Ivabradine in combination with beta-blocker improves symptoms and quality of life in elderly patients (≥ 75 years) with stable angina pectoris: age-related results from the ADDITIONS study

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Introduction

Several clinical trials have demonstrated the anti-anginal and anti-ischemic efficacy of ivabradine in combination with beta-blocker in patients with stable angina pectoris. The ADDITIONS (PrActical Daily efficacy anD safety of Procoralan In combinaTION with betablockerS) study evaluated the effectiveness and tolerability of ivabradine added to beta-blocker, and its effect on angina symptoms and quality of life in routine clinical practice.

Methods

This non-interventional, multicenter, prospective study included 2,330 patients with stable angina pectoris of different age groups treated with a flexible dose of ivabradine twice daily in addition to beta-blocker for 4 months. The parameters recorded included heart rate (HR), number of angina attacks, nitrate consumption, tolerability, and quality of life (QoL). A subgroup analysis was performed, focusing on the age group ≥75 years. Descriptive statistical methods were applied for data evaluation.

Results

Of 2330 patients (intention to treat, mean age 65.9 ± 10.7 years, 59% male) with chronic stable angina pectoris analyzed, 36% had a history of myocardial infarction. All patients in the study population received beta-blockers and also concomitant standard medication (e.g. aspirin 80%, statins 73%, ACEI/ARB 79%, long acting nitrates 14%, calcium antagonists 18%), 21% (n=479) of patients in the total cohort were elderly patients with at least 75 years of age. Patients of this elderly subgroup received beta-blocker treatment at baseline as follows: Metoprolol 43%, mean daily dose (mdd) 101.4 mg; Bisoprolol 35%, mdd 6.5 mg; Nebivolol 14%, mdd 4.6 mg; Carvedilol 7%, mdd 27.5 mg. At baseline, mean HR was 84.6 ± 12.2 bpm in elderly patients (Table 1). Average number of angina attacks per week was 2.0 ± 2.2 and the average consumption of short-acting nitrates per week reached 2.8 ± 3.6 units. 77% of patients were classified CCS grades II and III, 22% were CCS grade I. EQ-5D QoL index was 0.57 ± 0.28.

After 4 months of treatment, ivabradine (mean dose 11.60 ± 3.18 mg per day) reduced HR by 19.2 ± 11.6 bpm to 65.4 ± 8.3 bpm in the elderly patients subgroup (Fig. 1). The average number of angina attacks per week was decreased by 1.6 ± 1.8 to 0.4 ± 1.3 and the average consumption of short-acting nitrates per week dropped by 2.2 ± 3.2 to 0.6 ± 1.8 units (Fig. 2+3). At the end of the treatment period, a pronounced shift in CCS grade distribution could be seen. Most elderly patients (57%) were now classified CCS grade I, 42% were in CCS grades II and III (Table 4+5). This was also accompanied by an improvement in EQ-5D QoL index to 0.75 ± 0.22 (Fig. 6). No increases in beta-blocker dosages could be detected during the study period. Tolerability of ivabradine treatment was rated by the physicians "very good/good" for 72%-28% of elderly patients.

Conclusion

In this study over 4 months in daily clinical practice, ivabradine in combination with beta-blockers was effective in reducing HR, angina attacks and nitrate consumption in a cohort of elderly patients (≥75 years) with stable angina pectoris. In addition, treatment with ivabradine markedly improved CCS symptom scores and quality of life in these patients. Treatment was generally very well tolerated.

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