

Type 2 diabetes mellitus with hypertension at primary healthcare level in Malaysia: are they managed according to guidelines?

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ABSTRACT

Introduction: A study was conducted at primary healthcare level in the Melaka Tengah district of Malaysia to determine whether hypertension in patients with type 2 diabetes mellitus were managed according to guidelines.

Methods: A cross-sectional study involving 517 patients with diabetes mellitus from August to October 2003 was performed.

Results: All the subjects had type 2 diabetes mellitus. 350 (67.7 percent) patients had hypertension and about 25.7 percent of them were associated with microalbuminuria. The Malay ethnic group form the majority (54.6 percent), followed by Chinese (37.7 percent) and Indian (7.4 percent). Only 11 (3.1 percent) patients with type 2 diabetes mellitus and hypertension achieved the target blood pressure of less than 130/80 mmHg. For those who had not achieved the target goal, 39.5 percent of them were not on any antihypertensive drugs. 38.6 percent were on monotherapy and only 21.8 percent were on two or more antihypertensive drugs. Metoprolol was the most commonly used antihypertensive drug (22.4 percent), followed by Nifedipine (16.2 percent) and Prazosin (13.5 percent). Only 18.3 percent of patients with type 2 diabetes mellitus and hypertension were prescribed with angiotensin converting enzyme (ACE) inhibitors and 0.3 percent with angiotensin receptor blockers. For patients with type 2 diabetes mellitus, hypertension and microalbuminuria, only 14.1 percent of them were prescribed with ACE inhibitors.

Conclusion: A significant proportion of patients with type 2 diabetes mellitus had associated hypertension but they were not managed optimally according to guidelines. More intensive management of hypertension among patients with diabetes is essential to reduce the morbidity and mortality at primary healthcare level.

Keywords: clinical practice guidelines, diabetes mellitus, hypertension, primary healthcare

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INTRODUCTION

Hypertension (defined as a blood pressure (BP) $\geq 140/90$ mmHg) is an extremely common comorbid condition in diabetes mellitus, affecting about 20% – 60% of patients with diabetes⁽¹⁾. In Malaysia, about 10.7% patients with diabetes mellitus are associated with hypertension⁽²⁾. Hypertension substantially increases the risk of both macrovascular and microvascular complications in diabetes mellitus. People with both diabetes mellitus and hypertension have approximately twice the risk of cardiovascular disease⁽¹⁾, and five to six fold greater risk of developing end-stage renal disease, compared to nondiabetic people with hypertension⁽³⁾.

Studies show that glucose control is effective in reducing microvascular end-points but to date, only intermediate outcomes have been shown to be reduced⁽⁴⁾. In actual fact, “tight” hypertension control appears to be more effective than glycaemic control in reducing microvascular events^(5,6). To achieve optimal BP level in diabetes mellitus often requires a combination of two or more antihypertensive medications^(5,7). Some patients will not achieve aggressive goals, even while taking three or four different antihypertensive agents⁽⁸⁾. With regard to choice of antihypertensive drugs, thiazide diuretics, angiotensin converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) may be the preferred first-line agents for treatment of hypertension in diabetes mellitus⁽⁸⁾.

Malaysian clinical practice guidelines (CPGs) on the management of hypertension⁽⁹⁾ was developed based mainly on evidence-based reports and reviews, especially the sixth report of the Joint National Committee on high blood pressure, and World Health Organisation – International Society of Hypertension Guidelines 1999. The guidelines recommend that pharmacological treatment should be initiated if the BP is persistently ≥ 130 mmHg systolic and / or

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≥ 85 mmHg diastolic among patients with diabetes mellitus. The systolic BP should be targeted to < 130 mmHg and diastolic BP < 80 mmHg. ACE inhibitors and ARBs are the agents of choice for diabetes mellitus with hypertension, according to the practice guidelines.

The primary healthcare doctors in Malaysia could prescribe ACE inhibitors such as tablet Captopril (Pharmaniaga Ltd, Bangi, Selangor, Malaysia) and tablet Enalapril (Ranbaxy Pte Ltd, Sg Petani, Kedah, Malaysia). However, ARBs could only be initiated by medical specialists in hospitals and continued in health clinics with referral letters on discharge. CPGs on hypertension management are available in all the health clinics in the Melaka Tengah district. The availability of practice guidelines raises an important question: are these guidelines followed by the primary care doctors, especially in terms of achieving optimal blood pressure goals (BP $< 130/80$ mmHg) and using appropriate agents of choice (ACE inhibitors, ARBs)? This is a matter of great interest and importance, and these are the issues addressed in this study.

