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Successful Implementation of a P&T-Approved Therapeutic Interchange Program of Angiotensin II Receptor Blockers in a Medical Center in Taiwan

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A B S T R A C T

Objective: Therapeutic interchange is not a common practice in the medical society in Asia. We used clinic blood pressure readings, patients' tolerance, and cost saving as measures to evaluate the impact of a therapeutic interchange program implemented at a medical center in Taiwan. **Methods:** Taipei Medical University-Wan Fang Hospital initiated a therapeutic interchange program involving angiotensin II receptor blockers (ARBs). Data were retrospectively collected for 444 outpatients who were converted from other ARBs to candesartan. Evaluation of therapeutic efficacy, adverse effects associated with therapy, and drug costs was conducted before and after the program implementation. **Results:** Patients whose treatment was converted to candesartan experienced no statistically significant differences in blood pressure, and the average number of antihypertensive agents used per patient remained unchanged. A direct cost savings of US$62,237 was estimated for the 444 patients studied. Only 3.15% of the patients developed adverse drug reactions potentially related to candesartan, and none required hospitalization. **Conclusions:** Based on the results of this retrospective chart review, the present ARB therapeutic interchange program was successfully developed and implemented. This is the first study to establish the positive impact of a well-run ARB therapeutic interchange program in Taiwan.

Keywords: angiotensin II receptor blockers, candesartan, hypertension, therapeutic interchange.

Background

A well-managed hospital formulary system has been recognized as the most effective method to ensure that medically appropriate and cost-effective drugs are available for use within an institution [1,2]. The American Society of Hospital Pharmacists guidelines for formulary system management recommend that the Pharmacy and Therapeutics (P&T) Committee review the use and therapeutic effects of several drug classes each year [3]. After identifying the preferred agents within a pharmacological class, the P&T Committee can execute therapeutic interchange to substitute more expensive agents with less expensive ones while maintaining equal efficacy [4]. A survey in 2000 estimated that more than 80% of US hospitals had therapeutic interchange programs mostly involving H_2-receptor antagonists, proton pump inhibitors, cephalosporins, hydroxymethylglutaryl-coenzyme A reductase inhibitors, and so on [5]. This strategy has been used to effectively manage a variety of therapeutic classes in hospital systems in the United States [6–10].

Therapeutic interchange has not been a commonly accepted medical practice in Taiwan. Under the influence of aggressive promotion by pharmaceutical companies, physicians generally believe that patients respond differently to each drug in the same therapeutic class. In addition, most prescription medications on the market are covered by Taiwan's National Health Insurance, a single-payer nationwide insurance plan instituted in March 1995. The National Health Insurance enrolled 97.6% of the population by 2004 and increased the enrollment to 99.6% in 2009. It covers inpatient care, ambulatory care, dental care, and prescription medications with very low co-payments, usually around 5% to 10% of medication costs, for both brand-name and generic products. The National Health Insurance reimburses all brand-name drugs within the same therapeutic class with the same price at their equivalent doses and generics with 70% to 80% of the price of the brand-name products. It is not easy to persuade patients to switch their medications within the same therapeutic class, because they misunderstand that the hospitals were changing their brand-name drugs to generic ones. Many of our patients do not believe that the domestic generic version of a brand-name prescription drug is as good as the foreign imported one. As a result, it was commonplace for a hospital in Taiwan to have a formulary with more than 1000 drugs and many "me-too" agents in a therapeutic class.

Conflicts of interest: The authors have indicated that they have no conflicts of interest with regard to the content of this article.

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In 2004, the health-care system of Taipei Medical University (TMU) successfully replaced a significant number of trade-name prescription drugs with therapeutic equivalents on the formulary, which was truly revolutionary in Taiwan. A Joint P&T Committee was established in 1986 at TMU's health-care system, which consisted of TMU Hospital and TMU–Wan Fang Hospital (TMU-WFH), for managing the formulary system. A Pharmacy Management Group, consisting of several clinical pharmacists and pharmacy managers from both the teaching hospitals and a pharmacist consultant from the United States, was established in 2004 by adapting the principles from the American Society of Hospital Pharmacists' formulary management guidelines to promote rational drug use. The Pharmacy Management Group reviews both quarterly and yearly 80/20 reports (ranked by pharmaceutical costs) to identify potential areas for clinical and financial interventions. In 2004, cardiovascular agents accounted for about 30% of the total drug costs based on the first quarter 80/20 report. Angiotensin II receptor blocker (ARB), accounting for 7.5% of total drug expenditures as the top therapeutic class, was determined by the P&T Committee as a potential class for the first therapeutic interchange program at TMU-WFH.

