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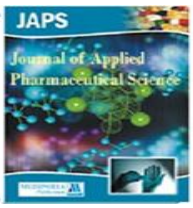

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Medication adherence and achievement of glycaemic targets in ambulatory type 2 diabetic patients

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ABSTRACT

The present study was conducted to determine the prevalence of nonadherence to antidiabetic medications in a Malaysian tertiary hospital and its association with patients' glycaemic outcomes. A cross-sectional study was conducted in the diabetes clinic of a tertiary hospital in Malaysia. Data was collected from patients' medical records and also via personal interviews of type 2 diabetic patients. Of the 405 respondents recruited, 41.7% (95% CI, 36.9-46.4%) did not adhere to their antidiabetic medications. Only employment status of the respondents and the types of diabetic treatment were significantly associated with medication nonadherence. All the respondents were on antidiabetic medications, including 49.9% on insulin but only 17.4% (95% CI, 13.7-21.1%) achieved HbA_{1c} of less than 6.5%. Those who were adherent to their antidiabetic medications were significantly more likely to achieve glycaemic control. Pharmacists should educate diabetic patients on the use of their medications and the importance of medication adherence. Such services will bring the healthcare system a step closer to achieving better clinical outcomes in this group of patients.

Key words: Medication adherence, glycaemic control, HbA_{1c}, type 2 diabetes mellitus.

INTRODUCTION

The prevalence of diabetes is increasing and approximately 171 million people worldwide have diabetes, with 82 millions in the Association of South East Asian Nations (ASEAN) region (WHO, 2009). In Malaysia, a drastic increase in the prevalence of diabetes has been reported, from 8.3% to 14.9% among those aged 30 years and above within a 10-year period (Ministry of Health Malaysia, 2006). Studies have demonstrated that poor glycaemic control resulted in the development of long term complications and was also associated with disease progression, hospitalization, premature disability and mortality (DCCT, 1993; Holman et al., 2008; Pladevall et al., 2004; UKPDS, 1998). A study conducted in Malaysia found that 58% of diabetic patients had neuropathy, 53% retinopathy, 8.6% with cardiovascular diseases, 5.6% stroke and 1.9% amputation (Zaini, 2000). The recommended glycaemic goal is a glycated haemoglobin (HbA_{1c}) of less than 6.5% (Asia-Pacific Type 2 Diabetes Policy Group, 2005; Clinical Practice Guidelines, 2009) although the American Diabetes Association (ADA) recommended less than 7% (ADA, 2008).

Nonadherence to long term treatment of chronic diseases, including diabetes is a global problem, with an average adherence rate of 50% in developed countries and expected to be worst in developing countries (Asefzadeh, et al., 2005; WHO, 2003). A retrospective analysis concluded that the adherence rate to oral antidiabetic agents ranged from 36 to 93% (Cramer, 2004). Adherence to antidiabetic agents was found to be positively associated with a decrease in HbA_{1c} (Pladevall et al., 2004; Schectman et al., 2002). For each 10% increase in adherence, HbA_{1c}

decreased significantly by 0.14 to 0.16% (Pladevall et al., 2004; Schectman et al., 2002). Nonadherence to medications among diabetic patients resulted in poor glycaemic control and hence increased risk of developing chronic complications as well as increased hospitalization and mortality (Kuo et al., 2003; Sokol et al., 2005). Accurate assessment of medication adherence is necessary for effective management of diabetes. However, there is no gold standard for such assessment although various methods have been reported in the literature (Donnan et al., 2002; Hernshaw and Lindenmeyer, 2006; WHO, 2003).

Not many studies on medication adherence among diabetic patients in Malaysia have been documented. Therefore, the present study was conducted to determine the prevalence of nonadherence to antidiabetic medications in a Malaysian tertiary hospital and its association with patients' glycaemic outcomes.

METHODS

A cross sectional study was conducted in the diabetes clinic of a tertiary teaching hospital. Data was collected via personal interviews using a structured questionnaire and also from the patients' medical records. A structured questionnaire was developed and reviewed by a senior pharmacist and an endocrinologist, and tested on 20 patients with type 2 diabetes in a pilot study.