METHODS

This was a cross-sectional study conducted in the Melaka Tengah district in Melaka, state of Malaysia, from August to October 2003. Melaka Tengah district is one of the districts in the Melaka state. There are 11 government health clinics providing primary healthcare, including diabetes and hypertension treatment, in the district and all of them were involved in this study. There are a few primary care doctors with basic medical degrees in each health clinic. Systematic sampling was done, i.e. every fifth registered patient with diabetes mellitus who came for follow-up would be selected for this survey. These patients should be Malaysian citizens and had been diagnosed and were on treatment for diabetes mellitus for at least 12 months. Patients who were newly diagnosed, defaulted treatment for more than six months, critically ill, had mental health problems or difficulty in communication were excluded. After the doctor had seen the selected patient, a trained medical assistant would use a data collection form to gather data from the patient's medical record. Data included demographical characteristics, duration of having diabetes mellitus, last blood pressure measurement, latest microalbuminuria results, and type of antihypertensive drugs used.

The standard mercury sphygmomanometer (Accoson Works, London, England) was used with an appropriately-sized cuff on the right arm of the patient who was adequately rested for at least five minutes and seated with the arm supported at his/her heart level. The systolic BP (Korotkoff phase 1)

and diastolic BP (Korotkoff phase 5) were recorded. In this study, hypertension was taken as systolic BP of 140 mmHg or greater and/or diastolic BP of 90 mmHg or greater, or the taking of antihypertensive medication⁽⁹⁾. The patients had an average of at least two readings taken two minutes apart, and the reading was rounded to 2 mmHg. Initial elevated blood pressure readings would be confirmed on at least two subsequent visits over one week or more. Patients with suspected white-coat hypertension would be referred for ambulatory blood pressure monitoring.

Microalbuminuria was semiquantitatively detected by using CLINITEK[®] 50 urine analyser (Bayer Corporation, Pittsburgh, PA, USA). The patient would be considered to have microalbuminuria with two separate positive results, after excluding other causes, e.g. urinary tract infection. Microalbuminuria is indicated at a ratio result of 30 - 300 mg/g (3.4 - 33.9 mg/mmol) and clinical albuminuria (macroalbuminuria) at a ratio result of > 300 mg/g (> 33.9 mg/mmol). Statistical Package for the Social Sciences (SPSS) software version 11.0 (Chicago, IL, USA) was used for data analysis. The association between ethnicity, age group, number of antihypertensive drugs and mean blood pressure were analysed with One-way Analysis of Variance (ANOVA).

RESULTS

A total of 517 patients with diabetes mellitus from various ethnic groups were enrolled in this study. All of them had type 2 diabetes mellitus, and four of them were on an adjunctive insulin regime. There were 350 patients with type 2 diabetes mellitus (67.7%) associated with hypertension. The Malay ethnic group formed over one-half of patients with diabetes mellitus and hypertension i.e. 191 (54.6%), while Chinese and Indian ethnic groups contributed 132 (37.7%) and 26 (7.4%), respectively. This distribution of ethnicity of this study was quite representative of the total registered diabetic patients in the Melaka Tengah district in year 2003, in which 53.6% of the registered diabetic population were Malay, 36.0% were Chinese and 9.0% were Indian⁽¹⁰⁾. The mean age of the patients was 59.0 years (range 24 to 91 years, standard deviation [SD] = 10.4 years); 219 (62.2%) patients were female. The mean duration of having diabetes mellitus was 7.1 years (range 1 to 31 years, SD = 6 years). Table I summarises patients' demographical characteristics in the Melaka Tengah district.

Based on Malaysian practice guidelines, only 11 (3.1%) of patients with type 2 diabetes mellitus and hypertension had achieved the target blood pressure of $< 130/80$ mmHg, with mean blood pressure (\pm SD) of $112.9/66.0 \pm 10.3/4.4$ mmHg. Table II illustrates

Table I. Demographical characteristics of patients with type 2 diabetes mellitus and hypertension (n=350).

