Patient compliance and therapeutic coverage: comparison of amlodipine and slow release nifedipine in the treatment of hypertension

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Abstract To study patient compliance in hypertensive outpatients amlodipine (5 mg once daily) and slow release nifedipine (20 mg twice daily) were compared in an open, crossover study in general practices.

Four methods of assessment for patient compliance (pill count, taking compliance, days with correct dosing, timing compliance) were used in both study arms. For the latter three assessment a special device, the medication event monitoring system, was used to record the time and date of each opening and closure of the container.

The compliance of the 320 hypertensive patients with once-daily amlodipine was markedly superior to twice-daily slow release nifedipine. Therapeutic coverage was also significantly better for amlodipine in the hypertensive patients. Amlodipine was better tolerated than nifedipine slow release.

Patient compliance and therapeutic coverage with the calcium antagonist amlodipine given once daily was superior to slow release nifedipine b.d. in hypertensive outpatients recruited in general practice.

Key words Amlodipine, Nifedipine, Compliance; slow release formulation, hypertension, therapeutic coverage

Patient compliance remains one of today’s major challenges to the physician. Despite the ever-increasing level of sophistication of pharmacological intervention and methods of drug delivery, patient compliance with therapy often remains poor. The problem of compliance is influenced by many factors, such as the effectiveness of the drug the complexity of the dosing schedule, side effects caused by therapy, the patient’s perception of the illness, communication with the physician, and etc. [1]. Another major factor influencing compliance in patients suffering from chronic illnesses is the large number of different medications that many are required to take simultaneously.
Compliance may be defined as the extent to which the actual time history of dosing corresponds to the prescribed regimen [2]. Patient compliance with therapy is a problem widely underestimated by practicing physicians, who frequently anticipate that their patients will simply take their medication according to the treatment schedule. Patients are sometimes dissatisfied with their physicians and do not respect the prescriptions written by them, often ignoring the advice given. At other times, poor compliance may be caused unintentionally by errors of information, lack of motivation and forgetfulness. Measurement of patient compliance is of variable importance in the interpretation of randomised clinical trials [3].

Patient compliance is of variable importance in different diseases but it is especially important in cardiovascular diseases, such as hypertension and ischaemic heart disease. In hypertension, for example, compliance is frequently low because of the asymptomatic nature of the condition [4] and poor compliance has been associated with an increased risk of death in postinfarction patients [5]. Interruption of medication by the patient can sometimes precipitate cardiovascular complications and, in some cases, the abrupt cessation of therapy can induce potentially serious withdrawal symptoms [6, 7].

It is also worthwhile mentioning the cost of non-compliance; according to the National Pharmaceutical Council [8], non-compliance in the US may result in an $8.5 billion extra cost for hospital admissions and physicians' visits. In the area of cardiovascular disease, considerable advances have been made by pharmaceutical companies in the development of drugs which have simple dosing regimens. In this open study, the compliance rates was compared in patients treated with slow release nifedipine 20 mg twice daily and amlodipine 5 mg once daily for the treatment of arterial hypertension.

**Material and methods**

**Patient selection**

Outpatients of either sex (age < 70 y) included in the study had been treated with slow release nifedipine or amlodipine for at least 4 weeks before inclusion. Their concomitant medications remained unchanged throughout the study. The diagnosis of hypertension was based on retrospective evaluation of mild to moderate hypertension (sitting diastolic blood pressure > 95 mm Hg to < 114 mm Hg, sitting systolic blood pressure > 150 mm Hg to < 200 mm Hg). Blood pressure was routinely monitored as the study was not designed to evaluate the comparative efficacy of the two drug regimens; at each of 3 visits, sitting systolic and diastolic BP were recorded with a standard mercury sphygmomanometer, after the patient had been sitting for at least 3 minutes. Excluded from the study were patients with severe or uncontrolled hypertension, unstable angina pectoris, serious heart failure or liver failure. Patients were asked to note adverse events in their diaries.

The study protocol was approved by the Ethics Committee of each participating centre (see title page). Written informed consent was obtained from each patient before entry into the study.

**Study design**

An equal number of patients, already receiving treatment with slow release nifedipine or amlodipine for a minimum of 4 weeks, was included in this multicentre study by each investigator. Patients were crossed over after the first 6 weeks of treatment, from slow release nifedipine to amlodipine or vice versa (Fig. 1).

**Compliance assessment**

Compliance over a period of 12 weeks was measured using two methods. The first was the pill count and the second was the Medication Event Monitoring System (MEMS). With this innovative technology, a small microprocessor in the cap of the tablet container records the time and date of each opening and closure of the container. Patients were informed that a device was being used to measure their drug intake. The parameters used to describe patient compliance are defined in Table 1. In these studies "correct" dosing is defined as % of days with correct dosing schedule (one a day or twice a day) as prescribed by the physician.

![Fig. 1 Trial scheme](image)