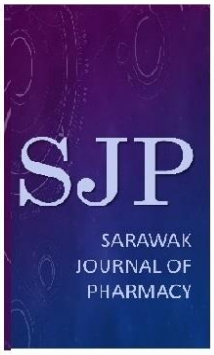

Perceived use and comparison of usage of sitagliptin and vildagliptin in Miri Hospital

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Abstract:

Introduction: Malaysia has the highest rate of diabetes in Asia. Patients with diabetes normally will initially treat with lifestyle intervention and followed by pharmacological treatment. Dipeptidyl peptidase-4 (DPP-4) inhibitors are a newer class of oral diabetes drugs that has recently gain attention in treating diabetes through increases and prolonged incretin hormone activity which in turn helps to increase release of insulin and minimize glucagon secretion. A study was carried out in Medical outpatient clinic of Miri Hospital in year 2016 and 2017 to find out the average maintenance dose per day (or Defined Daily Dose, DDD) for two selected DPP-4 inhibitors, namely vildagliptin and sitagliptin for adults diagnosed with type 2 diabetes.

Methods: The data collected measured in daily defined dose (DDD) which is the average maintenance dose per day for a drug used for its main indication in adults. The processed and total dose of each pharmaceutical agent linked to appropriate ATC code and DDD from WHO

ARC/DDD system. The drug utilisation for both sitagliptin and vildagliptin compared based on DDD per 1000 inhabitants to provide rough estimate of the proportion of patients in Medical outpatient clinic of Miri Hospital treated with sitagliptin and vildagliptin.

Results: Overall usage of DPP-4 inhibitors in Hospital Miri increased by about 6% from 2016 to 2017. The number of prescribed vildagliptin increased by 167.3%% from 0.098 DDD/1000 inhabitants/day to 0.262 DDD/1000 inhabitants/day while sitagliptin reduce by 22.3% from 0.555 DDD/1000 inhabitants/day to 0.431 DDD/1000 inhabitants/day from 2016 to 2017. Prescribers had slowly shifted their preference over to vildagliptin because it is cheaper and it shown to be more effective in term of glycemic control when compared to sitagliptin. However, sitagliptin still preferred over vildagliptinin 2016 to 2017 as it was the first DPP-4 inhibitor approved to be used in Malaysia.

Conclusion: Sitagliptin was more frequently prescribed than vildagliptin in Hospital Miri. However, the proper utilisation pattern was not clear due to money constraint, leading to restricted usage of both DPP-4 inhibitors. Hence, they were reserved for certain group of patients and depend on the preference of prescribers.

Keywords: *Define daily dose; diabetes; dipeptidyl peptidase-4 inhibitor; DPP-4 inhibitor, Miri Hospital, Malaysia*

Introduction

In 2017, there were total of 3,492,000 diabetic cases reported in Malaysia with prevalence of diabetes in adult of approximately 16.9% (1). This made Malaysia having highest rate of diabetes in Asia [1]. A report in 2007 stated that cost of antidiabetic medications ranked the second highest in healthcare expenses for medications in Malaysia (2).

Patients diagnosed with diabetes will initially approach with lifestyle intervention and followed by pharmacologic treatment. Dipeptidyl peptidase-4 (DPP-4) inhibitors are a newer class of oral diabetes drugs that has recently gain attention in treating diabetes through increases and prolonged incretin hormone activity which in turn helps to increase release of insulin and minimize glucagon secretion. As a consequence, DPP-4 inhibitors improve glycemic control by reducing fasting and postprandial glucose level (3). Sitagliptin, linagliptin, alogliptin, saxagliptin, and vildagliptin are the examples of DPP-4 inhibitors. As a result from growing scientific and medical evidence in validating the therapeutic benefits of DPP-4 inhibitors, increase in medical market needs, growth in worldwide healthy lifestyle campaigns and incline in investment by pharma companies, the demand of DPP-4 inhibitors has increase drastically in global as well as in Malaysia. Despite being well tolerable, most DPP- 4 inhibitors are yet to be established with strong information on durability of their effects in long run.

This study was carried out to find out the average maintenance dose per-day (or Defined Daily Dose, DDD) for two selected DPP-4 inhibitors, namely; vildagliptin and sitagliptin for treating adult with diabetes type 2 in Medical outpatient clinic of Miri Hospital in year 2016 and 2017. The usage pattern of DPP-4 inhibitors in Hospital Miri was compared to DDD trend of DPP-4 inhibitors in Malaysia.

Methods

In this study, we enrolled patients from Medical outpatient clinic of Miri Hospital who were taking sitagliptin and vildagliptin in year 2016-2017.

The data collected measured in daily defined dose (DDD) which is the average maintenance dose per day for a drug used for its main indication in adults. The drug utilisation measured in DDD may not be same as the recommended or prescribed daily dose of individual. In this study, the processed and total dose of each pharmaceutical agent linked to appropriate ATC code and DDD from WHO ATC/DDD system. The drug utilisation for both sitagliptin and vildagliptin were compared based on DDD per 1000 inhabitants (4). Data presented in DDD per 1000 inhabitants could provide rough estimate of the proportion of patients in Medical outpatient clinic of Miri Hospital treated with sitagliptin and vildagliptin.

$$DDDs\ per - 1{,}000\ inhabitants\ per - day = \frac{T\text{^}\ x\ 1000}{DDD\ x\ P\ x\ 365}$$

***T*^ =** An estimate of the total dose of the drug by ATC code utilised in the year under consideration.

DDD = DDD assigned for the drug according to WHO ATC/DDD system.