Patients included were those with type 2 diabetes, 18 years old and above and had been on antidiabetic medications for at least 3 months. Patients with severe cognitive impairment, could not understand Bahasa Malaysia, Mandarin or English and those who were too ill to answer questions, were excluded.

During each clinic day, the first patient to be interviewed was randomly selected (using a random table) based on the seating places in the clinic. This was followed by patients who sat on alternate seats. Patient was requested to participate in the study by a researcher and if he/she agreed, the interview was conducted using the structured questionnaire. Information provided by respondents was counter-checked with their medical records. These included antidiabetic medications and other prescribed medications. Presence of comorbidities and clinical outcomes such as HbA_{1c}, fasting blood glucose levels and blood pressure measurements were also obtained from the medical records.

Patients' adherence to antidiabetic medications and the reasons for nonadherence were assessed by direct self-reporting since this was the most practical method with limited time and resources and also an accepted method used in the literature (DiMatteo, 2004; Hernshaw and Lindenmeyer, 2006). This study was approved by the Medical Ethics Committee of the tertiary hospital before commencement of the study.

All data collected were analysed using the Statistical Package for the Social Sciences (SPSS), version 16 software. Associations between two categorical variables were tested using Pearson's chi-square test while Mann-Whitney U test was used for numeric data which did not fulfill the normal distribution. Multiple logistic regression was conducted to determine the predictors of medication nonadherence and also the level of HbA_{1c}. A p value of < 0.05 was considered as statistically significant.

RESULTS AND DISCUSSION

A total of 405 respondents participated in this study. The demographic and clinical characteristics of the respondents are shown in Table 1. There were more female than male respondents in this study which corresponds with the gender proportion reported in the Diabcare-Asia study, conducted in 12 Asian countries (Nitiyanant et al., 2002). The proportion of Indian respondents in this study is higher than that of the population in Malaysia but this corresponds with the higher prevalence of type 2 diabetes among Indians than among the Chinese and Malays (Ministry of Health Malaysia, 2006).

Table 1. Demographic and clinical characteristics of respondents.

Demographic data	Frequency (n = 405, %)	Mean (SD)[#] (Median) [Range]
Gender		
Male	180 (44.4)	
Female	225 (55.6)	
Ethnic		
Malay	153 (37.8)	
Chinese	122 (30.1)	
Indian and others*	130 (32.1)	
Age (years)		
≤ 40	9 (2.2)	60.3 (10.3)
41 – 64	275 (67.9)	(60.0)
≥ 65	121 (29.9)	[25 – 93]
Educational level		
None or Primary school	106 (26.1)	
Secondary school	216 (53.3)	
College/University	83 (20.5)	
Income group		
No income	218 (53.8)	
< RM3000	134 (33.1)	
RM3000 – 5000	36 (8.9)	
> RM5000	17 (4.2)	
Employment status		
Not working	300 (74.1)	
Working	105 (25.9)	
Diabetes duration (years)		
1-5	103 (25.8)	
6-10	89 (22.3)	13.2 (8.9)
11-15	65 (16.3)	(11.0)
16-20	58 (14.5)	[1 – 44]
> 20	84 (21.1)	
No. of prescribed medications		
1 – 5	168 (41.5)	6.0 (2.1)
6 – 10	229 (56.5)	(6.0)
> 10	8 (2.0)	[1 – 13]
Types of Antidiabetic agents used		
Oral antidiabetic agent(s)	203 (50.1)	
Insulin(s)	83 (20.5)	
Oral antidiabetic agent(s) + Insulin(s)	119 (29.4)	
HbA_{1c} (%), n = 397		
< 6.5	69 (17.4)	8.2 (2.0)
< 7.0	120 (30.2)	(7.7)
< 7.5	171 (43.1)	[4.4 – 15.7%]
≥ 7.5	226 (56.9)	

