Angina and hypertension

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Case report

The majority of patients with stable coronary heart disease (SCHD) have diverse comorbidities, such as hypertension (HTN), dyslipidaemia, diabetes mellitus (DM), and heart failure with reduced or preserved ejection fraction. Because they are already under treatment with RAS and/or beta-blockers, their blood pressure (BP) and heart rate (HR) probably should be low. In the CLARIFY study,1,2 in patients with angina, 70% and 75% of the patients had a history of arterial HTN and dyslipidaemia, respectively, while 30% suffered also from DM. Individualizing antianginal treatment taking into consideration comorbidities and concurrent drug indications or contraindications, represents a reasonable option for patients with stable angina, since drug treatment may confer benefits that go beyond angina relief3,4 (Table 1).

This is a case study of a 72-year-old male patient referred to a community doctor with long-standing history of HTN, previous inferior myocardial infarction with right coronary artery percutaneous coronary intervention, and frequent episodes of angina in effort. The patient was obese and had a medical history of hyperlipidaemia, DM, and chronic obstructive pulmonary disease (COPD). The patient was under treatment with: ramipril 5 mg o.d., metoprolol 50 mg b.i.d., atorvastatin 20 mg o.d., acetylsalicylic acid 100 mg o.d., and long-acting nitrates.

On physical examination, the patient was in good general condition. The BP levels were 126/70 mmHg, while the electrocardiogram was in sinus rhythm of 74 b.p.m. with Q waves in II, III AVF leads. The patient also provided an echocardiogram with no signs of LVH, inferolateral akinesia, with global left ventricular ejection fraction of 40%. The laboratory exams were within normal limits. The patient was referred for coronary angiography without previous non-invasive test which demonstrated: right coronary artery without in stent re-stenosis, other coronary vessels: atheromatous without significant obstructive lesions [fractional flow reserve of a 60-70% stenosis at mid in left anterior descending artery under maximal hyperaemia was (0.88)]. The decision of his physician was to proceed with optimization of medical regiment adding a new antianginal drug.

After the assessment of the clinical condition and the laboratory exams of the patient several clinical questions regarding the therapeutic strategy emerged.

What is the BP Target? Current American College of Cardiology/American Heart Association guidelines but also the new European Society of Hypertension/European Society of Cardiology guidelines advocate lowering BP levels below 130/80 mmHg in patients with CAD receiving BP-lowering drugs.5 In the contrary, ESH/ESC guidelines recommend that systolic blood pressure levels in those patients should not be decreased below 120 mmHg since there are studies proving that lowering BP levels below this threshold could be deleterious. Actually, in the CLARIFY registry they noticed that a BP lower than 120/70 mmHg was accompanied with higher cardiovascular risk.

Which antianginal drug to use? Based on the ESC guidelines for SCHD, the following options are available: (i) increasing the dose of the beta-blocker, (ii) adding diltiazem or calcium channel blocker, (iii) adding ivabradine, (iv) adding ranolazine, (v) adding nicorandil, and (vi) adding trimetazidine. In this patient, administrating an antianginal drug with BP-lowering effects (as calcium channel blockers) could be deleterious since his SBP levels were near 120 mmHg. Nitrates have shown to increase oxidative stress and may cause endothelial dysfunction, while there are no new data and strong evidence supporting the use of nitrates in SCHD. Thus, an antianginal drug with no or minimal effects on BP and such as ivabradine, ranolazine, or trimetazidine should be preferred. Since his heart rate is 74 b.p.m., ivabradine could be an option. In addition, the patient also suffered from COPD and DM. Thus, an antianginal drug with favourable effect on DM such as ranolazine or trimetazidine will be preferred. Moreover, since the patient has COPD a cardioselective beta-blocker other than metoprolol should be preferred, such as bisoprolol. Finally, based on the EUROPA and SMILE-4 trial, I would suggest as Ace inhibitors, either perindopril or zofenopril.
From the aforementioned approach, it is clear and proven from the literature, that some antianginal agents when compared to others possess auxiliary properties, not only limited to the relief of anginal symptoms. Improving glucose profile in patients with DM and angina, achieving HR control or avoiding high or low arterial BPs must also be objectives when considering a particular therapeutic approach. Thus, treatment has to be tailored taking into account patients’ risk factors and comorbidities (and the favourable and unfavourable effects of a given antianginal drug to them) but also the haemodynamic parameters as HR and BP levels. Using an algorithmic approach to tailor antianginal therapy is strongly advocated.

In this case, I would propose the following treatment for this person:

For event prevention: perindopril or zofenopril, atorvastatin, and aspirin.

For angina relief: bisoprolol, discontinuation of LAN and addition of ivabradine, ranolazine, or trimetazidine.

Consent statement

The patient’s consent to report the case has been obtained.

Conflict of interest: A.J.M. has received honoraria for steering committee membership from Bayer, Cardiorentis, and Novartis; received support for travel to study meetings from the same companies; and received personal fees for speaking activities from Amgen, Lilly, Sanofi, and Servier. M.S.K. has received honoraria for participation in advisory boards and/or speaker fees from Servier Hellas, Elpen, Menarini, Win. L.E.P. has received honoraria for participation in advisory boards and/or speaker fees from Astra Zeneca, Bayer, Boehringer Ingelheim, Menarini, Merck Sharp Dohme, Sanofi. The authors didn’t receive any financial support in terms of honorarium by Servier for the supplement articles.

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Table 1  Stable angina and specific conditions

| Preferred drugs (listed alphabetically) | Intolerance to BB/non-DHP CCB | DHP’s, ivabradine, LA nitrates, nicorandil, ranolazine, trimetazidine |
|----------------------------------------|-------------------------------|-------------------------------------------------------------|
| Low HR                                 | DHP’s, ivabradine, LA Nitrates, nicorandil, ranolazine, trimetazidine |
| AF                                    | DHP’s, ivabradine, LA Nitrates, nicorandil, ranolazine, trimetazidine |
| CHF                                    | Dihydropyridines, ivabradine, LA Nitrates, nicorandil, ranolazine, trimetazidine |
| Microvascular ischaemia               | Beta-blockers (rate control), non-DHP’s (rate control), ranolazine |
| Diabetes mellitus                     | Beta-blockers, ivabradine, possibly nitrates |
| COPD                                   | Beta-blocker, DHP, nicorandil, ranolazine |
|                                        | Beta-blockers, ranolazine, trimetazidine, vasodilating |
|                                        | Beta-blockers (cardioselective), DHP’s, ivabradine, LA Nitrates, nicorandil, ranolazine, trimetazidine |

AF, atrial fibrillation; AV, atrioventricular; BB, beta blockers; BP, blood pressure; CHF, chronic heart failure; COPD, chronic obstructive pulmonary disease, DHP, dihydropyridines; HR, heart rate; LA, long acting.