P = Total registered outpatients in Medical department

365 = Refers to 365 days in a year.

Results and Discussion

Table 1. Use of sitagliptin and vildagliptin in Medical outpatient clinic of Miri Hospital, year 2016 – 2017 (DDD per 1000 inhabitants per day)

ATC	Drugs	DDD per 1000 inhabitants per day	
		2016	2017
A10BH01	Vildagliptin	0.098	0.262
A10BH02	Sitagliptin	0.555	0.431

Table 2. Summary of total usage of drugs used in treating diabetes and DPP – 4 inhibitor agents in government hospital and private sector of Malaysia, year 2011 – 2014 (DDD per 1000 inhabitants per day) (4)

ATC	Therapeutic Group/Drug	Sector	2011	2012	2013	2014
A10H	Drugs used in diabetes	Public	44.6470	56.5723	62.3295	68.4853
		Private	10.5030	10.6507	11.0561	12.0008
Total			**55.1500**	**67.2230**	**73.3856**	**80.4861**
A10BH	Dipeptidyl peptidase 4 (DPP – 4)	Public	0.0240	0.0367	0.0474	0.0813
		Private	0.3305	0.4105	0.4167	0.4628
Total			**0.3545**	**0.4473**	**0.4642**	**0.5441**
A10BH01	Sitagliptin	Public	0.0235	0.0331	0.0359	0.0555
		Private	0.2601	0.2862	0.2447	0.2354
Total			**0.2836**	**0.3193**	**0.2806**	**0.2909**
A10BH02	Vildagliptin	Public	0.0005	0.0018	0.0046	0.0068
		Private	0.0393	0.0501	0.0431	0.0434
Total			**0.0398**	**0.0519**	**0.0477**	**0.0502**

Based on Malaysia Statistic on Medication (MSOM) data in 2011-2014, consuming oral blood glucose lowering drugs were in increasing trends. The use of the drugs increased by 45.9% from

55.1500 DDD/ 1000 inhabitants/day to 80.4861 DDD/1000 inhabitants/day which indicate more diabetes patients treated with medication (shown in Table 2) (4). Total DPP-4 inhibitors usage had increased by 53.5% over the 4 years, and it mainly contributed by the private sector (shown in Table 2). It wasreported that the usage in government hospital sector was limited due to cost factor (4). The similar issue wasfaced inMiri Hospital in 2016 to 2017, where the overall DPP-4 inhibitors prescribing was very low due to usage restriction.

As presented in the result, there was a drastic increase consumption of vildagliptin by 167.3% from 0.098 DDD/1000 inhabitants/day to 0.262 DDD/1000 inhabitants/day and sitagliptin reduced by 22.3% from 0.555 DDD/1000 inhabitants/day to 0.431 DDD/1000 inhabitants/dayfrom 2016 to 2017. Nonetheless, sitagliptin remained as the preferred prescribed DPP-4 inhibitor in Miri Hospital; DDD per 1000 inhabitants per day of sitagliptin is roughly 5 folds (470%) higher than vildagliptin in 2016 and about 60% higher in 2017. Similar pattern shown in MSOM 2011-2014 (4). This is expected as sitagliptin was the first DPP-4 inhibitor approved for use in Malaysia in June 2007 (5). Although vildagliptin has been licensed for use in Malaysia, it has not yet been approved by the U.S. FDA.

In Miri Hospital, both sitagliptin and vildagliptin reserved for selected patients, mostly in those with moderately to severely impaired renal function. Glycemic control with single oral hypoglycemic agent in this group of patientsis generally tougher and challenging, choices of add on agents are limited as use of certain drugs are contraindicated. Both vitagliptin and sildagliptin are safe to be used in renal failure patient with proper dose adjustment, however, as according to a crossover pilot study (J-VICTORIA study) (6), continuous glucose monitoring showed that mean daily blood glucose, highest blood glucose level after supper and after breakfast were

significantly lower in patients with type 2 diabetes mellitus taking vildagliptin than those taking sitagliptin. The study supports the trend of shifting preference from sitagliptin to vildagliptin in 2017 where overall use of; sitagliptin decreased by 22.3% while vildagliptin increased by 167.3%.

In government hospital sector, cost of a drug frequently become the main concern in doing purchasing after ensuring its effectiveness and safety profile. Thus, attributable to similar safetyprofile of both drugs in severely renal malfunction patient (7),vildagliptin is favoured solely due to its cheaper price (RM 1.68/50mg tablet) as compared to sitagliptin (RM 3.72/100mg tablet, RM 3.78/50mg tablet). This further explain why the use of sitagliptin declined instead over that two years as the price is doubled of what vildagliptin cost when compared in equivalent effective dosage.

Conclusion

As a summary, sitagliptin was more frequently prescribed than vildagliptin. Selection of DPP-4 inhibitors in Miri Hospital is based on the cost as well as the efficacy and safety profile of the drug. While interpreting this finding, there are few limitations that need to be aware of, such as prescribing of both DPP-4 inhibitors in Miri Hospital were restricted due to money constraint, they are generally reserved for patients with renal impairment that require stricter glycemic control and it also depend on the preference of prescriber. Moreover, no proper guideline available in Malaysia on appropriate use of DPP-4 inhibitors. Therefore, a study needs to be done to explore the utilisation pattern of DPP-4 inhibitors in more hospitals in Malaysia.

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