Fasting glucose levels (mmol/L), n = 398			8.5 (3.7) (7.6) [2.3 – 23.7]
Adequate	(≤ 6.1)**	107 (26.9)	
Inadequate	(> 6.1)	291 (73.1)	
SBP:	**≤ 130 mmHg**, n = 398**	198 (49.7%)	138.3 (18.5) (132.0) [100 – 240]
DBP:	**≤ 80 mmHg**, n = 398**	305 (76.6%)	80.3 (9.2) (80.0) [50.0 – 120.0]
TC:	**≤ 4.5 mmol/L**, n = 399**	196 (49.1%)	4.8 (1.2) (4.6) [1.3 – 10.5]
TG:	**≤ 1.5mmol/L**, n = 395**	214 (54.2%)	1.8 (1.3) (1.5) [0.40 – 14.4]

*One respondent of Punjabi origin is included under "Indian and others"
**Clinical Practice Guidelines, 2009
#SD = Standard deviation

A majority of the respondents (76.4%) were on more than one antidiabetic agent with 49.9% of the respondents being on insulin. Metformin was the most commonly used antidiabetic agent (68.6% of the respondents), followed by gliclazide (42.5%). Although all the respondents were on antidiabetic medications, only 17.4% (95% CI, 13.7-21.1%) and 26.9% (95% CI, 22.6-31.2%) achieved the target HbA_{1c} < 6.5% and fasting blood glucose level of ≤ 6.1 mmol/L, respectively. Whether the target HbA_{1c} is taken as below 7.0 or 6.5%, previous studies in Malaysia reported lower proportion of patients achieving these targets than the present study (22 to 27 versus 30.2% and 13 versus 17.4%, respectively) [Eid et al., 2003; Nitiyanant et al., 2002]. The average HbA_{1c} and fasting blood glucose in the Diabcare-Asia Study (Nitiyanant et al., 2002) were also higher than the present study, with 8.5(2.0) versus 8.2(2.0)% and 8.9(3.4) versus 8.5(3.7) mmol/L, respectively. A recent study in another tertiary hospital in Malaysia reported a very similar average HbA_{1c} of 8.20(3.4)% [Goldhaber-Fiebert et al., 2010]. However, glycaemic control in the present study is still suboptimal and this calls for more aggressive management of these patients. A total of 161 respondents (39.8%) reported experiencing side effects attributed to their antidiabetic medications. These included feeling bloated (11.4% of the respondents), weight gain (5.7%), belching (4.7%), nausea and vomiting (4.4%), skin irritation (4.2%), extreme hunger (2.5%), diarrhoea (2.2%), constipation (2.2%), tremor (1.7%), tiredness (1.7%), headache (1.7%) and dizziness (1.5%). These were mainly gastrointestinal disturbances but signs and symptoms of hypoglycaemia were also noted. Patients should be warned of such problems and also advised on action to be taken. Only 59% of the respondents knew the name of their antidiabetic medications while 29.9% knew only the description and 11.1% did not know at all. This shows that the respondents were not very familiar with their antidiabetic medications. Therefore, healthcare providers should play a more active role in educating diabetic patients about their disease conditions and medications.

Nonadherence to antidiabetic medications

Of the 405 respondents, 169 or 41.7% (95% CI, 36.9-46.4%) did not adhere to their antidiabetic medications. This is similar to that reported in the literature (Asefzadeh et al, 2005; Cramer, 2004; WHO, 2003) and implies that nonadherence to medications is also a significant problem among patients with chronic diseases in Malaysia. Reasons for not adhering to antidiabetic therapies were: forgetfulness (27.2% of the respondents), inconvenient (6.7%), did not bring the medication (4.9%), no more supply (4.4%), side effects (3.2%), busy (3.0%) and did not feel any difference to his/her health (1.5%). Most of the respondents missed their antidiabetic medications due to forgetfulness which is similar to that reported by other authors (Asefzadeh et al, 2005).

Initial bivariate analysis showed that younger respondents, those with higher income, currently working, those who reported side effects and on combinations of oral antidiabetic agents and insulin, were less likely to adhere to their antidiabetic medications ($p < 0.05$). However, multiple logistic regression found that only employment status and the types of diabetic treatment were associated with nonadherence to antidiabetic medications (Table 2).

Table 2. Factors associated with nonadherence to medications, using multivariate analysis.

