Hypotension, Nitroglycerin, and Acute Myocardial Infarction

It is widely recognized that hypotension may lead to serious consequences in the patient suffering an acute myocardial infarction. The fear of hypotension is amply justified and originates, in large part, from the poor outcome in patients who develop cardiogenic shock. Under these circumstances hypotension is a result of pump failure due to massive myocardial damage, but the diminished arterial pressure itself undoubtedly plays a causal role in the usually lethal cycle characterized by diminished coronary perfusion pressure, greater ischemic injury, more severe hypotension, etc. In addition, any baroreceptor-mediated increase in heart rate and myocardial contractility (caused by the reduction in arterial pressure) would tend to raise myocardial oxygen demand and thereby further augment the ischemic insult. These considerations understandably have focused the physician’s attention on the prompt treatment of hypotension and the avoidance of any drugs that may reduce blood pressure in patients with acute myocardial infarction.

An interesting paradox exists, however, insofar as most of us accept the dogma that the decrease in blood pressure produced by vasodilators (in particular, nitroglycerin) is potentially lethal in the patient with acute myocardial infarction, but almost invariably benefits the patient with angina pectoris. The relief afforded by nitroglycerin to the patient with angina pectoris has been well documented. The concept that nitroglycerin is deleterious during acute myocardial infarction, however, has been untested until very recently. Surprisingly enough, rather than supporting the clinical bias against the use of nitroglycerin during acute myocardial infarction, these recent studies suggest that, under certain circumstances, vasodilators may exert beneficial effects. For example, Franciosa and co-workers showed hemodynamic improvement in some patients with depressed cardiac output during acute myocardial infarction after administration of the vasodilator nitroprusside,1 and Gold et al. reported similar results following administration of nitroglycerin to patients with long-standing cardiac decompensation consequent to myocardial infarction.2 However, hemodynamic improvement is not necessarily indicative of reduced ischemic injury since the peripheral or reflex effects of a vasodilator could improve the net pumping performance of the heart at a time when the degree of ischemic injury of the involved portion of myocardium is unchanged or even increased.

To assess more directly the effects of nitroglycerin on the actual degree of ischemic injury occurring during acute myocardial infarction, the S-T segment changes recorded by intramyocardial electrodes were analyzed during occlusion of the left anterior descending coronary artery of the conscious dog.3 The results indicated that nitroglycerin could indeed cause an actual diminution of ischemic injury. Nitroglycerin also was found to minimize the decrease in ventricular fibrillation threshold caused by acute coronary occlusion.4 These effects were demonstrated despite the associated hypotensive action of the drug.

It might be postulated from these results that nitroglycerin-induced hypotension contributes to the beneficial effects of the drug during acute coronary occlusion by lowering myocardial oxygen requirements secondary to decreased afterload, a mechanism commonly cited as contributing to the salutary effects of nitroglycerin in relieving the pain of angina pectoris. Such an explanation presumes that this beneficial effect of hypotension counterbalances the deleterious effects accruing from both the decrease in coronary perfusion pressure and the reflex increase in sympathetic stimulation to the heart. However, some insight into the complexities of the interaction between blood pressure changes and myocardial ischemia is afforded by the observation that when a reduction in blood pressure equivalent to that produced by nitroglycerin is produced by hemorrhage, the intensity of the ischemic insult during coronary occlusion tends to increase.5 More dramatically, when the reduction in blood pressure caused by nitroglycerin is abolished by simultaneous administration of either methoxamine or phenylephrine, ischemic injury diminishes to an even greater extent than when nitroglycerin is

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given alone and pressure allowed to fall. It therefore seems likely that the reduction of ischemia produced by nitroglycerin does not depend upon a diminution of systemic arterial pressure. Indeed, these results suggest that nitroglycerin-induced hypotension actually augments the degree of ischemia during acute coronary occlusion; its deleterious effects, however, seem to be overridden by other actions that lead to a net reduction in ischemic injury. Whether the net benefit results from actions of nitroglycerin that increase blood flow to ischemic areas (by effects on coronary arterial or collateral flow), or from the capacity of nitroglycerin to decrease myocardial wall tension and, thereby, MVO₂ (by causing venous pooling and decreased ventricular volume) is unknown. It also is unknown whether desirable effects will accrue to the patient with acute myocardial infarction who has critical narrowing of more than one major coronary artery, since, under these conditions, nitroglycerin theoretically could be deleterious by predisposing to intracoronary pressure changes that would lead to a "coronary steal" situation.

Definitive answers regarding the proper approach of the physician toward hypotension occurring spontaneously (in the absence of cardiogenic shock) or induced pharmacologically during acute myocardial infarction do not as yet exist. It is apparent, however, that hypotension cannot be considered as an isolated, independent phenomenon, but must be evaluated in the context of the specific conditions in which it occurs; different hemodynamic changes occur when hypotension is produced by vasodilators than when it is the result of hemorrhage or massive cardiac necrosis. Therefore an a priori estimate of net beneficial or deleterious effect of vasodilators on the course of acute myocardial infarction cannot be inferred from the risks associated with hypotension occurring secondary to pump failure. Similar considerations apply to the mild-to-moderate hypotension that not infrequently accompanies the bradycardia present in many patients during the early phases of acute myocardial infarction. Thus, it is not at all clear that the risk of such patients is increased; and, while administration of atropine in this situation may raise blood pressure, it would also evoke the potentially deleterious effects a faster heart rate has on the degree of myocardial ischemia and on the electrical stability of the ischemic ventricle.

Although the relation between hypotension and ischemic injury is complex, it is clear that the long-standing clinical admonition not to administer nitroglycerin or other hypotensive agents to patients with acute myocardial infarction needs reevaluating. Moreover, if further clinical studies confirm a wider role for vasodilators in acute myocardial infarction, it would be reasonable to consider whether patients should be advised to self-administer nitroglycerin (in the supine position with legs elevated to minimize the risk of excessive hypotension) during the prehospital phase of acute myocardial infarction; if the drug does improve hemodynamics, decrease ischemic injury, and increase electrical stability of the ventricle, its use in this circumstance may decrease the incidence of arrhythmic death.

Regardless of the final answers that emerge relating to the specific questions raised in this discussion, it is to be hoped that a greater understanding of the effects various pharmacologic interventions have on the myocardial, electrophysiologic, and arrhythmic changes induced by acute myocardial infarction will lead to new modes of therapy capable of ameliorating ischemic injury and of reducing the morbidity and mortality of acute myocardial infarction.

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References

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