EDITORIAL

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A new perspective on calcium channel blockers in vasospastic angina

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Vasospastic angina (VA) is characterized by chest pain and electrocardiogram changes caused by reversible coronary artery spasm, and is common among Asians [1]. Compared to atherosclerotic coronary artery disease, VA has a good prognosis because it responds well to vasodilators. However, VA can be fatal by causing acute myocardial infarction or ventricular arrhythmia [1,2]. To prevent such complications, VA patients should take medications appropriately and avoid trigger factors for coronary artery spasm such as cigarette smoking. Coronary vasodilators are effective drugs for the prevention of vasoconstriction episodes in VA patients, and include calcium channel blockers (CCBs) and nitrates. CCBs are effective for the prevention of episodes of coronary vasospasm [1,3-5], and are recommended as first line treatment in VA. CCBs noncompetitively block voltage-sensitive L-type calcium ion channels in coronary smooth muscle, causing coronary artery dilatation. According to their mechanism of action, CCBs are classified into three categories: dihydropyridines such as nifedipine, amlodipine, and felodipine, phenylalkylamines such as verapamil, and modified benzothiazepines such as diltiazem. CCBs are also classified according to the time they were developed. First generation CCBs such as verapamil, diltiazem, and nifedipine were developed in the 1980s, and have been used for angina. Newer CCBs such as amlodipine and benidipine were developed in the 1990s [3]. Because diltiazem has been available longer, there are more data on its use, and diltiazem is the most commonly prescribed CCB for VA patients in Korea [6] and Japan [7]. Although the efficacy of newer CCBs such as amlodipine and benidipine for the prevention of VA has been proven in several studies [3,8,9], their use in VA patients remains less than that of diltiazem. Diltiazem is effective in VA patients and has few side effects, and the use of second generation CCBs has not increased as much as expected in VA patients. Because cardiovascular effects and adverse reactions are slightly different for each CCB [10], increasing the number to choose from should be beneficial to clinicians and patients. For example, if similar efficacy for prevention of a VA episode is guaranteed, the second generation CCBs could replace diltiazem, particularly in VA patients with bradycardia, because they do not have the side effect of bradycardia. It is important to know which CCBs are most effective in different clinical situations to provide the best personalized treatment to VA patients. However, comparative analyses of effectiveness

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among CCBs in large numbers of patients with VA have been scarce [7,8]. In particular, there are insufficient data on whether the new generation CCBs are as effective as the first generation CCBs [8]. Thus, the research results presented by Kim et al. [6] deserve clinical attention. The authors of this study investigated 1,586 patients with significant or intermediate vasospasm using an ergonovine provocation test, and demonstrated that the occurrence of composite events including death, acute coronary syndrome (ACS), and symptomatic arrhythmia during a 3-year clinical follow-up did not differ between patients treated with first (nifedipine and diltiazem) and second (amlodipine and benidipine) generation CCBs. However, the ACS incidence rate was significantly lower in patients treated with second generation CCBs. In addition, benidipine was more effective than other CCBs in reducing symptoms of angina in this study. In terms of the occurrence of clinical events in VA patients, this study suggests that second generation CCBs can be effectively used for VA patients like the first generation CCBs. Considering that second generation CCBs are more effective than the first generation CCBs in lowering ACS events, it is necessary to strongly consider the use of second generation CCBs for patients at high risk of ACS development in the future. Amlodipine, the most widely used second generation CCB for VA, is also widely used as an antihypertensive agent, because it has excellent blood pressure lowering effects. For VA patients who need blood pressure control, amlodipine may be the first choice. In addition, the once-daily dosing with long-acting CCBs such as amlodipine has an advantage in terms of drug adherence compared to diltiazem, which requires multiple daily doses. The CCB benidipine is not used frequently in Korea. However, the effect of benidipine in improving clinical outcomes in VA patients has been reported in several studies in Japan [8,9]. As a VA treatment drug, with the same or a superior prognosis compared to diltiazem, benidipine may be a better therapeutic option for VA patients with frequent symptomatic episodes. We can now expand our treatment options for VA patients, and not just use diltiazem. It may even be necessary to use amlodipine or benidipine as the primary treatment option for some VA patients. However, it is important to recognize a limitation of the Kim et al.'s [6] study; a relatively small number of patients taking second generation CCBs was enrolled. Further study of a larger number of patients taking second generation CCBs is warranted to clarify the role of second generation CCBs in the treatment of VA patients.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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