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ORIGINAL ARTICLE

Are we evidence-based in prescribing for hypertension?

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Abstract

Background: Adherence to clinical guidelines for treating hypertension would improve cardiovascular outcomes for patients, but might not result in lower drug expenditure. We sought to evaluate our prescription standard and the benefits of following guidelines in our practice.

Aims: To estimate the proportion of prescriptions for hypertension that were evidence-based, investigate the differences in clinical and economic outcomes between prescriptions that were evidence-based or not, and identify the factors associated with evidence-based prescription.

Methods: We reviewed all records of hypertensive patients attending our clinic from 1 October to 15 October 2005. We collected patients' demographic data, estimated the proportion of evidence-based prescriptions and investigated their associations with drug cost, blood pressure, hypertensive complications and doctors' qualifications.

Results: The mean age of the 149 subjects was 55.7 ± 10.3 years. They had a mean duration of hypertension of 2.5 ± 1.8 years, mean systolic blood pressure 139.3 ± 14.4 mmHg, and mean diastolic pressure 81.3 ± 7.9 mmHg. There were 85.4% of prescriptions being guideline-based. Including the old version of the Unit Guideline as the prescription standard, there was no significant association between evidence-based prescription and various outcome variables. If only the new edition was used as the reference standard, there was significant lowering in drug cost without significant changes in clinical outcomes. Higher postgraduate qualifications were associated non-significantly with evidence-based prescription.

***Conclusions**:* The majority of prescriptions were evidence-based. Adherence to the clinical guideline may give rise to cost reduction and potential benefits in clinical outcomes.

Key words: evidence-based, guideline, hypertension, prescription, drug cost

Introduction

Hypertension is a highly prevalent risk factor for cardiovascular and cerebrovascular diseases throughout the industrialized world. In Hong Kong, 16–18% of adult population and more than 50% of the elderly have hypertension.[1] Primary care physicians play an essential role in treating hypertension, particularly in an ageing population. Effective management of hypertension has been associated with about 40% reduction in the risk of stroke and about 15% reduction in the risk of myocardial infarction.[2] The complications of untreated hypertension constitute a substantial clinical and economic impact to the medical and healthcare system.

Over the past years, concerted effort worldwide to promote the development of clinical practice guidelines for hypertension not only reiterate the importance of blood pressure control, but also assist practitioners to assimilate clinical evidence into daily practice. However, despite widespread availability of evidence-based prescribing guidelines for hypertension, the standard of prescription remains suboptimal.[3–5] Recent studies have demonstrated that only 50% of physicians have complied with those recommendations.[6]

From an economic point of view, evidence-based practice does not necessarily lower the costs of healthcare. It only enables doctors to identify and apply the most efficacious therapeutic options to maximize the quality and quantity of life for individual patients. However, a recent study suggested that adherence to evidence-based prescribing guidelines for hypertension would result in substantial savings in prescription costs.[7] The economic implications derived from that study were based on a number of assumptions in the estimates of potential therapeutic substitutions instead of directly interviewing patients or reviewing primary medical records, and could have given rise to discrepancy in cost estimations varying from the real situation.

To achieve a high standard of management for hypertension and to investigate the benefits of practising evidence-based medicine in our setting, we sought to evaluate our prescription standards for hypertensive patients, investigate the difference in clinical and economic outcomes between evidence-based and non evidence-based prescriptions, and identify the factors associated with evidence-based prescription. We did these by reviewing every individual medical record in the study period. We determined the proportion of drug prescriptions that was grounded on evidence-based guidelines, investigated the differences in blood pressure control, prevalence of hypertensive complications and drug expenditure between patients receiving evidence-based or non-evidence-based medications, and revealed the relationship between professional training and evidence-based prescription.

Methods

Patients and procedures

We identified all hypertensive patients attending Kowloon Families Clinic, Hong Kong, for follow-up during a 2-week period from 1 October to 15 October 2005. For patients who filled a prescription for hypertension, we required chart reviews for those started with medications from January 2002, when the first edition of our *Unit Hypertension Guideline* was published. We excluded patients who started medications before the date of guideline implementation or by doctors not working in our clinic.

To minimize Hawthorne's phenomenon (the potential bias associated with subjects being aware that they were being observed), none of the participating doctors involved was aware of the study during the

recruitment period. After each consultation session, we retrieved all the required medical records and collected a predefined, standardized set of data. These included: (i) patients' demographics; (ii) smoking status; (iii) medical co-morbidities (diabetes mellitus, peripheral vascular disease, congestive heart failure, ischaemic heart disease, asthma, chronic obstructive pulmonary disease, gout, and benign prostatic hyperplasia); (iv) duration of hypertension; (v) regimen of the first and the last hypertension prescriptions; (vi) whether prescribing guidelines had been followed; (vii) average drug cost per month over the last year; (viii) mean blood pressure over the last three consecutive consultations; (ix) target organ damage (hypertensive retinopathy, left ventricular hypertrophy, ischaemic heart disease, heart failure, stroke or transient ischaemic attack, renal damage defined as a rise in serum creatinine or the presence of persistent proteinuria, and peripheral arterial disease); and, (x) availability of home blood pressure monitoring. We also collected data on doctors' ages, gender, training status and professional qualification(s).

