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Original Article

PRESCRIBING OF ANTIHYPERTENSIVE AGENTS IN PUBLIC PRIMARY CARE CLINICS – IS IT IN ACCORDANCE WITH CURRENT EVIDENCE?

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Conflict of interest: None

ABSTRACT

Background: Large population surveys in Malaysia have consistently shown minimal improvement of blood pressure control rates over the last 10 years. Poor adherence to antihypertensive medication has been recognized as a major reason for poor control of hypertension. This study aimed to describe the prescribing pattern of antihypertensive agents in 2 public primary care clinics and assess its appropriateness in relation to current evidence and guidelines.

Methods: A cross-sectional survey to describe the prescribing pattern of antihypertensive agents was carried out in 2 public primary care clinics in Selangor from May to June 2009. Hypertensive patients on pharmacological treatment for ≥1 year who attended the clinics within the study period of 7 weeks were selected. Appropriate use of antihypertensive agents was defined based on current evidence and the recommendations by the Malaysian Clinical Practice Guidelines (CPG) on the Management of Hypertension, 2008. Data were obtained from patients' medical records and were analysed using the SPSS software version 16.0.

Results: A total of 400 hypertensive patients on treatment were included. Mean age was 59.5 years (SD ±10.9, range 28 to 91 years), of which 52.8% were females and 47.2% were males. With regards to pharmacotherapy, 45.7% were on monotherapy, 43.3% were on 2 agents and 11.0% were on ≥3 agents. Target blood pressure of <140/90mmHg was achieved in 51.4% of patients on monotherapy, and 33.2% of patients on combination of ≥2 agents. The commonest monotherapy agents being prescribed were β-blockers (atenolol or propranolol), followed by the short-acting calcium channel blocker (nifedipine). The commonest combination of 2-drug therapy prescribed was β-blockers and short-acting calcium channel blocker.

Conclusion: This study shows that the prescribing pattern of antihypertensive agents in the 2 primary care clinics was not in accordance with current evidence and guidelines. β-blockers and short-acting preparations were commonly used both as monotherapy and combination treatment. Thiazide diuretics, ACE inhibitors and long acting calcium channel blockers were underutilised in this study, despite robust evidence to support their use. Evidence have also shown that simplifying the number of daily doses is effective in improving adherence, therefore a wider use of generic once daily preparation should be strongly advocated in public primary care clinics.

Keywords: Evidence-based, guideline, hypertension, prescribing, primary care.

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INTRODUCTION

Hypertension was estimated to affect 972 million adults worldwide, with 66% of those affected were from low and middle income countries.[1] The overall burden of hypertension-related diseases is rapidly rising in the developing world as a consequence of the aging population and increasing urbanisation.[2] Malaysia is experiencing similar epidemiological transition as the national prevalence of hypertension among adults ≥30 years in the year 2006 stood at 43%, a staggering 30% increase from that of 10 years earlier.[3] Almost two thirds were unaware that they have hypertension, and although the

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treatment rate has slightly increased, only 26% achieved the target blood pressure.[3]

While therapeutic lifestyle changes remain as first-line therapy for all patients with hypertension, the majority would eventually require antihypertensive therapy in order to achieve control targets. An ideal antihypertensive agent should be efficacious in terms of lowering blood pressure and preventing complications, tolerable, affordable and simple to use. Ample selections of antihypertensive agents are currently available in the public primary care setting. However, adherence to antihypertensive agents is estimated between 50% to 70%,[4,5] and lack of adherence has been recognized as being a major factor of poor control.[6] A World Health Organization (WHO) report has called for actions to improve adherence to long-term therapies.[7]

Evidence-based hypertension guidelines are now widely available, and this include the recently updated Malaysian Clinical Practice Guidelines (CPG) on the Management of Hypertension, 2008.[8] Although evidence-based practice has previously been thought to not necessarily lower the cost of healthcare, recent evidence suggested that adherence to evidence-based prescribing guidelines for hypertension would result in substantial savings in prescription costs.[9]

