JCN Chan 陳重娥
JYF Wu 吳雁飛
GMC Chan 陳曼姿
WYS Leung 梁潤成
BSC Lee 李成章

Promoting the appropriate use of chronic medications

Key Messages

1. Both doctors and patients have concordance problems with adhering to treatment guidelines and regimens.
2. Inappropriate prescribing of medications by doctors and poor drug compliance by patients can lead to treatment failure despite the proven efficacy of many chronic medications.
3. To enhance the cost-effective use of chronic medications, our interventional programmes, which emphasise teamwork between doctors and pharmacists, as well as patient education, to ensure continuity of care and adherence to therapy, led to a significant improvement in prescribing habits, patient compliance and clinical outcomes.

Hong Kong Med J 2006;12(Suppl 3):S11-4

Department of Medicine and Therapeutics, The Chinese University of Hong Kong
JCN Chan
Chief Pharmacy Office, Pamela Youde Eastern Hospital
JYF Wu
Department of Pharmacy, Prince of Wales Hospital
GMC Chan, BSC Lee
Department of Pharmacy, Queen Elizabeth Hospital, Kowloon
WYS Leung

HCPF project number: 226103

Principal applicant and corresponding author:
Prof Juliana CN Chan
Division of Clinical Pharmacology, Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Shatin, Hong Kong SAR, China
Tel: (852) 2632 3138
Fax: (852) 2632 3108
E-mail: jchan@cuhk.edu.hk

Introduction

According to the World Health Organization, 60% of global deaths are due to four chronic diseases (diabetes, cardiovascular diseases, cancer, and respiratory diseases), which in turn are closely related to ageing and unhealthy lifestyles.[1] Due to the asymptomatic nature of these diseases during remission, poor treatment compliance often results in relapse or deterioration in the clinical course.[2] Patients with chronic diseases have multiple needs in terms of knowledge, skills, and psychological support. Chronic disease management advocates an approach that emphasises coordinated, comprehensive care along the disease continuum and across health care delivery systems. It also emphasises the translation of evidence into practice and teaching that integrate the pathophysiological rationale, caregiver experience, and patient preferences with valid, current clinical research evidence. To make evidence-based chronic disease management effective, a multidisciplinary team is often required in order to develop, lead, and implement preventive, diagnostic, and therapeutic decisions.[3]

In Hong Kong, cardiovascular and respiratory diseases are the leading causes of death and hospital admissions. After discharge from hospital, many patients are managed at public hospital out-patient clinics where they are often seen in busy settings by different doctors, with long intervals between clinic visits. A local prescription review survey has documented high use of cardiovascular (50%), anti-diabetic (9%), and respiratory (15%) drugs by patients attending general medical clinics.[4] These drugs are also among the leading items in out-patient drug expenditure, accounting for over 60% of the overall drug expenditure in a typical medical unit, because of high volume use, high unit costs, or both.

Although many of these chronic medications have been shown to improve clinical outcomes and are cost-effective, it is often difficult to achieve maximal therapeutic benefits in actual clinical practice due to inappropriate or ineffective drug use. Local data have demonstrated that patients' compliance with chronic medications is often suboptimal.[5] National audits frequently show suboptimal adherence to recommended treatment guidelines by prescribers as well.[6,7] Together these factors can lead to increased health care costs, such as an increased number of hospital admissions and/or visits to the emergency room and, more importantly, poor clinical outcomes and a reduced quality of life for patients.

Aims and objectives

The objectives of this programme were to improve the cost-effective use of chronic medications by (1) promoting doctors' adherence to recommended treatment guidelines, (2) improving patients' compliance with chronic medications, and (3) examining the impact of patient education from pharmacists on clinical outcomes.

Methods

The study was conducted from July 1997 to July 1999 at the Prince of Wales Hospital, a regional hospital serving a catchment population of one million. There are 22 general and subspecialty clinics in the medical unit with an average weekly attendance exceeding 2200 patient visits. From August 1997, a series of

programmes to improve drug use were started in the unit.