Unit guidelines

Our *Unit Hypertension Guideline*, was used as the reference prescribing standard for the analysis. The first edition of our *Guideline* primarily followed the recommendations of the World Health Organization and the British Hypertension Society.[8–9] We updated it 2 years later because of new evidence and recommendations published in the Joint National Committee VII Report (JNC VII).[10]

The first edition of the guideline, considered both thiazides and beta-blockers to be appropriate first-line hypertension therapies for patients without specific contraindications or indications for another drug. In the second edition, beta-blockers were no longer recommended as equivalent to thiazides as first-line treatment for uncomplicated hypertension.

We also incorporated some compelling indications for certain classes of anti-hypertensives into our guidelines. For patients with congestive heart failure or diabetes mellitus and nephropathy, we considered ACE inhibitors to be indicated as first-line therapy.[10–14] For patients with a history of ischaemic heart disease, we considered beta-blockers as first-line therapy,[10,15] except in patients with diagnoses of asthma, chronic obstructive pulmonary disease or congestive heart failure. We followed JNC VII in allowing alpha-blockers as potentially favorable treatment for patients with coexisting prostatic disease.

Statistical analysis

We applied the Statistical Package for the Social Sciences version 10.0 (SPSS Inc. Chicago, IL, US) for data analysis. Descriptive statistics were used for patients, doctors and prescribing characteristics. We classified the drug prescription as evidence-based or not on basis of the first hypertensive medication(s) initiated for the patient, and assessed if it followed the particular edition of the *Unit Guideline* which was current at the time of prescribing. To investigate the clinical and economic differences between evidence-based and non-evidence-based prescriptions, the two groups of prescriptions were compared in terms of outcome measures including average drug cost per month over the last year, mean blood pressure control and presence of target organ damage adjusted for other confounding variables, for example the duration of hypertension. Univariate associations of an evidence-based prescription with various outcome variables were assessed using Mann–Whitney U-test for continuous variables and Chi-squared test for categorical variables. Similarly for the factors associated with evidence-based prescribing, we used the Chi-squared test to determine the relationship between an evidence-based prescription and doctors' professional qualifications. A P-value < 0.05 was considered significant. Furthermore, as the 2004 *Unit Guideline* was based on the latest available evidence, we performed an additional analysis based on the new reference standard alone to compare the differences in outcome measures with the older standard. In this scenario, we reviewed all data and reclassified the drug prescription as appropriate or not with reference to the new guideline only, that is thiazide should be used as a first-line anti-hypertensive agent in cases of uncomplicated hypertension. The same statistical analysis was repeated to estimate the differences in drug cost and clinical outcomes between the guideline-based and non-guideline-based prescriptions.

Results

Baseline patient and doctor characteristics

We identified a total of 486 medical records during the study period, of which 149 had fulfilled the inclusive criteria for in-depth chart review. Excluded were those who started medications before implementation of the *Unit Guideline* or those whose medications were initiated by doctors working outside our clinic. The baseline patient characteristics are illustrated in Table 1. The mean age of the subjects was 55.7 years. More than half were males. The majority never smoked. Less than a quarter had coexisting diabetes mellitus. The subjects had a mean duration of hypertension of 2.5 years and a mean blood pressure of < 140/90 mmHg. Out of the 149 subjects, 130 (87.2%) required the use of anti-hypertensive agents. Less than one-sixth suffered from target organ damage. Around 70% of our patients had home monitoring of blood pressure. Their mean office blood pressure control (139.9 ± 13.7/82.1 ± 7.3 mmHg) was non-significantly higher than the ones without home monitoring (138.1 ± 15.9/79.7 ± 9.0 mmHg) (P = 0.1 for mean systolic blood pressure and P = 0.3 for mean diastolic blood pressure). For the characteristics of the doctors in the clinic, most of the prescriptions were filled by doctors aged between 31 and 40 years (21–30 years: 16.8%; 31–40 years: 71.1%; 41–50 years: 12.1%). Fifty-two percent of the drug prescriptions were filled by female doctors. All the doctors were either trainees or trainers in family medicine. Doctors with a higher qualification in family medicine accounted for 69.8% of the prescriptions (no additional postgraduate qualification: 30.2%; Fellowship of Royal Australian College of General Practitioners [FRACGP] / Fellowship of Hong Kong College of Family Physicians [FHKCFP]: 49.7%, Fellowship of Hong Kong Academy of Medicine – Family Medicine [FHKAM – Family Medicine]: 20.1%.).