Despite the availability of clinical guidelines and effective drugs, hypertension control in the community is far from optimal. Published evidence have shown that only 50% of physicians complied with guideline recommendations.[10] In Malaysia, several cross-sectional surveys and clinical audits on hypertension management conducted in primary care have consistently demonstrated suboptimal management and poor control.[11-13]

The objective of this study was to describe the prescribing pattern of antihypertensive agents in the 2 public primary care clinics and its appropriateness in relation to current evidence and recommendations made by clinical practice guidelines.

METHODS

A cross-sectional survey to describe the prescribing pattern of antihypertensive agents in 2 public primary care clinics in Selangor was carried out in 7 weeks period from May to June 2009. These 2 clinics were teaching sites for medical students and both were located in urban areas. This study was conducted in collaboration with the local district health office, as an effort to improve antihypertensive prescribing in both primary care clinics.

10% of hypertensive patients who had been followed up in each clinic for 1 year were selected for this study. Medical records were systematically selected using registry number which ended with number 1, 3, 6, and 8 to give a balanced male: female ratio. Patients with co-existing diabetes mellitus were excluded as similar study on the management of diabetes has been conducted. Appropriate use of antihypertensive agents was defined based on current evidence appraised by the Malaysian CPG on the Management of Hypertension, 2008.

Data were obtained from patients' medical records and prescription scripts with regards to the types of antihypertensive agents used as monotherapy and combination treatments. SPSS software version 16.0 was used to analyse the data.

RESULTS

A total of 400 hypertensive patients on treatment (20% from the total hypertensive patients who attended the 2 health clinics over 7 weeks) were included in this study. Table 1 shows the demographic characteristics of the study sample. The mean age was 59.5 years (SD ±10.9, range 28 to 91 years).

Table 1: Demographic characteristics of the subjects (n=400)

Characteristics	Number (%)
Gender	
Male	189 (47.2%)
Female	211 (52.8%)
Ethnic groups	
Malays	199 (49.8%)
Chinese	160 (40.0%)
Indians	40 (10.0%)
Others	1 (0.2%)

With regards to pharmacotherapy, 183 patients (45.7%) were on monotherapy, 173 patients (43.3%) were on 2 antihypertensive agents and 44 patients (11.0%) were on 3 or more agents. Blood pressure target was achieved in 94 patients (51.4%) on monotheraphy and 72 patients (33.2%) on combination of ≥2 agents.

The commonest monotherapy agents being prescribed were β-blockers (atenolol and propranolol), followed by the short-acting calcium channel blocker (nifedipine) (Figure 1).

The top 3 commonest combinations of 2-drug therapy prescribed were β-blockers (atenolol and propranolol) and short-acting calcium channel blocker (nifedipine), diuretics and short-acting calcium channel blocker, followed by diuretics and β-blockers; comprising 56.3% of the total number of 2-drug therapy prescriptions.

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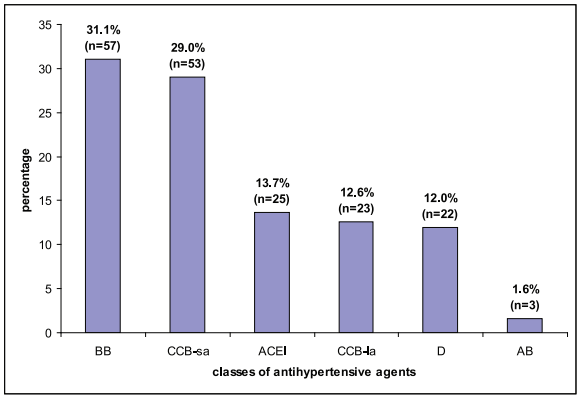
Figure 1: Frequency distributions of various antihypertensive agents used as monotherapy (n=183)



AB=±-blockers; D=thiazide diuretics; CCB-la=long-acting calcium channel blockers; ACEI=ACE inhibitors; CCB-sa=short-acting calcium channel blockers; BB=β-blockers.
Note: There was no prescribing of angiotensin receptor blocker (ARB) as monotherapy.