Structured prescription forms

Structured prescription forms outlining the recommended treatment guidelines for prescriptions of four classes of chronic medications were developed. These included a class of lipid-lowering drugs (statins), long-acting airway dilator inhalers (β_2 agonists), a corticosteroid nasal spray (fluticasone), and a cardiovascular drug (angiotensin II antagonists). The rationale for this programme was presented to all medical staff before commencement. Doctors were requested to complete these forms for all patients newly started on the studied drugs. Pharmacists performed regular audits to monitor the quality of prescribing and the pattern of drug use.

Table 1. Doctors' adherence to the recommended guidelines for prescription of lipid-lowering drugs (statins) in a public hospital clinic from 1997-1999

Local recommendations on prescription of lipid-lowering drugs*	Adherence rate (%)	
	Before using prescription forms	After using prescription forms
Availability of two lipid profiles	55	91
Availability of high-density lipoprotein C level	76	86
Levels within treatment criteria	83	86
Provision of dietary advice	59	91

* These prescription guidelines have been further modified since the publication of several landmark studies showing the efficacy of lipid lowering in patients with both medium to high risk for coronary heart disease

Compliance and refill clinic

A pharmacist-manned compliance and refill clinic was established to assess patients' compliance with chronic medications and provide patient education on the appropriate use of drugs. Between June 1998 and February 1999, patients given prescriptions from medical clinics containing any of the four studied drugs for more than 16 weeks' duration were recruited. Their prescriptions were split into two lots, obliging patients to return at 8 to 10 weeks for a refill. The purpose was to reduce drug wastage and to reinforce patient compliance. Tablet counting and direct patient questioning were employed to assess the level of patient compliance. Patients were considered compliant if they took 80 to 120% of the prescribed daily dose. The reasons for non-compliance were identified and patient counselling on disease management and the importance of good compliance was provided. The change in compliance after receiving education from a pharmacist was assessed at the patient's second attendance at the refill and compliance clinic. All intervention activities were documented and information regarding the patient's level of compliance and other medication-related problems was provided to the relevant doctors.

Disease management programme

Patients receiving multiple chronic medications were at risk of non-compliance due to the complexity of their treatment regimen. In a separate initiative, a randomised controlled trial was conducted to test the effect of telephone counselling, which was used to ensure continuity of care and reinforce compliance, on clinical outcomes. Between October 1998 and June 1999, patients receiving five or more chronic medications were recruited from the general medical, geriatric, cardiac, respiratory, asthma, and renal clinics. Together with the clinic nurses, a research pharmacist interviewed these patients and assessed their medication compliance using both pill counts and direct questioning before their clinic visits. Patients found to be non-compliant at the screening visit were invited to participate in a telephone intervention programme at the next clinic visit scheduled 12 to 16 weeks later. At this next visit, the pharmacist again assessed patients' compliance levels and all eligible patients were randomised, by an independent nurse, to either the intervention or control group. The intervention group received a phone call from the same pharmacist halfway between clinic visits, while the control group did not. All patients had a face-to-face interview with the pharmacist at the end of 2 years for assessment of their compliance. The primary end-points were death, emergency department visits, and hospital admission rates.

Results

Use of structured prescription forms

The impact the introduction of prescription forms had on doctors' prescribing practices concerning lipid-lowering drugs was examined by a review of the case notes of 92 patients treated with statins. The overall adherence to treatment guidelines rate increased from 23% before to 45% after introduction of the form (P=0.032) [Table 1].

Compliance and refill clinic

During the study period, 2038 patients (mean±standard deviation: age, 61±12 years; male 49%) attended the compliance clinic. The mean number of drug items received by each patient was 4.3±2 (range, 1-14). Of the 2038 patients, 17% asked their relatives to collect their medications. Of the remaining patients (83%), 24% were considered non-compliant. A change in dose frequency (34%) was the commonest reason for non-compliance. Other reasons included omission of doses (27%), change in drug dosage (20%), or a combination of both (19%).

