Effects of Atrial Natriuretic Factor on Baroreceptor Reflexes

Akira Takeshita

Editorial Comment

It is now evident that atrial natriuretic factor (ANF) exerts neural effects in addition to vasorelaxant, depressor, and renal effects. The study by Ferrari et al. examined the effects of intravenous ANF at doses within the pathophysiological range on arterial baroreceptor reflex control of heart rate and vascular resistance in conscious rats. Their results indicate that ANF markedly potentiated reflex bradycardia in response to phenylephrine but attenuated reflex tachycardia in response to nitroprusside and did not alter reflex increases in vascular resistance caused by carotid occlusion. What might be the mechanisms underlying these complex effects of ANF on arterial baroreceptor reflex function?

Previous investigators have shown that ANF markedly affects reflex control of sympathetic nerve activity. Thoren et al. and Imaizumi et al. demonstrated that, in anesthetized rats with intact baroreceptors, ANF inhibited sympathetic nerve activity or prevented expected reflex increases in sympathetic nerve activity during hypotension. The sympathoinhibitory effect of ANF was abolished by bilateral vagotomy, which suggested that this effect was mediated by activation of afferent vagal activity. These results could account for the findings in the earlier studies that bilateral vagotomy attenuated hypotension induced by the administration of crude atrial extracts. ANF decreases venous return and thus cardiac filling pressure, which would deactivate cardiopulmonary receptors and induce reflex increases in sympathetic nerve activity. Therefore, the findings of Thoren et al. and Imaizumi et al. strongly suggest that ANF sensitizes cardiopulmonary receptors as activation of afferent vagal activity by ANF occurs despite decreased cardiac filling pressure. Other studies have reported increased sympathetic nerve activity during intravenous infusion of ANF in animals with intact baroreceptors. However, the latter results do not necessarily contradict the suggestion made by Thoren et al. and Imaizumi et al. The reflex changes in sympathetic nerve activity in vivo are a function of the competing influences of altered reflex control by ANF and hemodynamic changes.

Previous investigators have also investigated the effect of ANF on arterial baroreceptor reflex control of sympathetic nerve activity. It has been demonstrated that anticipated reflex increases in sympathetic nerve activity did not occur during hypotension caused by ANF in rats with the vagi sectioned and with intact arterial baroreceptors. These results suggest that, in addition to the effect on vagal afferents, ANF alters arterial baroreceptor reflex control of sympathetic nerve activity. Hirooka et al. demonstrated in anesthetized rabbits that the aortic diameter and aortic nerve activity remained unchanged during hypotension caused by ANF, whereas they were decreased during hypotension caused by nitroprusside. During hypotension caused by ANF, aortic nerve activity remained unchanged because ANF dilated the aorta, and thus the strain of aortic baroreceptors did not decrease despite hypotension. These results suggest that reflex increases in sympathetic nerve activity do not occur during hypotension caused by ANF as aortic nerve activity does not decrease despite hypotension. Because ANF did not alter the relation between changes in the aortic diameter and those in aortic nerve activity, it is unlikely that ANF sensitized aortic baroreceptors. Thus, it appears that ANF alters arterial baroreceptor reflex control of sympathetic nerve activity by causing vasodilatation, whereas ANF augments sympathoinhibition mediated by cardiopulmonary baroreceptor reflex by sensitizing receptors.

Thus, ANF prevented changes in aortic nerve and sympathetic nerve activity expected to occur during ANF-induced hypotension. However, previous investigators also have shown that ANF did not modulate changes in aortic nerve and sympathetic nerve activity in response to rapid changes in arterial pressure caused by phenylephrine or nitroglycerin. A possible explanation for these complex effects of ANF on the arterial baroreceptor reflex might be that ANF causes vasodilatation of the vessels where baroreceptors are located but does not modulate changes in the aortic diameter associated with changes in arterial pressure caused by other means. Thus, the previous results could explain the finding by Ferrari et al. that ANF failed to modify pressor...
response to carotid occlusion. However, the results of Ferrari et al\(^1\) do not indicate that arterial baroreceptor reflex control of vascular resistance is unaltered by ANF. As discussed previously, reflex increases in sympathetic nerve activity and thus vascular resistance mediated by arterial baroreceptors do not occur during hypotension caused by ANF. Also, the effect of ANF on arterial baroreceptor reflex control of vascular resistance could not be adequately evaluated by carotid occlusion alone.\(^1\)

Ferrari et al\(^1\) demonstrated that ANF markedly potentiated reflex bradycardia but attenuated reflex tachycardia. As discussed by the authors, the diverse effects of ANF on arterial baroreceptor reflex control of heart rate cannot be fully explained by the known effects of ANF on arterial and cardiopulmonary baroreceptors. Activation of vagal afferents by ANF should attenuate arterial baroreceptor reflex control of heart rate, which is different from the findings of the study. Ferrari et al\(^1\) considered the possibility that ANF increased vagal influences on the heart. Volpe et al\(^7\) came to the same conclusion with the findings that ANF potentiated reflex bradycardia, and this effect of ANF was prevented by vagotomy and atropine. However, there are questions to be answered in this regard. First, Volpe et al\(^7\) noted that increases in resting heart rate caused by vagotomy and atropine were small and comparable before and after intravenous ANF. The latter results appear to contradict the suggestion of increased resting vagal activity induced by ANF. Is it possible that ANF potentiates a reflex increase in vagal activity without augmenting resting vagal activity? Second, the mechanisms by which ANF increases vagal influences on the heart are not known. Ferrari et al\(^1\) and Volpe et al\(^7\) suggested the possibility that this action of ANF might be related to functional antagonism of a central or peripheral vagolytic effect of angiotensin II. This interesting consideration needs to be verified. Erminio et al\(^8\) recently suggested that ANF might directly excite neurons of the solitary nucleus and thus cause hypotension and bradycardia. However, other studies have questioned the central nervous system as the site of action for the reflex effects of ANF.\(^9\)

Thus, experimental evidence indicates that ANF markedly influences control of sympathetic nerve activity and heart rate by modulating cardiopulmonary and arterial baroreceptor reflex mechanisms and possibly by acting on the central nervous system. The hemodynamic changes induced by ANF (decreases in arterial and central venous pressure) should cause reflex increases in sympathetic nerve activity and heart rate, which must oppose the direct vasodilator and natriuretic effects of ANF. The neural effects of ANF can play an important role in the physiological effects of ANF by opposing the reflex responses evoked by hemodynamic changes. The cardioinhibitory effect of ANF can contribute to its depressor action by reducing cardiac output. Furthermore, the results by Ferrari et al\(^1\) suggest that the neural effects of ANF can occur with plasma ANF levels within the pathophysiological range before a substantial decrease in blood pressure occurs.

### References


*KEY WORDS* • atrial natriuretic factor • baroreceptor reflex • editorials

*Hypertension* 1990;15:168–169
Effects of atrial natriuretic factor on baroreceptor reflexes.
A Takeshita

Hypertension. 1990;15:168-169
doi: 10.1161/01.HYP.15.2.168

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/15/2/168.citation