Clinical trials versus clinical practice in the secondary prevention of myocardial infarction

A. Agustí, J. M. Arnau, J.-R Laporte
Unitat de Farmacologia Clínica, Universitat Autònoma de Barcelona, Servei de Farmacologia Clínica, CSU Vall d’Hebron, Barcelona, Spain

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Abstract. To examine whether the results of trials on the secondary prevention of myocardial infarction have led to a change of prescription practice, the discharge forms of a random sample of 737 patients admitted to a university hospital with a diagnosis of acute myocardial infarction (MI) with Q wave from 1982 to 1988 were examined.

Information about cardiovascular and other risk factors, contraindications, and prescription of β-adrenoceptor antagonists (βAA), acetylsalicylic acid (ASA) and calcium channel blockers (CCB) was collected. The prescription of these drugs was analysed in relation to clinical variables and the date of patients’ discharge from hospital.

During the 7 years of follow-up, the prescription of βAA increased gradually from 20% to 30–35%; the prescription of CCB was above 30% during the same period and did not change significantly with time. The prescription of ASA increased from 0% to 30–35% in the last 3 years of follow-up. Contraindications to βAA were present in 23.2% of cases and contraindications to ASA in 14.4%. In a multivariate analysis, hypertension (odds ratio 2.29, 95% confidence interval 1.55–3.38) and the period 1986–1988 (OR 2.27, 95% CI 1.57–3.30) were associated with the prescription of βAA, although the prescription of βAA decreased significantly with advancing age. Other variables inversely associated with the prescription of βAA were contraindications (OR 0.41, 95% CI 0.24–0.66) and the presence of heart failure during admission (OR 0.08, 95% CI 0.03–0.20). The prescription of CCB was inversely associated with the prescription of βAA (OR 0.41, 95% CI 0.27–0.63); the preference for CCB over βAA was notable among patients with the following characteristics: age > 70 years (39.3% vs 9.3%), heart failure during admission (25.5% vs 3.2%), and contraindications to the use of βAA (28.1% vs 11.1%).

The only clinical variable which was significantly (and inversely) associated with the prescription of ASA was the presence of contraindications (OR 0.13, 95% CI 0.04–0.41).

These results suggest that clinical trials on the secondary prevention of ischaemic heart disease have had some influence on cardiologists’ prescription habits. However, they document a large underuse of efficacious drugs such as βAA and ASA, especially among the elderly and among those patients with more severe cardiovascular disease. The frequent prescription of CCB recorded in the present study, in spite of their unproven efficacy in this condition, suggests that these drugs are often preferred to βAA for the survivors of an acute MI, especially in certain groups of patients.

Key words: Myocardial infarction, Drug utilization; secondary prevention, β-adrenoceptor antagonists, acetylsalicylic acid, calcium channel blockers

During the last decade much progress has been made in the secondary prevention of coronary heart disease [1–9]. However, little is known about the potential influence of this progress on clinical practice [10–15]. At present, the efficacy of β-adrenoceptor antagonists (βAA) and of acetylsalicylic acid (ASA) in the secondary prevention of myocardial infarction (MI) is well established [16], but scarce data are available on the proportion of patients who may benefit from these drugs and on the factors (if any) which are associated with the prescription of βAA and ASA in routine clinical practice. The efficacy of calcium channel blockers (CCB) in this indication has also been evaluated, but the results of clinical trials have yielded conflicting results, and a meta-analysis could not document any benefit from these drugs [17]. In patients who have survived an acute MI, βAA and CCB may have some common indications (hypertension and angina).

The aim of the present study was to examine whether the results of secondary prevention trials have led to a change of prescription practice for patients who have survived an episode of MI at their discharge from hospital. The prescription of βAA and ASA to patients surviving
followed up. We have also examined the clinical variables describing the time trend of the prescription of CCB during the past few years in our hospital and in identifying and establishing the relationship, if any, between the prescription of flAA and that of CCB.

### Patients and methods

The study population was a random sample of patients who were discharged from our hospital with a diagnosis of acute MI with Q-wave from 1982 to 1988. This study period was selected because it was in 1982 that evidence on the efficacy of βAA was published for the first time [3,4]. Patients with non-Q-wave MI were excluded because the efficacy of βAA in this subgroup had been questioned in the reports of two of the biggest trials, the Beta-Blocker Heart Attack Trial (BHAT) [1] and the Norwegian Multicenter Study on Timolol (NMST) [2]. Information about diagnosis, other clinical variables (see Table 1) and treatments prescribed at discharge was obtained from the hospital discharge forms. The following were considered contraindications to the use of βAA: a history of chronic obstructive bronchitis or wheezing, intermittent claudication, heart failure before admission, and permanent A-V block (second or third degree). The presence of heart failure during admission (mild to severe according to Killip's classification) was analysed independently, because this is a marker of poor prognosis, rather than a contraindication. Contraindications to the use of ASA were previous gastroduodenal ulcer or its complications or a history of hypersensitivity to acetylsalicylic acid or to other non-steroidal antiinflammatory drugs.

The number of patients was calculated considering that 25 % of survivors of an acute MI would present with a condition (i.e. hypertension or angina) which would by itself be a clinical indication for βAA treatment. This proportion was extrapolated from previous studies [1,2]. We also expected a rise in prescribing of βAA and ASA to as many as 50% of eligible patients.

Analysis of the results was performed with the statistical package SPSSx. A value of P < 0.05 was considered as statistically significant. A logistic regression analysis with the statistical package BMDP was also performed. Prescription of βAA, prescription of ASA, and prescription of both βAA and ASA, ASA were considered as dependent variables, and the baseline clinical characteristics were considered independent variables (Table 1). The year of discharge (1982-1985 vs 1986-1988) and the treatment with CCB were also considered as independent variables.

To study the relationship between the prescription of βAA and that of CCB, the following variables have been taken into account: sex, age, presence of cardiovascular disease (i.e. hypertension and angina) before MI, contraindications to the use of βAA, heart failure during admission (according to Killip's classification), the location of the infarction and a history of previous MI.

### Results

The characteristics of the 737 patients included in the study are shown in Table 1. Table 2 shows the prevalence of drug prescription during the whole study period. The prevalence of the prescription of βAA, ASA, at least one of them (βAA and/or ASA), and CCB through the study period is shown in Fig. 1. The prescription rate was 0% for ASA and 20% for βAA in 1982 and 30-35% for both groups of drugs at the end of the study period. During the 7 years of follow up, the prescription of βAA increased abruptly, whereas the prescription of ASA increased more abruptly from 1985 and 1987. The percentage of patients discharged with a prescription of βAA and/or ASA increased mostly at the expense of an increase in ASA prescriptions. The prevalence of the prescription of CCB was higher than 30% and quite constant through the study period; it showed small annual differences which were not statistically significant. In 1988, 34% of the patients discharged with a diagnosis of acute MI from our hospital were prescribed βAA, while 44% were prescribed CCB.