Factors associated with nonadherence	Total no. of respondents	Nonadherence (%)	Adjusted p value	Adjusted OR (95% CI)
Antidiabetic medications	203	36.0		
Oral	119	58.8	<0.001*	3.0 (1.8 – 5.0)
Oral + Insulin	83	31.3		
Insulin	119	58.8	<0.001*	
Oral + Insulin				3.1 (1.7 - 5.7)
Currently employed	300	36.3		
Yes	105	57.1	<0.001*	2.4 (1.5 – 3.9)
No				

* Statistically significant at $p < 0.01$
** Statistically significant at $p < 0.05$

This is probably because patients who are still working are usually very busy and tend to forget to take their medications, or are more likely to be away from home and hence may not be convenient for them to take their medications. Combination therapy of insulin and oral antidiabetic agents was found to be significantly associated with lower medication adherence. Other studies also reported similar problems (Cramer, 2004). The different routes of administration may be inconvenient, confusing and thus the respondents tend to miss their medications.

Initial bivariate analysis found that respondents with longer duration of diabetes, on both oral antidiabetic medications(s) and insulin, were not using complementary medicines as well as non-adherent to their antidiabetic medications, were less likely to achieve glycaemic target ($p< 0.05$). The same factors were retained using multiple logistic regression (Table 3). The odds of those who adhered to their antidiabetic medications achieving glycaemic target was 2.0 times more than those who did not. Consequently, respondents who did not adhere to their antidiabetic medications had significantly higher HbA_{1c}

values as well as fasting blood glucose levels than those who adhered (median of 8.38 versus 7.38%, Z = -4.667 and p < 0.001; and median of 8.00 versus 7.20 mmol/L, Z = -3.431 and p = 0.001, respectively).

Table 3. Factors associated with glycaemic control (defined as HbA_{1c} < 6.5%), using multivariate analysis

Factors associated with glycaemic control	Tota1 no. of respondents	HbA_{1c} < 6.5% (%)	Adjusted p value	Adjusted OR (95% CI)
Antidiabetic medications				
Oral	199	28.1	<0.001*	14.8
Oral + Insulin	117	1.7		(3.5 – 63.2)
Insulin	81	13.6	0.001	9.0
Oral + Insulin	117	1.7		(1.9 - 42.0)
Duration of diabetes				
≤ 10 years	187	25.1		2.3
> 10 years	204	10.8	0.009*	(1.2 – 4.3)
Use of complementary medicines				
No	184	10.9		0.4
Yes	213	23.0	0.004*	(0.2 – 0.8)
Adherence to antidiabetic medications	231	21.6		2.0
Yes	166	11.4	0.035**	(1.1 – 3.7)
No				

* Statistically significant at p < 0.01
** Statistically significant at p < 0.05

The study showed that adherence to antidiabetic medications was associated with better glycaemic control. This finding is consistent with that of other studies (Pladevall et al., 2004; Schectman et al., 2002). Therefore, pharmacists should work in collaboration with other healthcare professionals to counsel patients on the use and importance of their medications and to promote better medication adherence.

The main limitation of the present study was that data was collected from only one hospital and hence may not be representative of all diabetic patients in Malaysia. In addition, direct self-reporting used in this study often results in underestimation of nonadherence to medications. However, the results obtained are comparable to that of other studies.

CONCLUSION

The present study found that 41.7% (95% CI, 36.9-46.4%) of the respondents did not adhere to their antidiabetic medications, mainly due to forgetfulness. Despite the use of multiple antidiabetic medications (both oral and insulin), only 17.4% (95% CI, 13.7-21.1%) of the respondents managed to achieve HbA_{1c} < 6.5%. In addition, those who were adherent to their antidiabetic medications were more likely to achieve glycaemic control. Therefore, pharmacists should educate diabetic patients on the use of their medications and the importance of medication adherence. Further studies to investigate the effects of pharmaceutical care on diabetic patients in developing countries such as Malaysia, may bring the healthcare system a step closer to achieving better clinical outcomes in this group of patients.

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Conflict of interests

The authors declare that they have no conflicts of interest to disclose.

REFERENCES

American Diabetes Association (ADA). Standards of medical care in diabetes - 2008. Diabetes Care 2008; 31: S12 – S54.