Prescribing pattern

Among the 130 hypertensive patients on regular drug treatment, 100 (76.9%) required one type of medication and 30 (23.1%) required two types of medications in the last consultation. No subjects had required more than two types of anti-hypertensive medication. Concerning the drug prescriptions for the 130 individuals, 111 (85.4%) were initiated in accordance with the recommendation in the *Unit Guideline*. Forty-seven (36.2%) hypertensive individuals were initially prescribed with thiazides, 51 (39.2%) with beta-blockers, 15 (11.5%) with ACE inhibitors, 9 (6.9%) with nifedipine retard, and the others (8/130 or 6.2%) were given other types of anti-hypertensives including amlodipine, felodipine, alpha-blockers and methyl-dopa. The average drug cost over the last year was US$2.13 ± 3.59/patient month (range, US$0.13–$15.95/patient month).

Comparing the first and the final consultation for hypertension follow-up in the 45-month study period, a similar proportion of patients had remained on thiazides (36.2% vs. 36.9%) and beta-blockers (39.2% vs. 38.5%), but more patients had used ACE inhibitors (11.5% vs. 16.2%), nifedipine retard (6.9% vs. 15.4%) and other types of anti-hypertensives (6.2% vs. 16.2%) in the last consultation.

Differences in drug cost and clinical outcomes between evidence-based and non-evidence-based prescriptions (Table 2)

The average drug cost per patient month was US$2.04 ± 3.50 for the evidence-based prescriptions, and US $2.65 ± 4.09 for the non-evidence-based prescriptions. The difference was not statistically significant (P = 0.50). The two groups of patients were similar in other confounding factors including patient age, gender, smoking status, body mass index, duration of hypertension, medical co-morbidities and the presence of target organ damage. Concerning the clinical outcomes, the mean blood pressure in patients receiving evidence-based prescriptions was not significantly lower than the ones on non-evidence-based prescriptions. (systolic blood pressure 138.7 ± 14.5 mmHg vs. 139.9 ± 14.6 mmHg, P = 0.73; diastolic blood pressure 80.1±8.2 mmHg vs. 82.1±7.9 mmHg, P = 0.54) There was no difference in the presence of target organ involvement between the two groups of patients. (P = 1.00)

Postulation analysis

If we reassessed the drug prescription using the updated *Guideline* 2004 as the only reference standard and then repeated the same statistical procedure, we found a significant reduction in drug expenditure (2.91–1.53/2.91 or 47.4%) for the evidence-based prescriptions (US$1.53 ± 2.64 vs. US$2.91 ± 4.42, 0.03), but a similar degree of systolic blood pressure (P = 0.73) and diastolic blood pressure control (P = 0.50), and a similar prevalence of target organ damages. (P = 0.25)

Factors associated with evidence-based prescription

Doctors with higher postgraduate qualifications more often prescribed evidence-based therapies (no additional postgraduate qualification: 81.0%; FHKCFP/FRACGP: 84.3%; FHKAM - Family Medicine: 92.3%) However, the association was not statistically significant (P = 0.70).

Discussion

Our study demonstrated that the majority of anti-hypertensive regimens (85.4%) prescribed by doctors in our unit were evidence- (or guideline-) based. The proportion of evidence-based prescriptions in our study was higher than the findings from other studies, where only around 50–60% of the prescriptions were found to be grounded on scientific evidence.[6,7] In line with the *Guideline* recommendations, in our unit, thiazides and beta-blockers were first-line anti-hypertensive agents in 75.4% (47 + 51/130) of the total prescriptions, while other groups of hypertensive medications, particularly the more expensive amlodipine and felodipine, were mainly used as second-line agents. Thiazides and beta-blockers were also better tolerated by our patients than those involved in other studies. At the last visit in the reviewing period, the majority of patients were still on thiazides and beta-blockers. In the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), the 1-year cessation rate was 12.9% for thiazide-type diuretics[16] and in recent trials of beta-blockers, the cessation rate was about 27%.[17,18] The racial difference in the development and perception of adverse effects and a clearer explanation of the drug regimen and mechanism to patients might have accounted for the lower rate of discontinuation.

Our study was performed in a family medicine training center which was a reason for our higher prescription standard. All the doctors involved were either trainees or trainers in family medicine. About 70% of the anti-hypertensive prescriptions were given by doctors with higher qualifications in family medicine. They were more experienced and aware of the evidence available in the literature. Some of them may even have been directly or indirectly involved in the development of the *Unit Guidelines* and this process would have better equipped them in practising evidence-based medicine. Moreover, the multifaceted strategies in the training centre, including educational activities, regular clinic meetings and case reviews, were useful for effective communication, dissemination and implementation of the guidelines.[19] The small sample size of this pilot research may have limited the power of the study to demonstrate the significant relationship between professional training and evidence-based prescriptions.

