Nitroprusside in Circulation

To the Editor:

I read with great enthusiasm the article by Pagani et al. as contributing to our understanding of the effects of nitroprusside in the intact circulation. However, their interpretation of data showing a decrease in left ventricular end-diastolic dimension due to "...venodilation which undoubtedly contributed to the reduction of preload," is regrettable. The interpretation lacks the necessary supportive measurements of venodilation of the peripheral blood vessels, and it fuels the controversy surrounding models of storage and resistance properties of the peripheral blood vessels.

Other investigators, cited by the authors in support of their interpretation, have also failed to make simultaneous measurements of left ventricular and peripheral blood vessel volume. One investigator reported qualitative decrease in heart and kidney volume and increase in leg volume. It is a common tautology to assume that when measurement of left ventricular volume or pressure decreases, that venous volume increases. This simple logic assumes that volume distribution is subdivided into a two compartment model with volume storage in the left ventricle and peripheral veins. Once having made this assumption, it can be stated that nitroprusside causes venodilation by observing a decrease in left ventricular volume alone. Even limited measurement of forearm venous tone, along with volume or pressure of the left ventricle, is not adequate information to understand changes of volume distribution in the circulation.

Other models of the circulation, in addition to two volume storage elements, may account for changes in volume distribution without venodilation. In one model, for example, a decrease in arterial resistance alone could increase peripheral blood volume without venodilation.

Intact circulatory physiology is greatly benefitted by the work these authors have contributed in unanesthetized animals. However, caution should be observed to avoid postulating physiological mechanisms in an unmeasured compartment of the circulation based on data from a measured compartment.

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References


The authors reply:

To the Editor:

We appreciate Dr. Rubin’s comments on our investigation “Hemodynamic Effects of Intravenous Sodium Nitroprusside in the Conscious Dog.” Dr. Rubin, however, disagrees with our analysis of the reduction in end-diastolic size, with particular regard to nitroprusside’s effects on the venous system. We stated that “The reduction in left ventricular dimensions induced by nitroprusside reflects the effects of both tachycardia and decrease in both preload and afterload.” We further went on to state that “the drug induces venodilatation which undoubtedly contributes to the preload.” The crucial role of venous tone in the regulation of venous return and hence cardiac size is well-recognized. There is considerable evidence in the literature, as well as in our investigation on nitroprusside, which support the concept that nitroprusside dilates peripheral veins and contributes to the reduction in preload. First of all, Miller et al. have found that nitroprusside reduces venous tone. Secondly, we observed that 5–10 minutes after cessation of nitroprusside infusion, left ventricular end-diastolic pressure and diameter were still significantly reduced at a time when the peripheral arterial circulation showed a significant elevation in vascular resistance, and heart rate and myocardial contractility were at the pre-infusion control levels. Therefore, at that time the reduction in end-diastolic diameter could not be attributed to arterial vasodilation, nor could it be attributed to tachycardia. Since end-diastolic cardiac size, as well as pressure, were significantly reduced at this time, it appears that this effect must have been due to persistent venodilation and peripheral pooling of blood.

In summary, we feel that Dr. Rubin’s comments are very important to consider, i.e., that more precise measurement techniques need to be developed to measure venous tone and volume in the intact animal and man, and that one should not extrapolate from other measurements to conclusions regarding the venous bed. However, in this particular situation, i.e., the action of nitroprusside, it is generally accepted from the measurements made by Miller et al., as well as those data in our study, which support the concept that nitroprusside also acts to dilate veins as well as arterioles.

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