The major reasons for non-compliance were given as (1) a lack of knowledge about recent modification of the treatment regimen by their doctors (58%), (2) forgetfulness (25%), (3) drug side-effects (7%), (4) decrease in severity or disappearance of symptoms (4%), and (5) attending multiple clinics or visiting different doctors (3%).

After counselling from the pharmacist, patient compliance improved from 76% to 91%. Among the 2038 patients, 12% reported adverse drug effects, although this

Table 2. Savings of different classes of drugs following introduction of the compliance and refill clinic midway between clinic visits due to default or suboptimal compliance

Drug class	Proportion of savings (%)
Cardiovascular drugs	47.5
Lipid-lowering drugs	36.4
Anti-diabetic drugs	3.5
Respiratory drugs	11.8
Others	0.8
Total	100

led to non-compliance in only 14% of all patients. There were significant differences between compliant and non-compliant patients in terms of age (60.6 vs 62.3 years, P<0.02) and number of drug items received (4.1 vs 4.8, P<0.001). Over 90% of patients expressed satisfaction with the education service. An average of HK$30 000 worth of drugs were returned per month mainly due to default at the refill clinic and suboptimal compliance. The proportion of savings by drug class is shown in Table 2. Feedback from the pharmacist to prescribing doctors about their patient's drug-taking patterns led to a simplification or modification of treatment in 30% of cases.

Disease management programme

Of 1011 subjects receiving multiple medications recruited at the screening visit, 562 (55%) were non-compliant. Patients were defined as compliant with a drug if they took 80 to 120% of the prescribed daily dose. To calculate a compliance score for the whole treatment regimen, the number of drugs that the patient was fully compliant with was divided by the total number of prescribed drugs and expressed as a percentage. Only patients who complied with all recommended drugs were considered compliant (100% score).

Among the non-compliant patients, 39% stopped taking their drugs, 29% omitted dosages, 22% modified the frequency of taking their drugs, 15% modified dosages, and 33% reported a combination of these habits. The major reasons leading to patient non-compliance included (1) a lack of knowledge about the treatment regimen (60%), (2) adverse drug effects (21%), and (3) patient forgetfulness (21%). Feedback from the pharmacist to the prescribing doctor about a patient's drug-taking behaviour resulted in simplification or modification of treatment in 46% of cases.

Sixty patients did not return for the randomisation visit 12 to 16 weeks later. Thus, only 442 patients were randomised. Two years into the study, 50% of defaulters had died. In the control group (n=223), 17.0% died compared to 11.4% in the intervention group (n=219) [Fig[8]]. After adjusting for confounders, the pharmacist's telephone counselling was associated with a significant 41% risk reduction of death (relative risk [RR)], 0.59; 95% CI, 0.35-0.97; P=0.039). The number needed to treat to prevent one death at 2 years was 16. Other predictors included age, living alone, prior hospitalisation rates, compliance levels at baseline, number of chronic medications, and non-treatment with lipid-lowering drugs at screening visits. In the entire cohort of 1011 patients, the adjusted RRs of death were 1.61 (1.05-2.48, P=0.029) and 2.87 (1.8-2.57, P<0.001) in those with 34-66% and 0-33% compliance levels respectively compared to those with ≥70% compliance level.[8]