Another reason for our better adherence to clinical guidelines was that our clinic served only government servants and was not making any profit out of the clinical services. This would have reduced the marketing effects of the drug industry trying to promote the use of newer and more expensive medications and divert physicians and patients to drug choices outside of published guidelines.

In our unit, there was a marked increase in patients with hypertension over the years. In the study clinic, drug spending on anti-hypertensives contributed about 40% of the total drug expenditure in 2004. With an ageing population, we are concerned with the expected rise in the number of hypertensive patients and a proportional increase in drug expenditure. Cost-effective use of drugs will be of utmost importance in this regard. In this study, we found that the use of the new clinical guideline based on JNC VII – which recommended thiazide-

type diuretics as the first-choice agent in uncomplicated hypertension – produced a significant reduction (47.4%) in drug expenditure, which included the cost on both the anti-hypertensive therapies and potassium supplements. Another study has projected similar results using the same guideline as a reference standard.7 Clinical practice guidelines need to be regularly revised and updated in response to the development of new evidence in order to bring about the most benefit from practising evidence-based medicine.

With a high standard in the use of hypertensive medications in our setting, the mean blood pressure of our study population achieved an optimal level of 139/81 mmHg. The non-significant differences in the associations between evidence-based prescriptions, degree of blood pressure control and the presence of target organ damage were probably related to the insufficient sample size and the short mean duration of hypertension of the subjects (2.5 ± 1.8 years). The small sample size constituted the major limitation in this study. However, as a pilot study, it provided us with useful clinical data for planning a larger-scaled and multi-centered study in the near future, which will hopefully bring us to a more valid and representative conclusion on this issue.

Conclusion

This study demonstrated that most of our prescriptions for hypertensive patients were evidence-based. Adherence to clinical practice guideline in our unit was associated with reduction in drug expenditure and potential benefits in clinical outcomes. More guideline-based prescriptions were filled by doctors with higher postgraduate qualifications, but the difference was not statistically significant.

Summary of implications for GPs

This pilot study reiterated the importance of evidence-based prescription for hypertensive patients and further encouraged evidence-based practice by suggesting that adherence to clinical practice guideline was associated with cost-effectiveness in health care and potential benefits in clinical outcomes for patients.

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Table 1 - Baseline characteristics of the 149 patients, Evidence-Based Prescribing in Hypertension, Hong Kong 2005

Age	55.7 ± 10.3 years. (34.7–86.9)
Gender	
Male	84 (56.4%)
Female	65 (43.6%)
Smoking status	
Never smoked	136 (91.3%)
Ever smoked	13 (8.7%)
Medical comorbidities	
Diabetic mellitus	33 (22.1%)
Ischaemic heart disease	3 (2.0%)
Asthma	2 (1.3%)
Gout	4 (2.7%)
Benign prostatic hyperplasia	7 (4.7%)
Atrial fibrillation	3 (2.0%)
Duration of hypertension	2.5 ± 1.8 years (0.0–7.8)
Mean systolic blood pressure	139.3 ± 14.4 mmHg (103.0–197.0)
Mean diastolic blood pressure	81.3 ± 7.9 mmHg (63.0–101.0)
Target organ involvement	
Left ventricular hypertrophy	6 (4.0%)
Ischaemic heart disease	2 (1.3%)
Stroke or transient ischaemic attack	1 (0.7%)
Renal damage	15 (10.1%)
Availability of home monitoring	
No	47 (31.5%)
Yes	102 (68.5%)

Table 2 - Baseline characteristics, clinical and economic parameters of patients receiving evidence-based and non evidence-based prescriptions with regard to the first edition of Unit Guideline, Hong Kong 2005

Patient characteristics	Evidence-based	Non-evidence-based	*P*-value
Age (years)	56.3 ± 10.4	56.0 ± 12.1	0.18
Gender			
Male	58	7	0.78
Female	53	12	
Smoking status			
Never smoked	101	17	0.69
Ever smoked	10	2	
BMI (kg/m^2)	24.7 ± 3.6	25.2 ± 3.1	0.44
Duration of hypertension (years)	2.6 ± 1.8	2.5 ± 1.3	0.17
Medical comorbidities			
Yes	33	6	0.19
No	77	13	
Mean systolic blood pressure (mmHg)	138.7 ± 14.5	139.9 ± 14.6	0.73
Mean diastolic blood pressure (mmHg)	80.1 ± 8.2	82.1 ± 7.9	0.54
Target organ damages			
Yes	20	3	1.00
No	91	16	
Drug cost/patient month (US$)	2.04 ± 3.50	2.65 ± 4.09	0.50

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