ARBs have been used commonly for the treatment of hypertension, heart failure, myocardial infarction complicated by heart failure, and diabetic nephropathy. In Taiwan, this therapeutic class accounts for more than one-third of the market share for antihypertensive agents. It is the second most used antihypertensive drug class after calcium channel blockers. The use of ARBs has been included in many clinical practice guidelines, such as the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, guidelines of the American College of Cardiology/American Heart Association regarding the management of patients with heart failure or following myocardial infarction, and guidelines published by the Kidney Disease Outcomes Quality Initiative of the National Kidney Foundation [11–13]. The National Quality Foundation in August 2009 also endorsed the medication possession ratios for angiotensin-converting-enzyme inhibitor or ARB by patients with chronic kidney disease or diabetes and hypertension as one of the standards for measuring the performance of health-care providers [14]. All ARBs are approved for the treatment of hypertension, and some have also been approved for other conditions, such as treating heart failure, treating myocardial infarction complicated by left ventricular dysfunction, or use in diabetic patients with nephropathy. Currently, there are no significant clinical advantages in terms of efficacy or risks that justify the use of one ARB over another [15–17].

A therapeutic interchange program involving ARBs was initiated at TMU-WFH, a 732-bed medical center, in May 2004, after being approved by the Joint P&T Committee of TMU health-care system. To our knowledge, this was the first therapeutic interchange program implemented in Taiwan. The objective of this study was to evaluate the impact of the therapeutic interchange program in WFH on patients' blood pressure control and cost saving.

Methods

Initiation of therapeutic interchange program

Four ARBs—valsartan (Diovan®, Novartis, Taiwan), irbesartan (Aprovel®, Sanofi-Aventis, Taiwan), telmisartan (Micardis®, Boehringer Ingelheim, Taiwan), and a combination of losartan and hydrochlorothiazide (Cozaar®, Merck, Taiwan)—were originally included in the TMU-WFH formulary. Using our formulary decision criteria, the P&T Committee decided to limit the ARBs on the formulary to candesartan and valsartan in 2004. The TMU's formulary decision criteria, which were similar to the System of Objectified Judgment Analysis, included appropriate indications, factors affecting patient compliance, bioavailability, interactions, clinical impact and efficacy, acquisition cost, and documentation supporting efficacy [18,19]. Candesartan was listed as the preferred agent with a high score in the formulary decision criteria due to its low acquisition cost and good documentation for hypertension, and valsartan was restricted to patients with heart failure. A dosage conversion guide was developed by referring to multiple clinical head-to-head comparison trials involving ARBs [20–23], and the guide was approved by the Joint P&T Committee at TMU health-care system in August 2004. The use of candesartan increased over time, and it accounted for more than 75% of the ARB market share as of October 2004. After the Food and Drug Administration approved candesartan for the treatment of heart failure (New York Heart Association classes II–IV and ejection fraction ≤40%) in 2005, the score of candesartan became the highest among ARBs in our formulary decision criteria. As a result, the Joint P&T Committee decided to remove valsartan and listed candesartan as the sole formulary ARB in May 2005.

Study design and subjects

A total of 899 patients with active prescriptions for candesartan were identified in the computerized outpatient database during the period of October 4–9, 2004. Medical records of these patients were made available for initial review. Inclusion criteria were hypertensive patients switched from other ARBs to candesartan during the study period. Exclusion criteria included 1) hospitalization during the study period not because of ARB-induced adverse drug reaction (ADR), 2) diagnosis of cancer, 3) younger than 18 years of age, 4) use of candesartan prior to the implementation of the therapeutic interchange program, and 5) incomplete blood pressure documentation. Incomplete blood pressure documentation was defined as having fewer than two blood pressure readings in the patient's medical records within 6 months before or after conversion. It is a standard practice in Taiwan to prescribe a 3-month refilled prescription to patients who have chronic diseases stably controlled by medications. Patients visit the doctor's office only every 3 months, unless there is any unusual condition, such as experienced new clinical signs/symptoms or any side effects. Excluding the patients with fewer than two blood pressure readings would not exclude the patients experiencing unwanted effects from the ARB switching program.

The data collected included patient demographics, pertinent diagnoses, blood pressure readings, and number of antihypertensive agents used per patient within 6 months pre- and postconversion, as well as any ADRs, such as headache, dizziness, angioedema, or increased serum potassium occurring in the postconversion period. To measure the number of patients who were successfully converted from their original treatment, the number of patients who discontinued angiotensin II receptor therapy within 1-year postconversion was also calculated. Cost savings from implementing this therapeutic interchange program for each patient was calculated by using the following formula:

Table 1 – Reasons patients were excluded from current study.

	Number of patients
Reason	
Hospitalization during the study period	14
Patients with cancer	7
Use of candesartan before the therapeutic interchange program implementation	5
Incomplete blood pressure documentation	202
Total	228