DISCUSSION

The Malaysian CPG 2008 recommends a wide selection of first-line monotherapy which includes ACEI, CCBs, Diuretics or ARBs for patients with newly diagnosed uncomplicated hypertension who have no compelling indications for any specific agent. β-blockers, however, are no longer recommended for first-line monotherapy for this group of patients.[8] In this study, 45.7% were found to be on monotherapy and the commonest antihypertensive agents being prescribed were β-blockers (atenolol or propranolol), followed by the short-acting CCB (nifedipine). β-blockers are no longer preferred as compelling evidence showed that they were associated with 16% increase in the risk of stroke when compared to other agents,[14] and an excess cardiovascular event risk of 18% in older patients (>60years).[15] It has also been shown to increase the incidence of new-onset diabetes compared to other drugs, especially in those with high metabolic risk.[16] They were the least effective agents in terms of LVH regression[17] and reduced central aortic pressure less effectively[18] than newer antihypertensive agents. β-blockers should only be prescribed when compelling indications such as heart failure and ischaemic heart disease coexist.[8]

The short-acting CCB (nifedipine) is regularly prescribed in the public primary care setting due to the perceived low cost of the drug. However, the cost of a 30-day prescription for nifedipine 10mg 3 times daily (RM2.70) is now more than amlodipine 10mg once daily (RM1.80), as shown in Table 2. In addition to this, improvements in adherence can be best achieved through the use of once-daily regimens.[19,20]

For stage 2 hypertension (160-179 and/or 100-109mmHg), combination therapy of at least 2 agents is often required to achieve target BP and it should be instituted early.[8] The benefits of combination therapy are not merely additive, but can be synergistic i.e. improving efficacy and reducing side effects.[21] This study shows that 54.3% of the patients were on combination of ≥2 agents and the commonest combination of 2-drug therapy were β-blockers (atenolol or propranolol) and short-acting CCB (nifedipine). The achievement of control target was found to be worse off in those on combination treatment, and this may be due to the complex dosage regimens of short acting preparations being widely used as combination treatment in this study. The combination of β-blockers and thiazide diuretics was also found to be commonly used, and this should be avoided especially in patients with

Table 2: Costs of antihypertensive agents

Generic name	Prescription class#	Cost per tablet*(RM)	Cost for a usual prescriptionper month (RM)
Propranolol	B	0.03/40mg	1.80 (60 tablets)
Atenolol	B	0.14/100mg	4.20 (30 tablets)
Metoprolol	B	0.15/100mg	9.00 (60 tablets)
Nifedipine	B	0.03/10mg	2.70 (90 tablets)
Amlodipine	B	0.03/5mg	0.90 (30 tablets)
			1.80 (60 tablets)
Perindopril	B	0.13/4mg	3.90 (30 tablets)
		0.28/8mg	8.40 (30 tablets)
Enalapril	B	0.08/5mg	2.40 (30 tablets)
		0.16/10mg	4.80 (30 tablets)
Prazosin	B	0.08/1mg	4.80 (60 tablets)
		0.11/2mg	6.60 (60 tablets)
Losartan	A/KK	1.00/50mg	30.00 (30 tablets)

* Costs of these agents were directly obtained from the drug purchasing invoice provided by the pharmacists at the health clinics
# Drug class B can be prescribed by Medical Officers
# Drug class A/KK can be prescribed by Medical Officers with Family Medicine Specialist's counter signature

high metabolic risks as it increases the risks of developing new-onset diabetes.[16] However, the use of thiazide diuretics as monotherapy or in combination with other agents (other than b-blockers) should be used in most patients with uncomplicated hypertension.[22]

