Mechanism of Cardiovascular Effects of Contrast Media: Evidence for Transient Myocardial Calcium Ion Imbalance*

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The current issue of the Journal contains two reports (1,2) relating to the cardiotoxicity of radiographic contrast media. Although complications of coronary arteriography directly attributable to contrast media are uncommon, these media induce hemodynamic and electrophysiologic changes in nearly all instances (3). The site of injection of contrast medium is a major factor in the type and severity of the cardiovascular effects (4). Injection into the coronary arteries or into the left ventricle can produce transient hypotension. With intracoronary injection the hypotension results from negative inotropic and chronotropic effects; with intraventricular injection it is a reflection of peripheral vasodilation.

Mechanisms of hemodynamic and electrophysiologic effects. Current experimental results (3) point to multiple mechanisms mediating the hemodynamic and electrophysiologic effects. The peripheral vasodilation seems to be closely related to the degree of hyperosmolality of the contrast medium. Likewise, inhibition of the function of sinoatrial and atrioventricular (A V) nodal tissues and other electrophysiologic actions parallel osmolality (4-6). However, the cause of the negative inotropic effects can be traced to hyperosmolality, introduction of excess sodium or other single valence cations and decreased levels of ionic calcium in the myocardium (3,6,7). The most important factor seems to be that the intracoronary injection of contrast medium produces a transient imbalance in the ratio of calcium ions to sodium ions (3,7,8). These reports demonstrated the decrease in myocardial calcium ion as a critical factor responsible for the cardiac effects of ionic contrast medium. Moreover, the negative inotropic effects are accentuated and prolonged in dogs with induced systemic hypocalcemia (7). Addition of calcium ions to contrast medium alleviates the chronotropic, dromotropic and inotropic effects of intracoronary injection of ionic contrast medium (8). The two reports (1,2) in the current issue provide further evidence for the importance of an imbalance in calcium ions in the myocardium as a proximate mechanism of the cardiac effects.

A study (7) reported by our group several years ago indicated a parallel decrease in the indexes of myocardial contractile state and ionic calcium in the coronary sinus blood. The study reported in this issue by Bourdillon et al. (2) supports this observation using a method capable of providing closer temporal correlation between contractile indexes and coronary sinus levels of calcium ion. Their study and earlier studies (8,9) showed that addition of calcium ion to contrast medium alleviates the negative inotropic effects.

Interaction of contrast medium and calcium antagonist drugs. Recognizing the importance of induced hypocalcemia in the myocardium as the mechanism of cardiotoxicity of contrast media, one is led to speculate on a possible interaction between contrast media and calcium antagonist drugs. Because coronary arteriography is frequently performed on patients being treated with calcium antagonists, this interaction could be frequent and important. Two recent reports (10,11) revealed not only an additive but probably a synergistic interaction of contrast media and verapamil in causing AV block in dogs (10,11). This deleterious interaction was not observed with nonionic (iophexol) or low osmolality (Hexabrix) contrast media (10,11).

The report by Morris et al. (1) in the current issue of the Journal reveals a more severe degree of hypotension after injection of ionic contrast media (Renografin-76 and Hypaque-76) into the left ventricle of patients treated with nifedipine or diltiazem compared with those who were not receiving calcium antagonists. No deleterious interaction between nonionic contrast medium and the calcium antagonist was apparent in this study. The results of prior canine studies and the current studies in patients indicate the advisability of discontinuing calcium antagonist therapy in patients undergoing coronary arteriography. With the anticipation of approval from the Food and Drug Administration for use of nonionic contrast media for intravascular injection, these studies identify a group of patients in whom it may be preferable to perform coronary angiography with nonionic contrast media. Despite the anticipated high cost of these media their added safety may indicate their use in certain clinical circumstances such as in patients being treated with calcium antagonists. They may also be indicated in patients at higher risk for complication such as those with severe aortic stenosis, congestive heart failure and low cardiac output states.

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Cardiac angiography is uneventful in most patients and, consequently, concern about cardiovascular side effects of contrast media is usually a remote theoretical consideration. However, we would warn against complacency regarding these pharmacologic agents. Studies revealing the mechanism of cardiotoxicity indicate some situations in which theoretical considerations can be manifested as clinical complications.

References