| Characteristics | | Malay (n=191) | Chinese (n=132) | Indian (n=26) | Others (n=1) |
|--|--------|---------------|-----------------|---------------|--------------|
| Age (in years) | Mean | 56.7 | 62.7 | 57.3 | 76.0 |
| | SD | 10.4 | 9.1 | 10.5 | – |
| Gender | Male | 69 (36.1%) | 52 (39.4%) | 9 (34.6%) | 1 (100%) |
| | Female | 122 (63.9%) | 80 (60.6%) | 17 (65.4%) | – |
| Duration of diabetes (in years) | Mean | 6.3 | 8.5 | 8.3 | 12 |
| | SD | 5.8 | 6.1 | 5.8 | – |

SD: standard deviation

Table II. Blood pressure among patients with type 2 diabetes mellitus who had not achieved the target goal (n=339).

| Age group (in years) | | Systolic blood pressure (mmHg) | Diastolic blood pressure (mmHg) |
|----------------------|-------|--------------------------------|---------------------------------|
| 20 - 29 (n=1) | Mean | 100.0 | 80.0 |
| | SD | – | – |
| | Range | 100 | 80 |
| 30 - 39 (n=9) | Mean | 137.1 | 91.6 |
| | SD | 8.4 | 3.4 |
| | Range | 130 - 150 | 90 - 100 |
| 40 - 49 (n=53) | Mean | 139.6 | 86.6 |
| | SD | 12.8 | 5.9 |
| | Range | 110 - 180 | 80 - 100 |
| 50 - 59 (n=101) | Mean | 142.1 | 85.7 |
| | SD | 13.6 | 7.9 |
| | Range | 110 - 200 | 60 - 100 |
| 60 - 69 (n=121) | Mean | 145.5 | 84.4 |
| | SD | 15.1 | 7.9 |
| | Range | 100 - 180 | 60 - 100 |
| 70 - 79 (n=47) | Mean | 144.3 | 83.2 |
| | SD | 15.4 | 7.2 |
| | Range | 100 - 180 | 60 - 100 |
| 80 and above (n=7) | Mean | 152.3 | 80.6 |
| | SD | 21.5 | 6.8 |
| | Range | 130 - 196 | 70 - 90 |
| Total (n=339) | Mean | 143.2 | 85.1 |
| | SD | 14.7 | 7.6 |
| | Range | 100 - 200 | 60 - 100 |

SD: standard deviation

the blood pressure of patients who had not achieved the target goal. Of the patients who had not achieved the target blood pressure (i.e BP \geq 130/80 mmHg), 134 (39.5%) of them were not on any antihypertensive drugs. For the rest who were on antihypertensive medications, 131 (38.6%) of them were on monotherapy and 63 (18.6%), 10 (2.9%), and one (0.3%) respectively received two, three and four antihypertensive agents. In addition, the mean systolic BP among treated patients aged 60 years and above was 144.9 ± 16.4 mmHg, which appeared to be higher than treated patients with age less than

60 years (139.1 ± 14.3 mmHg). This difference was significant statistically ($p < 0.01$). In those who achieved the target blood pressure, the average number of different antihypertensive medications prescribed was 1.3 compared with patients who had not achieved the target goal (1.4). Nevertheless, the difference was not significant statistically ($p > 0.05$).

With regard to the choice of antihypertensive agents, tablet Metoprolol (Pharmaniaga Ltd, Bangi, Selangor, Malaysia) was the most commonly used antihypertensive drug (22.4%), followed by short acting Nifedipine (Medochemie Ltd, Limassol, Cyprus,

Table III. Use of ACE inhibitors and ARBs in type 2 diabetes mellitus.

| Patients | ACE inhibitors | ARBs |
|---|----------------|------|
| Type 2 diabetes with hypertension (n=350) | 18.3% | 0.3% |
| Type 2 diabetes with hypertension and microalbuminuria (n=90) | 14.0% | 0% |

ACE: angiotensin converting enzyme

ARBs: angiotensin II receptor blockers

Europe) (16.2%) and Prazosin (Pharmaniaga Ltd, Bangi, Selangor, Malaysia) (13.5%). In the patients with type 2 diabetes mellitus, about 24% had microalbuminuria. The prevalence of microalbuminuria was even higher (25.7%) among the patients with both diabetes and hypertension. Table III illustrates the use of ACE inhibitors (Captopril and Enalapril) and ARBs i.e. Losartan (Merck Sharp & Dohme Ltd, Cramington, England) in type 2 diabetes mellitus.