Long acting ACE Inhibitors such as perindopril and enalapril has also been found to be underutilised in this study, despite the affordable cost of generic preparations and extensive evidence to support its use.[8,22,23] Due to cost implication, prescription for ARBs in primary care should only be reserved for patients who are not able to tolerate ACE Inhibitors.[23]

Large population surveys in Malaysia have persistently showed poor hypertension control rates, with minimal improvement over the last 10 years.[3,24,25] A systematic review of randomized controlled trials containing data on 15 519 hypertensive patients, found that simplifying dosing regimens improved adherence in 7 of 9 studies, with relative improvement in adherence increasing by 8% to 19.6%.[26] One randomized controlled trial showed an increase in adherence (90% vs. 82%; $p<0.01$) together with a reduction in systolic blood pressure of 6mmHg ($p<0.01$).[19] A wider use of generic long-acting once daily preparation of antihypertensive therapies should therefore be strongly advocated in public primary care clinics where most of the hypertensive patients are being treated.

Further discussion with the local district health office is necessary to plan for continuous quality improvement measures in order to improve the appropriateness of antihypertensive prescribing and the overall standard of hypertension management in both health clinics.

CONCLUSION

In conclusion, this study shows that the prescribing pattern of antihypertensive agents in the 2 primary care clinics was not in accordance with current evidence and guidelines. β-blockers and short-acting preparations were commonly used both as monotherapy and combination treatment. Thiazide diuretics, ACE inhibitors and long acting calcium channel blockers were underutilised in this study, despite robust evidence to support their use. The relatively poor blood pressure control rate of those on combination treatment may be explained by poor patients' adherence to the complex regimes of short-acting preparations. Since cheaper generic preparations of long-acting antihypertensive agents are now available in public primary care clinics, a wider use of such agents either as monotherapy or in combination should be advocated.

This study was conducted in 2 public primary care clinics and therefore the findings cannot be generalised to reflect the entire primary care setting in Malaysia. It is recommended that larger cross sectional surveys or clinical audits involving more public primary care clinics be conducted to assess the overall situation.

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Statins reduces mortality and cardiovascular events in people without cardiovascular events but with cardiovascular risk factors

Brugts JJ, Yetgin T, Hoeks SE, *et al.* The benefits of statins in people without established cardiovascular disease but with cardiovascular risk factors: meta-analysis of randomised controlled trials. *BMJ*. 2009;338(jun30_1):b2376.
In this meta-analysis of 10 trials, treatment with statins significantly reduced the risk of all cause mortality (odds ratio 0.88, 95%CI 0.81 to 0.96), major coronary events (0.70, 0.61 to0.81), and major cerebrovascular events (0.81, 0.71 to 0.93). No evidence of an increased risk of cancer was observed.

Long-term NSAIDs (but not aspirin) may prevent Parkinson's disease

Gagne JJ, Power MC. Anti-inflammatory drugs and risk of Parkinson disease: A meta-analysis. *Neurology*. 2010;74(12):995-1002.
A meta-analysis of 7 trials showed a 15% reduction in Parkinson's disease incidence was observed among users of non-aspirin NSAIDS (relative risk 0.85, 95CI 0.77 to 0.94). The protective effect of non-aspirin NSAIDs was more pronounced among regular users and long-term users

ARBs may increase risk of cancer

Sipahi I, Debanne SM, Rowland DY, Simon DI, Fang JC. Angiotensin-receptor blockade and risk of cancer: meta-analysis of randomised controlled trials. *Lancet Oncol.* 2010. [No volume, issue and page number yet]
Meta-analysis of 5 trials showed that patients randomly assigned to receive ARBs had a significantly increased risk of new cancer occurrence compared with patients in control groups (7.2% vs 6.0%, relative risk 1.08, 95% CI 1.01 to1.15; p=0·016).