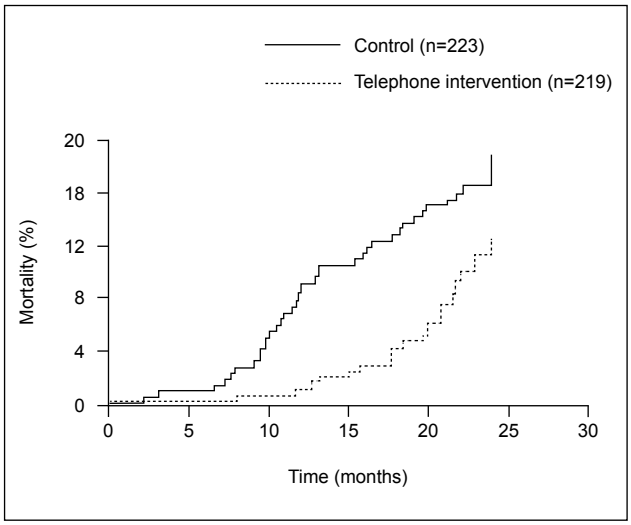

Fig. Kaplan-Meier estimates of effect of telephone intervention by a pharmacist on all cause mortality in patients receiving polypharmacy (relative risk for intervention, 0.59; 95% confidence interval, 0.35-0.97; P=0.039 after adjusting for confounding factors)[8]

Discussion

Despite the proven efficacy on clinical outcomes of many chronic medications, the effectiveness of these drugs in actual clinical practice remains uncertain. Our previous series of drug utilisation evaluations confirmed that both doctors and patients have concordance problems. Inadequate knowledge about disease management and treatment regimens was the main reason for suboptimal compliance among our patients. The intervention programmes emphasised patient education and teamwork between doctors and pharmacists. The programmes were comprised of (1) the use of structured prescription forms as an educational tool for doctors, (2) the establishment of a compliance and refill clinic, (3) the development of disease management programmes using telephone counselling from a pharmacist to ensure continuity of care. Together, these programmes improved doctors' prescribing habits and patients' compliance in the short term and reduced adverse clinical outcomes including use of hospital resources and death rates in the long term.[8] Importantly, in the latter study, non-compliant subjects who became compliant after the initial interview but did not receive subsequent reinforcement had a similar death rate to those who remained non-compliant

from the beginning. These findings support the importance of continuous or regular reinforcement to sustain behavioural modification.

Acknowledgements

This study was supported by the Health Care and Promotion Fund (#226103). The authors thank Dr Philip KT Li, consultant and clinical coordinator, and Ms MF Lau, nursing officer at the Prince of Wales Hospital for their support of the programmes. We also thank the nursing and medical staff of the medical unit and the Department of Pharmacy of the Prince of Wales Hospital for their assistance in this project.

Results of this study were published in full in the *British Medical Journal*: Wu JY, Leung WY, Chang S, et al. Effectiveness of telephone counselling by a pharmacist in reducing mortality in patients receiving polypharmacy: randomised controlled trial. BMJ 2006;333:522.

References

1. Ellrodt G, Cook DJ, Lee J, Cho M, Hunt D, Weingarten S. Evidence-based disease management. JAMA 1997;278:1687-92.
2. Preventing chronic diseases: a vital investment. World Health Organization website: http://www.who.int/chp/chronic_disease_report/en/index.html. Accessed 1 Jun 2006.
3. Defining adherence. Adherence to long-term therapies: evidence for action. Geneva: World Health Organization; 2003:4-5.
4. Yuen YH, Chang S, Chong CK, Lee SC, Critchley JA, Chan JC. Drug utilization in a hospital general medical outpatient clinic with particular reference to antihypertensive and antidiabetic drugs. J Clin Pharm Ther 1998;23:287-94.
5. Chong CK, Yuen YH, Chan JC, Chang S, Lee SC, Critchley JA. A patient compliance survey in a general medical clinic. J Clin Pharm Ther 1997;22:323-6.
6. Chang S, Tam BH, Tse BP, et al. Evaluation of losartan usage in a regional hospital in Hong Kong. J Pharm Tech 1999;15:170-5.
7. Saaddine JB, Engelgau MM, Beckles GL, Gregg EW, Thompson TJ, Narayan KM. A diabetes report card for the United States: quality of care in the 1990s. Ann Intern Med 2002;136:565-74.
8. Wu JY, Leung WY, Chang S, et al. Effectiveness of telephone counselling by a pharmacist in reducing mortality in patients receiving polypharmacy: randomised controlled trial. BMJ 2006;333:522.