DISCUSSION

The prevalence of hypertension in patients with diabetes in this clinic-based study was 67.7%, which was comparable to studies elsewhere (20%-60%)⁽¹⁾. However, the prevalence was higher if compared with the Malaysian national survey (10.7%)⁽²⁾. This could be due to the different setting and methodology of the studies. The national survey was population-based and was done in 1996, whereas the subjects in this study were confined to the current diabetic population in government health clinics. There was 100% type 2 diabetes mellitus in this study although the prevalence of type 2 diabetes mellitus in Malaysia was estimated to be about 95%⁽¹¹⁾. The reason could be due to the government hospitals which traditionally treat the bulk of patients with type 1 diabetes mellitus, especially adolescents and children.

Despite the enormous evidence indicating the benefits of treatment of diabetes mellitus and hypertension, some studies showed that only a very small percentage of patients were optimally managed^(12,13). Similar results were observed in this local study in which the target blood pressure was not achieved in the vast majority (96.9%) of patients with type 2 diabetes mellitus and hypertension. The poor control of hypertension may result from the inadequate use of antihypertensive agents. This was evidenced by the average number of antihypertensive drugs used, which was only 1.4 for those who had not achieved target BP in this study. A review of clinical trials indicates that more than 65% of people with diabetes mellitus and hypertension will require two or more different antihypertensive medications to achieve the target blood pressure of <130/80 mmHg⁽¹⁴⁾.

Moreover, the misconception that an elevation of systolic BP accompanying old age as a normal process may be another contributing factor for the poor result of BP control in this study. The mean systolic BP of the older patients (more than 60 years) in this study, though on medication, appeared to be higher compared with that of the younger group. It has been recommended that the treatment for older individuals with hypertension should follow the same principles outlined for the general care of hypertension⁽⁹⁾. Furthermore, data from the Cardiovascular Health Study suggest that the undertreatment of a systolic BP of 140 mmHg or higher may be the responsible for 22% of myocardial infarction and 34% of stroke in older adults⁽¹⁵⁾.

Besides reducing cardiovascular diseases and stroke incidence in patients with diabetes mellitus, both ACE inhibitors and ARBs can affect the progression of diabetic nephropathy and reduce albuminuria^(16,17). However, both ACE inhibitors and ARBs were not commonly prescribed to patients with diabetes compared with calcium channel blockers and β -blockers in this study. Evidence from recent trials has tended to extend the indications for ACE inhibitors, and limit or reduce the indications for calcium channel blockers and β -blockers in treating hypertension. This is because there is a higher risk of congestive heart failure and major cardiovascular events in the β -blocker group than in the diuretic group, based on the ALLHAT report⁽¹⁶⁾. Calcium channel blockers were associated with higher risks of myocardial infarction and heart failure in a meta-analysis of randomised controlled trials⁽¹⁸⁾ and many commentators now regard calcium channel blockers as second- or third-line agents, although they are still commonly used⁽¹⁹⁾.

It is clear from this study, that the management of patients with type 2 diabetes mellitus and hypertension was not optimal in the primary healthcare clinics. Although the patient-specific factors are often faulted for affecting the successful management of hypertension, such as lack of adherence to therapy, limited access to care, financial barriers and lack of knowledge about the seriousness of uncontrolled hypertension^(20,21), the physicians impose barriers that

need to be recognised. Some physicians may lack awareness and familiarity about CPGs. Cabana et al⁽²²⁾ reported that for 78% of the available guidelines, more than 10% of physicians were not aware of their existence. Even though some physicians are familiar with the guidelines for treating hypertension, they do not implement this knowledge into their everyday practice. This attitude was observed by a study conducted by Oliveria et al in which the physicians were aware of guidelines but did not treat hypertension more aggressively. They would only recommend pharmacological treatment when the patient's lowest systolic BP was 150 mmHg⁽²³⁾.

In another study where the hypertensive patients were regular users of healthcare that is free or available for a small co-payment, the physicians frequently failed to increase dosage of antihypertensive medications or to try new treatments in patients with elevated BP⁽²⁴⁾. There were several limitations to this study. The control of BP may be affected by the patients' adherence, life style and other risk factors, and the results of this study may not represent other districts or states of Malaysia.

In conclusion, a significant proportion of patients who had type 2 diabetes mellitus associated with hypertension were not managed optimally according to guidelines. Remedial measures should be taken to increase the adherence to practice guidelines, and improve both primary care doctors' and patients' knowledge of diabetes mellitus. Auditing the diabetic management in primary healthcare should be done regularly by senior doctors or family medicine specialists. These steps are essential in order to reduce the cardiovascular and end-stage renal diseases, as well as the associated morbidity and mortality among patients with type 2 diabetes mellitus.

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