Asefzadeh S, Asefzadeh M, Javadi H. Care management: adherence to therapies among patients at Bu-Alicina Clinic, Qazvin, Iran. J Res Med Sci 2005; 10: 343-348.

Asia-Pacific Type 2 Diabetes Policy Group and International Diabetes Federation, Western Pacific Region (IDF-WPR). Type 2 Diabetes: Practical Targets and Treatment, 4th edn. Melbourne: International Diabetes Institute (IDI); 2005.

Clinical Practice Guidelines: Management of Type 2 Diabetes Mellitus, 4th edn. Kuala Lumpur: Malaysian Endocrine and Metabolic Society, Ministry of Health Malaysia, Academy of Medicine Malaysia, Persatuan Diabetes Malaysia, 2009: MOH/P/PAK/184.09(GU)

Cramer JA. A systematic review of adherence with medications for diabetes. Diabetes Care 2004; 27: 1218-1224.

DCCT (The Diabetes Control and Complications Trial) Research Group. The effects of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med 1993; 329: 977-986.

DiMatteo MR. Variations in patients' adherence to medical recommendations: a quantitative review of 50 years of research. Med Care 2004; 42: 200-209.

Donnan PT, MacDonald TM, Morris AD. Adherence to prescribed oral hypoglycemic medication in a population of patients with type 2 diabetes: a retrospective cohort study. Diabet Med 2002; 19: 279-284.

Eid M, Mafauzy M, Faridah AR. Glycaemic control of type 2 diabetic patients on follow up at Hospital Universiti Sains Malaysia. Msian J Med Sc 2003; 10: 40-49.

Goldhaber-Fiebert JD, Li H, Ratanawijitrasin S, Vidyasagar S, Wang XY, Aljunid S et al. Inpatient treatment of diabetic patients in Asia: evidence from India, China, Thailand and Malaysia. Diabet Med 2010; 27: 101-108.

Hernshaw H, Lindenmeyer A. What do we mean by adherence to treatment and advice for living with diabetes? A review of the literature on definitions and measurements. Diabet Med 2006; 23: 720-728.

Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA. 10-year follow-up of intensive glucose control in type 2 diabetes. N Engl J Med 2008; 359: 1577-1589.

Kuo Y-F, Raji MA, Markides KS, Ray LA, Espino DV, Goodwin JS. Inconsistent use of diabetes medications, diabetes

complications, and mortality in older Mexican American over a 7-year period. Diabetes Care 2003; 26: 3054-3060.

Ministry of Health Malaysia. The Third National Health and Morbidity Survey (NHMS). Kuala Lumpur: Ministry of Health Malaysia, 2006. Available at http://www.nih.gov.my/NHMS Last accessed 9 June 2010.

Nitiyanant W, Tandhanand S, Mahtab H, Zhu XX, Pan CY, Raheja BS et al. The Diabcare-Asia* 1998 study - outcomes on control and complications in type 1 and type 2 diabetic patients. Curr Med Res Opin 2002; 18: 317-327.

Pladevall M, Williams LK, Potts LA, Divine G, Xi H, Lafata JE. Clinical outcomes and adherence to medications measured by claims data in patients with diabetes. Diabetes Care 2004; 27: 2800-2805.

Schectman JM, Nadkarni MM, Voss JD. The association between diabetes metabolic control and drug adherence in an Indigent population. Diabetes Care 2002; 25: 1015-1021.

Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS. Impact of medication adherence on hospitalization risk and healthcare cost. Med Care 2005; 43: 521-530.

UKPDS (UK Prospective Diabetes Study) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patient with type 2 diabetes: UKPDS 33. Lancet 1998; 352: 837-853.

WHO. Adherence to long term therapies: evidence for action. World Health Organization, 2003. Available at http://apps.who.int/ medicinedocs/pdf/s4883e/s4883e.pdf Last accessed 21 December 2009.

WHO. Diabetes programme: country and regional data. World Health Organization, 2009. Available at http://www.who.int/ diabetes/ facts/world_figures/en/ Last accessed 21 December 2009.

Zaini A. Where is Malaysia in the midst of the Asian epidemic of diabetes mellitus? Diabetes Res Clin Pract 2000; 50: S23-S28.